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CLINICAL RESEARCH TRENDS & INSIGHTS FOR 2020

Welcome to a new decade of tremendous opportunities for advancing human health.

At WCG, we enter 2020 with great anticipation for the ways in which clinical research will contribute to those advances.

In these pages, 16 subject matter experts from WCG and our partners share the important shifts, trends, regulations, and priorities that will inform clinical trial development in 2020 and beyond.

Science

DANIEL KAVANAGH, PHD, RAC
Senior Scientific Advisor,
Gene Therapy, WCG

With regard to clinical product development in the coming year, I am looking forward to seeing new proof-of-concept approaches to cancer treatment that make use of advanced synthetic biology. Synthetic biology is the application of engineering principles to molecular biology, especially through the combination of validated, modular synthetic DNA and RNA components. These approaches will make future human gene transfer products more effective and responsive to clinical needs.

Currently the FDA has approved two chimeric antigen receptor T-cell (CAR-T cell) products, both for the treatment of B cell malignancies. Both products are based on genetic modification of the patient's lymphocytes to recognize a single tumor antigen (CD19). Both products are always "on"—in attack mode, seeking to destroy CD19+ targets. These products, the result of heroic development efforts, represent the first generation of gene-modified immune therapies.

Ideally, future CAR-T therapies, will not be restricted to a single tumor antigen target; they will be "tunable," with response intensity under the control of the treating physician; they will be versatile in terms of the selection of cell contact-dependent and -independent immune effector mechanisms they deploy; and they will incorporate genetic logic circuits—molecular computers—to execute programmable responses to changing clinical needs at the cellular level. In principle, the necessary design elements exist today, but practical deployment of these ideas will require careful planning and intense efforts to address clinical, commercial, regulatory, and long-term safety needs.

Dr. Kavanagh was a principal investigator and Assistant Professor at the Ragon Institute of Massachusetts General Hospital, MIT, and Harvard prior to joining WCG. He was also Vice-Chair of the Partners Institutional Biosafety Committee, and a member of the Executive Committee of the Harvard Center for AIDS Research. Dr. Kavanagh has chaired clinical trials of an investigational human gene transfer vaccine in HIV-infected subjects, and is the author of more than 35 peer-reviewed publications in microbiology and immunology.

MARK OPLER, PHD, MPH
Chief Research Officer
WCG MedAvante-ProPhase

2020 will be another exciting year for psychiatry and neuroscience clinical trials. The overarching story for 2020 will be one of 'building momentum' - taking the achievements and gains of the past decade to the next level.

FDA approvals of new, rapid acting agents for mood disorders such as esketamine and brexanolone signal that the new era of CNS research is firmly rooted and poised to continue. Ongoing trials of PTSD, non-dopaminergic mechanisms for treatment of schizophrenia, and continued progress in rare neurodevelopmental disorders all show that the industry continues to blaze new trails. This exciting flurry of activity in drug development comes at a time when entirely new paradigms are being constructed in digital therapeutics, i.e. "Digital Medicine (DiMe)" and novel applications of devices. We need to remember, however, that these advances have coincided with some notable stumbles in the face of high placebo response, causing massive late-stage failures and killing off promising avenues of investigation.

The extent of the progress we make in the next decade depends on the degree to which we address the rising cost and complexity of research, refine the role of technology to enable progress, and confront the ever-present issue of placebo response in neuroscience and beyond. The challenges and the opportunities of 2020 and the years to follow are considerable, requiring all stakeholders to find common ground and work together to achieve success.

Dr. Mark Opler serves as Chief Research Officer, directing scientific research and development at WCGs MedAvante-ProPhase. Dr. Opler was the founder of ProPhase and served as its CEO and Chief Scientific Officer among other positions. He holds the titles of Adjunct Assistant Professor of Psychiatry at New York University and Assistant Professor of Clinical Neuroscience at Columbia University's College of Physicians and Surgeons. His academic research focuses on the etiology, phenomenology, and treatment of serious and persistent mental disorders. He is also leading the development of the new upcoming edition of the PANSS Manual.

KARMEN TRZUPEK, MS
Director, Clinical Trial Services
InformedDNA

Until recently, genetic testing in clinical trials has been performed primarily to screen patients with rare genetic diseases, such as cystic fibrosis. Increasingly, genetic testing is being used in more common multifactorial diseases, such as Alzheimer's disease and age-related macular degeneration (ARMD)- where multiple genetic risk factors, in combination with environmental and lifestyle factors, can ultimately lead to disease.

In "dry" ARMD, genetic risk variants are known to affect multiple disparate disease pathways, including

"Genetic testing is being used in more common multifactorial diseases, where multiple genetic risk factors, in combination with environmental and lifestyle factors, can ultimately lead to disease."

the complement cascade, lipid metabolism, and angiogenesis. This disease is both common and currently untreatable, making it a natural target for drug development, but previous clinical trials have proven unsuccessful. Precision therapies targeted to one of these pathways will likely be much more efficacious when the patient population is enriched for individuals known to have genetic risk factors directly involved in that pathway.

In the past 15 years, more than 500 clinical trials have been conducted in Alzheimer's disease, to nearly universally disappointing results. Trial sponsors are now being urged to test patients for different genetic risk variants in APOe, to balance the treatment and placebo arms of their studies. APOe4 is a genetic risk variant that can increase an individual's risk of developing Alzheimer's disease by up to 11-fold. Very recent data, published in November 2019, suggests that the APOe2 variant carries even more significant weight regarding disease risk- but this particular variant is *protective*. (Individuals who have 2 APOe2 variants have up to a 99.6% lower risk of developing Alzheimer's disease compared to someone with 2 APOe4 variants.)

Clinical trial participants in future studies will likely be tested for these genetic variants prior to assignment to a study arm, to ensure that observed disease progression differences can be attributed to the experimental therapy, and not underlying genetic risk.

It's clear that in the near future, genetic testing will be increasingly used to evaluate and stratify study populations even when the therapeutic isn't a gene therapy.

Karmen Trzupek currently directs clinical trial services at InformedDNA. Karmen first began working as a genetic counselor in 2001 at Oregon Health and Sciences University, specializing in inherited eye diseases and managing clinical research studies. In 2008, Karmen joined InformedDNA, where she developed the first national telemedicine program for ocular genetic counseling and genetic test coordination services. She has a longstanding passion for supporting patients with rare diseases, and has managed multiple rare disease outreach programs at InformedDNA, in collaboration with patient foundations, pharmaceutical companies, and advocacy organizations. Karmen now develops strategies and programs to increase the efficiency of patient identification and enrollment for clinical trials.

Study Design

MARK SUMMERS
President, Patient Engagement Division, WCG

Placebo response reduction represents a tremendous opportunity in studies with subjective outcomes measures such as those within the CNS specialties. Placebo response continues to cloud accurate signal detection and clinical endpoint measurements with huge costs in terms of inaccurate outcomes tracking and even failed trials.

New analytical tools have been introduced that allow clinical and data scientists to employ an automated rules engine, customized for the specific study design and patient population, to perform ongoing analysis of data in near real time to spot outliers while data is being captured during a study—rather than having to wait for an interim analysis or study completion—in much the same way an onboard computer monitors automotive engine performance while driving. A clinician can then perform root cause analysis to determine the reason for the anomaly and follow up with immediate implementation of corrective procedures such as retraining the site or patient in specific areas such as process control or symptom capture and reporting.

These new early warning tools are equipping scientists with the ability to significantly decrease placebo response along with corresponding risk and cost in studies with subjective outcomes.

Mark Summers is President of the Patient Engagement Division at WCG and with more than thirty years of experience in pharmaceutical and medical device clinical research, is widely recognized as a veteran entrepreneur and thought leader in the area of accelerating clinical trial patient enrollment. As the founder and CEO of ThreeWire, Inc., he has led the company through the development and patenting of its proprietary model for maximizing clinical trial patient enrollment. Prior to founding ThreeWire, Mr. Summers held executive positions at two early stage medical device firms where he drove more than $100 million in global growth following completion of extensive clinical trials. He is a graduate of the University of Michigan and is also a United States Navy veteran where he spent seven years flying F-14s from various aircraft carriers and at Topgun.

NATHANIEL KATZ, MD, MS
Chief Science Officer
WCG Analgesic Solutions

I see increasing awakening among clinical research professionals to the reality that the performance of all parties involved in clinical trials—investigators, coordinators, participants, and others—impacts the accuracy and reliability of the overall results of the trial. This is particularly important for trials with subjective endpoints, such as pain, headache, sleep, mood disorders, and urinary or bowel symptoms.

We now have methods to quantify the relationships between performance and results, such as how accurately participants report symptoms, levels of expectation that drive placebo responses, medication adherence, e-diary compliance, clinician ratings, etc. We can monitor these performance metrics in real-time using central statistical surveillance techniques, implement corrective actions targeted to the performance issues with the greatest impact on the validity of final study results, and watch the resolution of these issues before our eyes using the same surveillance techniques.

Training is the most common corrective technique, and we now have evidence from randomized controlled trials of the effectiveness of training, if it is designed and deployed following basic training principles.

The rather formless and chaotic responses to regulatory guidelines on "risk-based monitoring" will organize itself into rational and data-driven approaches to improve the reliability of study results in ways that yield measurable return on investment, simultaneously enriching the scientific literature on clinical research methodology and regulatory science.

Dr. Nathaniel Katz is a leading expert in treatment and clinical study design of pain clinical trials. He is a neurologist and pain management specialist at Harvard Medical School, Brigham & Women's Hospital, and Dana Farber Cancer Institute.

Dr. Katz founded Analgesic Solutions to modernize the design, conduct, and "scientific quality" of pain clinical research, and empower effective treatments for patients.

Dr. Katz's is an Adjunct Associate Professor of Anesthesia at Tufts School of Medicine. He has completed numerous clinical trials for treatments of pain, both industry-initiated and investigator-initiated, involving pharmaceuticals, non-pharmaceutical analgesics and devices, and has also conducted studies related to opioids, pain, addiction, and other issues related to opioid therapy.

LINDSAY MCNAIR, MD, MPH, MSB
Chief Medical Officer
WCG

In the next year, I expect that we will continue to see creativity, innovation, and variety in the design of clinical trials- especially clinical trials supporting novel therapeutic agents and mechanisms.

Over the past few years, it has been increasingly obvious that the Phase 1/Phase 2/Phase 3 development paradigm is becoming irrelevant to the way drugs are being developed now, especially in oncology; not surprising, since the basis of this framework was initially conceived more than 50 years ago by a statistician at the National Cancer Institute who proposed separating initial "drug-oriented" trials and later "patient-oriented" trials. New agents have been approved by regulatory agencies based on "Phase 1" clinical trials of more than a thousand patients, and early-stage studies with planned expansion cohorts to combine the assessment of initial safety and efficacy signals are now common.

"Master" protocols, including platform studies (looking at multiple agents which rotate through a protocol until either an efficacy or futility threshold is reached), umbrella trials (testing multiple agents for a single disease in sub-populations defined by genetic or histologic markers) and basket trials ("disease-agnostic" studies in which the population is defined by a genetic or histologic marker, regardless of the location of cancer or type of disease), are becoming increasingly common, and increasingly complex.

Sponsors are avoiding the delay and administrative burden of study start-up processes and looking for ways to move seamlessly from one development

Dr. Lindsay McNair has extensive experience in the pharmaceutical industry. Prior to joining WCG, she was a consultant to pharmaceutical and biotechnology companies, providing medical guidance on clinical development strategies and study designs for new drug studies, and medical oversight of all phases of clinical trials. Dr. McNair is also a member of the Human Subject Research Board at the Environmental Protection Agency, and teaches graduate-level courses on the scientific design of clinical research studies. She has been actively involved in IRB work for 18 years, and has a Master's of Science in Bioethics with a concentration in research ethics.

question to the next, without closing and re-opening clinical sites and stopping and starting study recruitment. We are also seeing design innovation in the form of decentralized and "virtual" trial designs or design components, intended to reduce the barriers to study participation for patients (logistic, geographic, financial) and to increase the opportunity to participate in studies and the diversity of study populations.

These changes are positive and important, but they also bring challenges to the administrative and regulatory structures for the review, oversight, and conduct of clinical trials, which are still based on the way studies were conceived and run decades ago. We'll have to be innovative in these areas as well, to keep up with the necessary advances that are being driven by therapeutic innovation.

"Over the last few years, it has been increasingly obvious that the Phase 1/Phase 2/Phase 3 development paradigm is becoming irrelevant to the way drugs are being developed now."

Study Conduct

JONATHAN ZUNG, PHD
Executive Vice President
Site Division, WCG

The role of independent sites in the conduct of clinical research continues to increase as a result of their ability to more predictably recruit patients from within their practices and/or through the databases they maintain, along with their ability to start up clinical trials faster and more efficiently than many academic medical centers (AMCs) and hospitals.

Independent sites can do this based on their size, agile processes they have in place, and their reliance on focused patient engagement. From a sponsor and CRO perspective there is a strong desire to work with those sites that can meet their enrollment commitments and have accelerated start-up processes in order to meet the sponsor's study timeline and budget.

In 2020 we can expect sponsors and CROs to continue to leverage the wealth of site performance data they have access to when evaluating and

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selecting which sites to include in their clinical trials. The ultimate goal in a given clinical trial is to identify the most appropriate sites that are focused on meeting or exceeding their enrollment commitments while meeting quality and ethical standards. This will allow sponsors to reduce the total number of sites that are required for a given trial. This means prospective sites will need to more accurately demonstrate their ability to not only meet enrollment commitments, but to also reduce startup timelines.

AMCs and hospitals who participate in clinical trials will need to streamline their internal processes for startup and enhance their effectiveness in patient recruitment. It is not uncommon for these larger institutions to take more than 90 days to complete startup activities, while independent sites can routinely do this in less than half that time. We can expect the AMCs and hospitals to more effectively leverage third party organizations who can more adroitly execute critical activities like budget development, contract negotiations, and patient recruitment. The reliance on third party organizations who can partner with AMCs and hospitals to reduce startup timelines through their agile processes and enhance enrollment effectiveness through their proprietary processes and best practices will continue to increase. This is necessary as the competition for qualified US sites continues to increase. This means institutions will need to be more open to modifying their current practices by partnering with providers who can not only augment their capabilities, but also make them more attractive to sponsors/CROs during the site selection process.

We can expect to see best practices embedded at the larger institutions in order to help them reduce startup timelines given the volume of patients that reside within their institutions and are under the care of their physicians.

Dr. Jonathan Zung has more than 25 years of pharmaceutical development experience in oncology, immunology, cardiovascular disease and other major therapeutic areas. He has held executive leadership positions in the pharmaceutical and pharmaceutical services industries. Most recently, Dr. Zung was group president, Clinical Development & Commercialization Services for Covance Drug Development where he led a global organization of over 8,000 employees in 60 countries spanning all phases of development (Phase I- IV), along with global market access services.Prior to Covance Dr. Zung was vice president and head of Global Clinical Sciences and Operations at UCB, with responsibility for clinical operations, data management, statistical sciences, contracting, medical writing and operational excellence across the United States,Europe and Asia.

JILL JOHNSTON
President, Study Planning and Site Optimization Division, WCG

From my perspective, one of the most interesting things is that after all this time, we are still surprised by how hard it is to start and launch a new clinical trial. In addition to study complexity, it is often the first time the study team is assembled to work together. It is not surprising that the challenges of planning a complex project with people who have likely never worked together ends up being a series of unfortunate events.

One challenge that is a perennial favorite is adequate site selection. It shouldn't be so difficult; it is quite straightforward on paper and yet, in reality, it is still astonishingly hard. On average, 11% of sites never enroll a patient. Original timelines end up doubling in order to meet the desired enrollment goals. When searching for a solution I think we should look to where we are succeeding in site selection. It is a mix of art and science; and a mix of technology and back to basics.

In no particular order, these are the attributes I have found, when done correctly, lead to more optimal outcomes and teams feel successful by achieving their intended milestones. Focusing on these attributes will be a priority for my site selection teams in 2020.

1. Data Insights: Accessing the right data, pulling insights, and taking the right actions
2. Customer Service: Start treating sites like long-term customers with a proper customer-service mentality
3. Technology: Leverage the power of natural language processing/artificial intelligence -- more automation; more visibility

Jill Johnston leads WCG's site identification, selection, and activation services. She is responsible for developing strategy, driving the vision, and delivering for customers as WCG continues to drive ingenuity in the clinical research space.

Her aim is to deliver transformational site activation solutions that stimulate growth, foster compliance, and maximize efficiency for those who perform clinical trials.

Prior to WCG, Jill was the vice president of Vault Clinical at Veeva, providing thought leadership, driving development of product and market strategy.

Before joining Veeva, Jill spent the majority of her career at Covance, where she held a variety of strategic roles in clinical operations, project management, and as a Six Sigma Black Belt.

4. Expertise: Under-estimating the value of experience often leads to missed clues
5. Focus: So many tasks at study start, so little time; finding the right sites takes intense focus – fewer distractions here mean better choices
6. Building Relationships: Relationships matter and can go a long way to building trust and reliability.

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LINDA SULLIVAN, MBA
Executive Director
WCG Metrics Champion Consortium

I predict substantial growth in the adoption of quality by design, risk-based quality management, and centralized monitoring approaches detailed in the ICH-E6(R2) and ICH-E8(R1) addendums. During 2020, clinical studies that utilized risk-based approaches will be completed and inspected by regulatory authorities. Early adopters will be able to share lessons learned and reassure others that risk-based, data-driven approaches are both effective and accepted by regulators.

Two key factors will limit the rate of adoption: access to the data needed to support analytics and the availability of staff trained to interpret and act on the data. These challenges can be addressed through the adoption of industry-based performance and quality metric standards that improve the quality and consistency of the data available to data analytic programs. Additionally, risk management and root cause analysis training programs—developed specifically for clinical research staff—can be deployed to reduce the workforce skills gap.

I believe that 2020 will be the year that the industry begins to realize the benefits of risk-based quality management and centralized monitoring – namely, using data to identify when human intervention is required to investigate whether patient safety and/or data integrity issues are occurring and take rapid action before they impact the integrity of the research.

Linda Sullivan has more than 30 years of experience working in the healthcare and clinical research industries helping organizations improve processes to improve financial and quality outcomes. She was a founder of Metrics Champion Consortium, an industry association dedicated to leading the drug development enterprise in the adoption and utilization of standardized metrics and benchmarks to drive performance improvement.

Ms. Sullivan has been a featured speaker at Performance Metrics, Risk-Based Monitoring, Quality Management & Clinical Trial Oversight industry meetings, published articles in leading journals and served on industry advisory boards such as the NIHNCATS Methods and Process Domain Task Force and the ACRP CRA Competency Steering Committee.

Technology & Data

APRIL MULRONEY
Senior Vice President &
Chief Data Officer, WCG

In the last few years, data analytics has proven to be extremely valuable in answering questions of how to run clinical trials more efficiently. It is obvious that improved efficiency in clinical trials will save time, and ultimately decrease the cost of drug development. This is good news for an industry passing through this turning point of leveraging data, as we aim to bring drugs to patients who need them, faster. However, why has something so obvious been so hard to adopt? The art and science of data analytics is complex.

Optimizing data analytics requires careful consideration of three key components: relevant data; technology to mine that data; and expertise to understand and apply the output. Most organizations are data-rich, having access to internal unique data sets from running decades of trials, data sets in the public domain, and other relevant commercial data sets (such as prescription and EHR data). The only way to make sense of it all is to leverage a technology platform that not only handles the entire data journey in an innovative way, but also provides for speed-to-value to help generate the much-needed insights to make real-time critical decisions on the trials. And lastly, and likely the most critical, is having people with the expertise to mine relevant real-time data, and literacy to understand what the data is saying.

Combining these components together resembles a three-legged stool, which establishes the baseline for engaging in the age of using data to transform the way clinical trials are run.

April Mulroney is responsible for the vision and direction of WCG's data and knowledge strategy. She brings a unique blend of general management, finance, strategic innovation and product development experience in life sciences to her role. A recipient of both the 2016 HBA Woman of the Year, and 2016 PharmaVOICE Top 100 awards, Ms. Mulroney holds a CPA certification and BComm from University of Toronto.

Prior to joining WCG, Ms. Mulroney was with Medidata Solutions as general manager of site payments and FMV benchmarking. During her tenure, she incubated and launched the financial products component of Medidata's industry leading clinical trial technology platform. Ms. Mulroney led the Payments EDC to Cash launch in 2016, resulting in the SCRIP Award for Best Technology of the year.

LINDA MARTIN
President
WCG KMR Group

The use of advanced data analytics within R&D will see substantial growth in 2020. Biopharma companies of all sizes are witnessing the benefits from their early investment and are now poised to embrace data analytics in a more systematic way. Advanced tools allow companies to solve complex questions and unearth deeper insights in an efficient, reliable manner. Using sophisticated techniques, companies can evaluate key business questions and understand the critical factors driving performance.

Advanced data analytics can be applied across the full R&D spectrum, including especially portfolio management and clinical development. Within clinical operations, advanced data analytics are improving crucial processes, such as precision planning, country optimization, site selection, and investigator management. Companies are able to better evaluate risk, time to market, and value while at the same time simplify decision making.

The essential foundation for data analytics is reliable data. Trusted source data is key and knowing where the data comes from, the curation, and the nuances around the methods and algorithms is essential to success. Seemingly small differences in actual to predicted site enrollment rates are, for example, magnified when considering studies with hundreds of sites across many countries.

An often overlooked aspect is the art of model development and application of statistics. Having consistent access to the right data is just the start; building on that foundation requires skill and experience and deep understanding of the industry and the nuances surrounding drug development.

Linda Martin was founder and President of KMR Group, a firm specializing in biopharmaceutical R&D performance, data, and analytics. Her areas of expertise include the measurement and evaluation of R&D productivity and clinical development, including subspecialties of enrollment and site performance. Ms. Martin has a Master of Management degree from Northwestern University's Kellogg Graduate School of Management and an undergraduate degree from the Illinois Institute of Technology.

EMMANUEL OLART, MS
Chief Technology Officer
WCG

In a world where convenience and ease of use is the name of the game, we are all getting used to a technology experience designed to be enjoyable, personalized, and efficient, largely led by personal devices imagined by Amazon, Google, and Apple. Personal assistants are commonplace in many homes and speaking to one's watch or phone an ordinary sight.

These technology solutions are making the life of the end users easy with the clear goal of having them use more of the provider's services as opposed to those of the competition.

A well-known concept in designing user experience for any technology or service is that there is now a constant competition for people's time and attention. The most enjoyable activities and the ones that are quick and easy to carry out get prioritized.

From my point of view, applying this concept to clinical trials is key to get to better patient compliance and retention. The clinical trial experience has historically been designed with clinical sites in mind. Shifting the focus to patients, and applying modern technology solutions and user experience principles to the various points of interaction with them, will lead to better outcomes.

Emmanuel Olart has 18+ years of experience in the clinical research and technology space leading global software engineering and IT teams and architecting solutions serving the pharmaceutical industry. Prior to joining WCG, Mr. Olart worked for BioClinica in a series of increasingly senior positions leading to vice president, systems architecture.

Public Policy & Regulatory Oversight of Research

DAVID FORSTER, JD, MA, CIP
Chief Compliance Officer
WCG

To me the most interesting question in 2020 is when, and to what extent, FDA will modify its IRB and informed consent regulations to harmonize with the changes that were made to the Common Rule. Most of the changes went into effect in January 2019. Eighteen federal agencies have adopted the Common Rule as the uniform set of regulations on IRB and informed consent requirements. The 21st Century Cures Act directed FDA to harmonize with the revised Common Rule to the extent possible. FDA is currently working on a Notice of Proposed Rule Making (NPRM) for that purpose, but has not indicated when the NPRM will be released for public comment.

Most of the changes to the Common Rule will have minimal effect on the pharmaceutical industry if adopted by FDA, since many of them apply to internal IRB processes, but three would be significant. The first is the requirement that each informed consent must begin with a concise and focused presentation

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of the key information that is most likely to assist a prospective participant or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This section must be short and succinct. Many investigators and IRBs have already begun to work with this requirement for federally funded research. Sponsors, CROs, and others who draft consent forms will need to implement policies to meet this requirement.

The second is the requirement for use of a single IRB for all US sites in multi-site research. This requirement was adopted by NIH in January 2018, and the Common Rule requirement goes into effect in January 2020. In the NIH and Common Rule versions, the funding agency or the institution receiving the grant determines which single IRB to use. Because FDA regulations do not directly apply to institutions, it is unlikely FDA will place this responsibility with institutions, and because FDA is not a funding agency, it is unlikely that FDA will take the responsibility itself. Therefore, the sponsor is the most likely candidate for ensuring that this requirement is followed, as the funder of the research. Under these provisions, there cannot be multiple IRBs unless there is a requirement for local review, such as tribal law.

The third is the requirement that for each clinical trial conducted or supported by a federal agency, an IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the federal department or agency component conducting the trial, on a publicly available federal web site. It is unclear how FDA will harmonize with this requirement, as the FDA does not award grants and is not a funding agency. The party likely to be made responsible for this task, if it is adopted by FDA, is the sponsor of the research.

David Forster has a JD and a Masters in Medical Ethics from the University of Washington. He joined Western IRB (WIRB) in 1996 and is currently the Chief Compliance Officer for WCG..

Mr. Forster co-chairs the Secretary's Advisory Committee on Human Research Protections (SACHRP) Sub-Committee on Harmonization (SOH). He previously served a four-year term as a member of SACHRP, and was a member of the SACHRP Sub-Committee on Inclusion of Individuals with Impaired Decision-Making in Research (SIIIDR). Mr. Forster also serves on the Certified IRB Professional (CIP) Council.

DAVID BORASKY, MPH, CIP
Vice President, IRB Compliance
WCG

In 2020 I see the research ethics field's struggles with data security and data privacy escalating.

While there has been a long-standing recognition of privacy issues around medical records—and regulations like HIPAA to protect that information—there is an ever-growing amount of personal data that is being converted for research use. From social media to Google searches, browsing Netflix and shopping on Amazon, we each contribute a vast amount of data about ourselves to various entities. Everyone with a smartphone, smartwatch, or wearable fitness device also contributes data about ourselves to the companies that make those devices. There is a wealth of research being done using these devices for medical purposes, such as the diagnosis of medical conditions and mobile apps to improve mental health. However, there is also research that is less obvious to the public, and fewer controls to protect the privacy of that data. When some of this research is revealed to the public, such as the Facebook emotional contagion study or the research done by Cambridge Analytica, members of the public often express outrage and surprise that their data is being used in this manner, even when they agreed to such use at the time they signed up for the service.

Outside of research there have been numerous data breaches in which personal financial information was stolen. If there is a data security event tied to the research use of data, it could have a significant impact on the public's perception of research uses of their data.

While research uses may be consistent with the terms of service or end user license agreements

David Borasky is responsible for leading the quality and compliance activities for all of the WCG institutional review boards (IRBs). He has 20 years of experience in managing IRBs in settings that include global public health organizations, large academic medical centers, and independent IRBs. In addition to his compliance oversight responsibilities at WCG, Mr. Borasky also serves as Co-Chair of the Subpart A Subcommittee of the Secretary's Advisory Committee on Human Research Protections (SACHRP) and previously sat on the Board of Public Responsibility in Medicine and Research (PRIM&R).

that individuals agree to when activating a device or setting up a social media account, most members of the public are unlikely to have given any thought to potential research use. It may not happen in 2020, but the chances of a research-related data breach are only going to increase. I'll be watching to see if there are any significant new developments in this area.

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JONATHAN SELZER, MD, MBA, MA
Chief Scientific Officer
WCG

Perhaps the only area of bipartisan agreement seems to be that the price of drugs is too high—and they must be lowered.

Recently, a two thirds majority of the Senate Finance Committee passed the Prescription Drug Pricing Reduction Act of 2019 which aims to cut drug spending by $100 billion over the next decade. According to the National Bureau of Economic Research (NBER), cutting prices by 40 to 50 percent will lead to between 30 and 60 percent fewer R&D projects being undertaken, whereas a modest reduction, such as 5 or 10 percent, may only impact R&D spending by about 5% (www.nber.org/digest/may05/w11114.html).

For those of us involved in drug, biotech, and medical product development, the implication is clear. Pressure to reduce the cost of clinical trials will be turned up a notch in 2020. This will require collaboration with regulators, sponsors, and academic institutions as we need to validate technologies and scientific approaches which enable us to reduce the size and time of clinical trials.

Dr. Jonathan Seltzer is a recognized leader in the area of cardiac safety, endpoint adjudication committees and data and safety monitoring committees. He has chaired and served as a committee member for scores of protocols, and has functioned as an advisor for dozens more. He is actively publishing in these areas and participating in thought leadership efforts focused on defining best practices. Currently, Dr. Seltzer is on the scientific programs committee for the Cardiac Safety Research Consortium (CSRC) and the steering committee for the Clinical Trials Transformation Initiative (CTTI). Previously, he served as the president and chair of Trustees for the Academy of Physicians in Clinical Research.

Patient Advocacy

STEVE SMITH
President, Patient Advocacy
WCG

In 2020 patient advocacy will continue to transform drug development, although positive results can be hard to see unless one takes a long-term look at the past for context. We see healthy skepticism that drug developers' patient-centric efforts create real change. Protocols are still overloaded with burdensome procedures, endpoints don't reflect what matters most to patients, and dialog with patient communities seems symbolic, even off-putting when informed consents and trial descriptions remain in complex language many patients don't understand. Patients note how warmly trial sponsors reach out to them at first, then disappear, sharing neither trial outcomes nor the patient's own data.

As discouraging as this sounds, patient/researcher collaboration continues the detailed work to transform this atmosphere. Today's hard work stems from profound legislative changes to regulatory processes which collaborating patient advocates brought about in the past. It takes years to realize the benefits of such change, e.g., The Orphan Drug Act (1983), PDUFA V (2012), 21st Century Cures Act (2016).

Five years from now, looking back at 2020, we will confirm improvements in the use of patient-friendly lay language, patient cohorts providing advice at trial design time, researchers sharing patient data with any legitimate researcher when collected in a federally funded trial, patient-friendly, online ways to search for trials, and increasingly better-informed patients who have something positive to say about participation in clinical research.

Steve Smith is a seasoned patient advocate with an extensive career in software, consulting, process transformation, health care systems and patient-focused drug development.

Steve's strong sense of mission to increase the rate at which new treatments for disease can be developed to address unmet medical need, is complemented by his conviction that we can develop drugs faster, while remaining safe. Paramount is the interests of patients whose needs include not only new medicines, but also quality of life. Modern science, modernizing regulatory processes, and modern computing technology, when combined with best practices in collaboration and process improvement, can give us new drugs developed faster, safely, and at a lower cost.

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WCG is built upon a 50-year legacy of ethical review, growing to what is today a suite of clinical services and technologies that maximize speed and efficiency for those who perform clinical trials.

WCG is proud to serve the individuals on the frontlines of science and medicine, and the organizations that strive to develop new products and therapies to improve the quality of human health. It is our role to empower them to accelerate advancement, while ensuring that the risks of progress never outweigh the value of human life.

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The WCG Institute curates actionable insights on the clinical research industry from our research Fellows and the WCG Knowledge Base.

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