Market Value Should be “Defendable,” Not “Fair,” Experts Say
By Brandon May

Establishing a fair market value for a clinical trial that both sponsors and sites can agree on often is easier said than done. There is little or no consensus on the “fair” price to be paid for clinical trial services. Instead, sites should focus on providing a solid defense for each expense they expect a sponsor to foot.

“Often, people say they can’t pay more than fair market value,” says David Vulcano, vice president of research compliance and integrity at the Hospital Corporation of America, “and that’s great, but not everybody agrees on the dollar amount of what fair market value actually is. Instead of fair market value, we should probably use the term ‘defendable market value.’”

Lack of Training Compromises Trial Results, Expert Says
By John Mitchell

At its very core, a clinical trial is a measurement system. But unlike other fields that rely on measurement and data reporting, the clinical trials industry has not focused enough on training for everyone involved, from the investigators all the way down to the patients.

Lack of training, particularly for patients, creates variability detrimental to trial findings, says Nathaniel Katz, founder and chief science officer of WCG Analgesic Solutions.

“People have had magical thinking about the way clinical trials generate data,” Katz told the audience of a recent WCG webinar. “There’s this strange belief that if you give some people the treatment and (others) the placebo ... the trial will generate an observed effect size that somehow will accurately characterize the pharmacology of the treatment,” Katz said.

That attitude, he stressed, has resulted in trials ending in expensive failure. Some of those failures could have been avoided with training to eliminate key causes of variability that undermine the scientific process.

The problem is that clinical trial research has not set a high enough training standard.

“Training is not really even viewed as a scientific topic in the world of clinical trials,” Katz said. “Training has been viewed as a checkbox activity or something to do to please regulators, but not something that has a direct impact on our ability to achieve our scientific objectives in clinical trials.”
FDA Plans Clinical Trial Regulatory Changes
The FDA has unveiled its agenda for upcoming proposed and final rulemakings, including several noteworthy proposals related to clinical trials.

The agency's plans for the remainder of 2019 include a proposed rule on responsibilities for initiating and conducting clinical trials; a proposed rule harmonizing several provisions of FDA regulations on human subject protection; proposed new reporting requirements under the Right to Try Act; and a proposed rule adding development safety update reports to IND application annual reporting requirements.

Additionally, a proposed rule is being considered that would require any U.S. institution participating in multi-site cooperative research to rely on approval by a single IRB for research conducted in the U.S. “with some exceptions.”

Read the Unified Agenda here: https://bit.ly/2whya8S.

Feds Dole Out $9 Million for Alzheimer’s Candidate Trial
Federal officials have awarded $9 million to a North Carolina drugmaker to help bring an anti-Alzheimer’s drug through a clinical trial.

Pharma firm T3D Therapeutics says the money will be doled out over the next four years to support its T3D PIONEER study, a Phase II trial designed to test the safety and efficacy of its candidate pill, T3D-959.

PIONEER hopes to recruit 252 adults with mild-to-moderate Alzheimer’s disease and give them either one of three doses of T3D-959 or a placebo for 24 weeks. The trial is supposed to start next year.

The money comes from a grant through the National Institute on Aging.

Drug Giants Partner with Data Company to Ramp Up Clinical Trials
Verily, a subsidiary of Google parent company Alphabet, is partnering with drug giants Novartis, Otsuka, Pfizer and Sanofi to explore novel methods for generating real-world data.

Verily’s evidence generation platform, Project Baseline, will help the partners collect health information from electronic health records, sensors and other digital sources.

The companies plan to use the data to inform future trials in various therapeutic areas, including cardiovascular disease, oncology, mental health, dermatology and diabetes.

The collaboration aims to make clinical trials more accessible to patients and accelerate the clinical research process.

Drugmakers Comment on FDA’s Guidance on Natural Histories for Rare Diseases
Ionis, Merck, Lundbeck and six other companies offered feedback on the FDA’s guidance for developing natural history studies for rare disease drug development, praising some parts of the guidance but calling for more details.

Responding to the agency’s call for comments on the guidance, which closed on May 24, Ionis suggested that the agency add three additional uses for natural history studies to the guidance — establishing the burden of disease, characterizing genetic mutations and biological consequences and reducing trial burden in interventional studies.

The guidance should strongly encourage sponsors to share with the public and community “not only methods, practical aspects and results, but also subject-level data in a timely fashion,” the drugmaker said.

It also called for greater emphasis on interim analyses.

Lundbeck noted that many rare diseases have established disease registries made available by clinicians and institutions, calling on the agency to acknowledge that it may not always be feasible for sponsors to influence registry development.

Establishing a free-standing prospective natural history study can be challenging in terms of recruitment as well, the drugmaker added.

The company also suggested electronic health records as a potential source for creating a control group, and requested a separate section on methods to deal with bias. The agency should also look into how the guidance’s principles could apply to other vulnerable populations and pediatric development, it said.

Merck asked the agency to clarify its expectations for data submissions. The company said it’s unclear if sponsors should submit only external control data or the whole natural history study.

It also stressed the importance of outside organizations and programs running natural history studies to improve the characterization of rare diseases, and urged the agency to emphasize that industry collaboration with them could be beneficial.

Read all nine comments here: https://bit.ly/2HOQOdM.

continues on next page »
Genentech Added to Corrona Multiple Sclerosis Registry
Roche’s Genentech has become the first pharmaceutical company to have its data be included in a national registry of multiple sclerosis patients.
The Multiple Sclerosis Registry is one of six efforts created by Corrona to collect data on diseases ranging from rheumatoid arthritis to inflammatory bowel disease. The registries collaborate with more than 400 participating investigator sites and the data have been used in more than 140 peer-reviewed manuscripts. More than 700 patients have enrolled in the multiple sclerosis registry alone.

MAGI, ACRP Call for Proposals and Speakers
Clinical research professionals looking for speaking opportunities can look to two upcoming national conferences.

MAGI has issued a call for proposals for sessions at its October 2019 conference in Las Vegas. The conference will feature more than 100 sessions and workshops in six tracks.
ACRP will open a call for proposals on June 3 for its ACRP 2020 conference to be held in Seattle next May.
This feature highlights changes in clinical research companies’ personnel.

**Eisai**  
Luca Dezzani has been appointed as vice president, U.S. medical affairs, of Eisai’s Oncology Business Group. He will also oversee Eisai’s health economics and outcomes research, medical science liaison and medical information and education teams. Dezzani previously held senior medical roles in Europe and the U.S. at Novartis Oncology.

**Arch Oncology**  
Kirk Christoffersen has been named chief business officer at California-based Arch Oncology. Christoffersen was previously head of corporate and business development at Compugen.

**Protalix BioTherapeutics**  
Dror Bashan has been selected to be the new president and chief executive officer at Protalix BioTherapeutics, Inc. Bashan previously held a number of senior positions at Teva Pharmaceutical Industries Ltd., most recently as Teva’s senior vice president of global business development.

**Arcutis**  
Arcutis, Inc., a privately held immunodermatology drug development company, has named John W. Smither as chief financial officer. Prior to this appointment, Smither held CFO positions with Sierra Biopharmaceuticals and Kite Pharma.

**Eger BioPharmaceuticals**  
Eger BioPharmaceuticals, Inc., has announced that David Apelian will step down as the company’s chief operating officer and executive medical officer, effective June 14, to become the chief executive officer at a private biotech company. Eger plans to announce a new senior executive medical lead in the near future.

**CSL Behring**  
Paul McKenzie has been named as the new chief operating officer at CSL Behring, the drug and plasma unit of CSL Ltd. McKenzie was previously executive vice president of pharmaceutical operations and technology at Biogen.

**Voyager Therapeutics**  
Voyager Therapeutics, Inc., has announced the retirement of Dinah Sah as chief scientific officer, to be replaced by Omar Khwaja, the current chief medical officer, in an expanded role that includes head of research and development.

**RedHill Biopharma**  
RedHill Biopharma Ltd. has named Rob Jackson as vice president of marketing, Robert Gilkin as vice president of market access and Steven Thomasian as vice president of supply chain. Jackson most recently served as the national director of market access for the surgical business unit at Bioventus. Gilkin was previously vice president of market access at Synergy Pharmaceuticals. Thomasian most recently held the position of president of supply chain at Kala Pharmaceuticals.

**Akrevia Therapeutics**  
Akrevia Therapeutics, a privately held biopharmaceutical company, has announced the appointment of René Russo as chief executive officer. Russo most recently served as president and chief executive officer of Arsanis, Inc.

**Seattle Genetics**  
Seattle Genetics has named Robin Taylor as the company’s first chief commercial officer. Taylor spent the past seven months as the franchise head for immune-oncology at AstraZeneca. Prior to his stint with AstraZeneca, Taylor led the cancer immunotherapy franchise at Genentech.

**Locana**  
Locana, Inc., a start-up gene therapy company, has named Jeffrey Ostrove as CEO. Ostrove was formerly the chief executive officer of AbVitro and Ceregene.

---

Clinical study leads and business opportunities

**Research Center Profile**  
A Research Center Profile highlights your site’s expertise to patients and industry experts alike

- When you create a Research Center Profile page, you can list an unlimited number of clinical trials on the Clinical Trials Listing Service™
- Profiles are selected for a monthly feature in our CWWeekly publication to showcase your site to Sponsors and CROs

**Clinical Research of West Florida, Inc.**

Visit store.centerwatch.com to learn more
Market Value
continued from page 1

says Vulcano. But if 70 percent to 80 percent of sites accept the lower price, he says, then the average could drop to $90 the next time a sponsor checks the price. And the cycle continues from there.

“Sometimes, sponsors call us and tell us that their budget is non-negotiable and that they’re only paying as high as they can without exceeding fair market value,” explains Vulcano. “But that’s their fair market value for research-naïve sites,” he says. “And about six months later, we often get a call from these sponsors and they tell us that they’re not recruiting very well and they’re looking for new sites and they’ve increased their budget.”

To determine value, sites generally must look at various aspects of the study, including payments toward nurses, physicians and administrative staff, says Russell John, global director of grants management at Clintrax Global. “Sites that do less research don’t build a granular financial budget and don’t consider how much time it’s going to take,” John adds. “I think it’s important for sites to build up a dossier or database of their own on how much time they spend on certain services that are not subject-related, such as administrative time-related costs.”

“Sites need evidence to support what they ask for,” agrees Wendy Tate, director of analytics at Forte Research. “Many research sites don’t have empirical data on how long it takes to do something,” Tate says. “One of the things I highly recommend from an analytics perspective is to determine how long it takes to do something, like obtaining consent of participants or how long it takes to prepare a sample. That way, sites have a little more justification for their line items and aren’t just pulling a number out of the air.”

“It can be very valuable to discuss what considerations go into determining a dollar amount,” explains Laura Hilty, vice president of product management & strategy at Forte Research. “Documenting this and sharing these details with the sponsor can go a long way in helping them understand the real reason and justification for costs,” Hilty says.

In addition to the challenges of establishing a fair market value that ensures a well-run clinical trial, both payers and payees are responsible for navigating the regulatory framework that governs clinical trial funding. “Sponsors, sites, investigators and certain downstream contractors may be wise to have policies and procedures to ensure that payments made in the context of clinical trials are in each case fair market value for legitimate, reasonable and necessary items or services,” says Andrea Ferrari, a partner at HealthCare Appraisers in Florida.

Ferrari suggests a “toolkit” of policies that include a summary of and/or access to previously determined fair market value ranges for services that are most common in clinical trials of a similar nature. This toolkit might do well to include general guidance for how to apply the fair market value ranges in the context of applicable laws and regulations, she says. “Guidance should focus on how to deconstruct a budget to match budget line items to actual items/costs, caveats to applying the fair market value ranges to certain specific circumstances and triggers for higher-level or more specific review than can be accomplished through the tools in the general toolkit.”

Using KPIs to Improve Site Performance
A CenterWatch Webinar presented by Kelly Smith, CCRP, Sr. Solutions Consultant for Bio-Optronics

Tuesday, June 11, 2019 · 1:30–3:00 pm EDT
Location: Your office or conference room (no need to travel!)

Transform your raw and unstructured data into meaningful information. This presentation will illustrate how technology can assist in streamlining your operations and improve your business decisions based on intelligence derived from the clinical trial data.

Learn more about this webinar at store.centerwatch.com.

REGISTER TODAY!
Lack of Training

continued from page 1

This is especially clear when it comes to training trial participants to report accurately on their reactions and experiences.

“Although pharma, device companies, CROs and regulatory agencies invest heavily in internal training, the concept of training clinical trial participants to perform their tasks better has scarcely filtered into the clinical trials managed by these organizations,” Katz said.

He cited one example in which participants had not been appropriately trained on how to use electronic diaries the trial used to gather patient data. It resulted in skewed and flawed findings on drug effectiveness.

“It’s rare that the skill we are asking people to do (in a trial) has been defined, yet that’s what’s necessary if you want (them) to do it,” he explained.

“Training has been viewed as a checkbox activity or something to do to please regulators, but not something that has a direct impact on our ability to achieve our scientific objectives in clinical trials.”

—Nathaniel Katz, founder and chief science officer, WCG Analgesic Solutions

Katz laid out a best practice training model for clinical trial staff and subjects based on adult learning principles used widely in other industries.

First, it’s vital to understand the difference between education and training. Education is about what you know, he said, and training is about what you do. Giving someone a manual to read is education. Showing them how to perform tasks discussed in the manual and allowing them to practice is training. Education doesn’t necessarily change behavior, but training does.

Practice should progress from simple to more advanced tasks and be followed by constructive and diagnostic feedback, Katz said. To facilitate the transfer of new skills to action, training and practice conditions should be increasingly difficult, trainer support should gradually decrease and practice conditions should increasingly resemble real-world conditions.

Katz also made a strong case for validating that any training done has achieved verifiable process improvement. It is the responsibility of leadership to demonstrate that there is a return on investment through more reliable clinical trial outcomes, he said.

Together, we’re helping our partners deliver on the promise of precision medicine.

The Center for Genetics and Precision Medicine in Clinical Trials

Genetics-oriented solutions to support clinical trials

Protocol design • Study design • Patient engagement
Genetic testing & counseling

www.wcgclinical.com
<table>
<thead>
<tr>
<th>Company</th>
<th>Drug/Device</th>
<th>Medical Condition</th>
<th>Status</th>
<th>Sponsor Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inovio and CEPI</td>
<td>INO-4500</td>
<td>Lassa virus</td>
<td>Phase I trial initiated enrolling 60 volunteers</td>
<td>inovio.com CEPI.net</td>
</tr>
<tr>
<td>Compugen, Ltd.</td>
<td>COM701 in combination with Opdivo (nivolumab)</td>
<td>advanced solid tumors</td>
<td>Phase I trial initiated enrolling 140 subjects at ten sites in the U.S.</td>
<td>cgen.com</td>
</tr>
<tr>
<td>Atriva Therapeutics GmbH</td>
<td>ATR-002</td>
<td>influenza</td>
<td>Phase I trial initiated enrolling 60 healthy volunteers in Belgium</td>
<td>atriva-therapeutics.com</td>
</tr>
<tr>
<td>Compugen, Ltd.</td>
<td>COM701 in combination with Opdivo (nivolumab)</td>
<td>advanced solid tumors</td>
<td>Phase I trial initiated enrolling 140 subjects at ten sites in the U.S.</td>
<td>cgen.com</td>
</tr>
<tr>
<td>Atriva Therapeutics GmbH</td>
<td>ATR-002</td>
<td>influenza</td>
<td>Phase I trial initiated enrolling 60 healthy volunteers in Belgium</td>
<td>atriva-therapeutics.com</td>
</tr>
<tr>
<td>Axovant Gene Therapies, Ltd.</td>
<td>AXO-AAV-GM1 (also known as AAV9-GLB1)</td>
<td>GM1 gangliosidosis</td>
<td>Phase I trial initiated</td>
<td>axovant.com</td>
</tr>
<tr>
<td>Dicerna Pharmaceuticals, Inc.</td>
<td>DCR-HBVS</td>
<td>chronic hepatitis B virus (HBV) infection in adults</td>
<td>Phase I trial initiated enrolling healthy volunteers (HV) and subjects with non-cirrhotic chronic HBV infection</td>
<td>dicerna.com</td>
</tr>
<tr>
<td>NeuClone Pharmaceuticals, Ltd.</td>
<td>Stelara (ustekinumab)</td>
<td>moderate to severe plaque psoriasis in adults and children 12 years or older, active psoriatic arthritis and moderate to severe Crohn’s disease in adults</td>
<td>Phase I trial initiated enrolling subjects in Australia</td>
<td>neuclone.com</td>
</tr>
<tr>
<td>ImaginAb, Inc.</td>
<td>$^{99}$Zr-Df-IAB22M2C</td>
<td>cancer</td>
<td>Phase II trial initiated enrolling metastatic cancer subjects</td>
<td>imaginab.com</td>
</tr>
<tr>
<td>IO Biotech</td>
<td>IO102 in combination with KEYTRUDA (pembrolizumab)</td>
<td>metastatic non-small cell lung cancer (NSCLC)</td>
<td>Phase II trial initiated enrolling 96 subjects at more than 20 sites across the U.S. and Europe</td>
<td>iobiotech.com</td>
</tr>
<tr>
<td>Respivant Sciences</td>
<td>RVT-1601</td>
<td>idiopathic pulmonary fibrosis (IPF)</td>
<td>Phase IIb trial initiated enrolling 180 subjects in the U.S., Canada and Europe</td>
<td>respivant.com</td>
</tr>
<tr>
<td>Rigel Pharmaceuticals, Inc.</td>
<td>fostamatinib disodium hexahydrate (fostamatinib)</td>
<td>warm antibody autoimmune hemolytic anemia (AIHA)</td>
<td>Phase III trial initiated enrolling 80 subjects in the U.S.</td>
<td>rigel.com</td>
</tr>
<tr>
<td>Perrigo, Co.</td>
<td>Voltaren Gel, 1% (diclofenac sodium topical gel, 1%)</td>
<td>osteoarthritis</td>
<td>ANDA approval granted by the FDA</td>
<td>perrigo.com</td>
</tr>
<tr>
<td>Mayne Pharma Group, Ltd.</td>
<td>SORILUX (calcipotriene Foam, 0.005%)</td>
<td>plaque psoriasis of the scalp and body in patients aged 12 years and older</td>
<td>Approval granted by the FDA</td>
<td>maynepharma.com</td>
</tr>
<tr>
<td>Pfizer, Inc.</td>
<td>Vyndaqel (tafamidis meglumine) and Vyndamax (tafamidis)</td>
<td>cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults</td>
<td>Approval granted by the FDA</td>
<td>pfizer.com</td>
</tr>
<tr>
<td>UCB</td>
<td>NAYZILAM</td>
<td>acute treatment of intermittent, stereotypic episodes of frequent seizure activity that are distinct from a patient’s usual seizure pattern in patients with epilepsy 12 years of age and older</td>
<td>Approval granted by the FDA</td>
<td>ucb.com</td>
</tr>
<tr>
<td>Takeda</td>
<td>GATEX (teduglutide) for injection</td>
<td>pediatric patients one year of age and older with Short Bowel Syndrome (SBS)</td>
<td>Approval granted by the FDA</td>
<td>takeda.com</td>
</tr>
<tr>
<td>Pfizer, Inc.</td>
<td>Fragmin (dalteparin sodium) injection</td>
<td>symptomatic venous thromboembolism (VTE) in pediatric patients one month of age and older</td>
<td>Approval granted by the FDA</td>
<td>pfizer.com</td>
</tr>
</tbody>
</table>
CWMarketPlace

CWMarketPlace is a monthly section featuring a range of clinical research service providers who have Industry Provider Profile pages posted on CenterWatch.com. Included in their annual subscriptions, company profiles are randomly selected to appear in this section, providing added exposure for their products and services. To learn more about becoming an Industry Provider Profile page subscriber, contact Sales at (617) 948-5100 or sales@centerwatch.com.

Click on any provider to view the company’s complete online profile or click here to search more profiles.

<table>
<thead>
<tr>
<th>CONTRACT RESEARCH ORGANIZATION</th>
<th>LABORATORY SERVICES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accell Clinical Research, LLC</strong>&lt;br&gt;Culpeper, VA&lt;br&gt;+7 981 844 10 48&lt;br&gt;<a href="mailto:svetlana.kazanskaya@accellclinical.com">svetlana.kazanskaya@accellclinical.com</a></td>
<td><strong>LabConnect, LLC</strong>&lt;br&gt;Seattle, WA&lt;br&gt;(206) 322-4680&lt;br&gt;<a href="mailto:info@labconnectllc.com">info@labconnectllc.com</a></td>
</tr>
</tbody>
</table>

ACCELL has been providing clinical CRO services to pharmaceutical and biotechnology companies since 2007. They are a full-service CRO specializing in Phase I-IV clinical trials in Eastern Europe, Russia and the CIS.

| **Confidence Pharmaceutical Research**<br>Burlington, CA<br>(401) 965-3377<br>anna.ravdel@confidenceresearch.com | **Consolidated Clinical Trials, Inc.**<br>Monroeville, PA<br>(412) 273-9100<br>smh@consolidatedclinicaltrials.com |

Confidence Pharmaceutical Research is a CRO and a vendor management organization that helps clinical trial sponsors run better trials. Our focus is on transparency, reducing waste and producing rigorous metrics.

| **CROMSOURCE**<br>Waltham, MA<br>(617) 871-1128<br>april.mccall@cromsource.com | **Complion**<br>Cleveland, OH<br>(800) 615-9077<br>contact@complion.com |

CROMSOURCE was among the first CROs to become active in Central & Eastern Europe and Russia. Their successful growth over has been built on stability, integrity, high levels of customer satisfaction and repeated business.

| **Medpace**<br>Cincinnati, OH<br>(513) 579-9911<br>info@medpace.com | **Virtrial**<br>Scottsdale, AZ<br>(480) 462-2222<br>kimkundert@virtrial.com |

Medpace employs approximately 2,500 people across 35 countries and provides Phase I-IV clinical development services to the biotechnology, pharmaceutical and medical device industries.

| **Pivotal S.L.**<br>Madrid, Spain<br>0034 679 488 022<br>bd@pivotal.es | **Palm Beach Research Center**<br>West Palm Beach, FL<br>(561) 689-0606<br>david@palmbeachresearch.com |

Pivotal was founded in 2001 by Dr. Ibrahim Farr on the principle that strategic medical advice and support should be the backbone of all clinical trials. Pivotal currently employs 200 cross-functional professionals.