CDER Drug Trials Report Shows Declining Enrollment

By James Miessler

CDER released its fourth annual Drug Trials Snapshots report, which shows a significant drop in the number of participants in pivotal novel drug trials that led to agency approvals.

The overall number of participants dropped by more than half from approximately 106,000 in 2015 to 44,000 in 2018, according to the latest report.

Mark Summers, president, patient engagement, WCG Clinical, noted that clinical studies — especially those for cancer drugs — don’t need as many people as they used to. “In areas like oncology everything’s moving toward biomarkers. You don’t need as large a population. That could be a factor as well,” Summers said, cautioning that the report doesn’t speak for overall participation in clinical studies because it only covers the enrollment rate of pivotal studies for FDA approved drugs.

Another significant trend was a shift in the trial demographics toward inclusion of more female and black or African American participants. The overall percentage of women increased from 40 percent in 2015 to 56 percent in 2018, while black or African American participation doubled from 5 percent in 2015 to 10 percent in 2018. Hispanics were not recorded in the first two snapshot reports but accounted for 14 percent in 2017 and 2018.

“In recent years, the representation of certain subgroups, such as women and minorities, has improved, but there is still a long way to go,” Summers said.

Keep Investigator’s Brochure Updates Clear, Concise and Timely, Experts Advise

By Mike Ingram

Most of the information in a clinical trial’s annual report is contained — often in greater detail — in the investigator’s brochure, so it makes sense to produce those documents in parallel, Guckin says. She notes, however, that an IB would need to be updated immediately if any crucial safety-related information came to light.

Beyond timing, Guckin says investigators often struggle with keeping IB updates clear and concise, balancing the need to provide all the relevant information with the need to produce a document that an IRB can quickly and easily digest. She suggests including with each IB revision a brief, easy-to-read summary of changes since the last iteration of the brochure. This summary can perform the same function as a table of contents, Guckin says. See Investigator’s Brochure on page 5 >>

ORDER TODAY

Accelerate your CRA career and get instant answers to your toughest clinical research procedural questions

The most complete guide to successful practices of high-performing CRAs.

New edition for 2019!

ORDER TODAY

Service providers:
Showcase your expertise with an Industry Provider Profile page.

• Generate new business leads and highlight products and services
• Increase visibility to Sponsors, CROs and research sites

POST AN INDUSTRY PROVIDER PROFILE

Order Today!

A crash course in what you should and shouldn’t say in a CTA

Reduce confusion and speed the negotiation of clinical trials by using clearly understood words and phrases.

ORDER TODAY

February 11, 2019

Industry Briefs…2

Drug & Device Pipeline News…7

Twelve drugs and devices have entered a new trial phase this week.

Research Center Spotlight…8

Research center profiles.
Industry Briefs

FDA to Review Trial Data in Real Time for Kadcyla Expanded Indication Study

The FDA will review Roche’s breast cancer drug Kadcyla (Trastuzumab emtansine) under its Real-Time Oncology Review and Assessment Aid pilot program, the drugmaker confirmed last week.

Kadcyla will be Roche’s first reviewed under the FDA’s Real-Time Oncology pathway, in which the agency can assess trial data as soon as it is generated rather than waiting until a drugmaker submits its formal application. The agency has approved four drugs under the real-time review pilot since July 2018.

The drug is currently indicated for treatment of previously treated HER2+ metastatic breast cancer, but Roche recently applied to expand its indication to HER2-positive early breast cancer patients who don’t fully respond to drug therapy before surgery.

Roche CEO Bill Anderson said in a January conference call that, between the real-time review and the agency’s breakthrough therapy designation, the company hopes to secure an FDA decision in the first quarter of 2019.

In December, the company presented data from its Phase III trial comparing Kadcyla to Herceptin, the company’s earlier breast cancer drug. In 1,500 patients and found that Kadcyla reduced risks of death or recurrence in early-stage patients with residual disease by 50 percent compared to Herceptin. Kadcyla had cut the risk of recurrence by 11 percent three years after treatment, according to Roche.

WCG Partners with Prudentia Group

WCG Clinical is partnering with drug safety and pharmacovigilance consulting firm Prudentia Group, the companies have announced.

Prudentia, headquartered in India, will work with WCG subsidiary Vigilare. Company officials hope the partnership will add “critical elements that will make our solution more powerful for clients, helping them make better, faster decisions with a greater degree of confidence,” WCG CEO Don Deieso said in a news release.

FDA Clarifies Efficacy Trials for Anti-Opioid Treatment

Sponsors that can provide specific data based on existing products won’t have to conduct new efficacy trials for the anti-opioid treatment buprenorphine injections or implants, says a new final guidance issued last week.

The FDA says it wants to clarify expectations for improving and speeding up other anti-opioid delivery mechanisms by specifying what kind of data can help bypass the efficacy stage, including:

- The proposed drug/device’s pharmacokinetic profile;
- The length of time a given treatment takes to reach a blood-plasma level that will block opioid reception;
- The maximum and minimum plasma concentration;
- The drug’s accumulation after several doses; and
- An estimate of how long a drug will take to clear a patient’s system.


FDA Issues Recommendations for Eosinophilic Esophagitis Drug Trials

The FDA has released draft guidance on clinical trial designs for treatment of eosinophilic esophagitis (EoE), including recommendations for selecting trial participants.

Randomized, double-blind, placebo-controlled trials should include a pre-specified screening period before patients are randomized to confirm their eligibility, the guidance says. Trials should evaluate a drug’s effect on both symptoms and the underlying inflammation of the disease by assessing the coprimary endpoints in Phase III trials.

Following the initial efficacy assessment, the FDA strongly recommends a randomized withdrawal design to assess the incidence of relapse, the need for redosing and persistence of the drug’s effects.

The trial population should include patients with a history of mild to moderate esophageal strictures because they may be responsive to treatment. Patients with a history of severe strictures requiring dilation, strictures preventing passage of a standard, diagnostic upper endoscope, or any critical esophageal stricture that requires dilation at screening should be excluded, as they’re unlikely to respond to drug therapy.


Informed Consent Doesn’t Equal Data Privacy Waiver, European Board Warns

Clinical trials operating in the EU need more clarity on data privacy and informed consent requirements, Europe’s top privacy regulator says.

In a document issued late last month, the European Data Protection Board (EDPB) says that a guidance on the impact of the
EU’s new General Data Protection Regulation (GDPR) on clinical trials doesn’t go far enough in explaining more restrictive rules for informed consent.

EDPB’s opinion is in response to a request from the European Commission to evaluate the EU’s new Clinical Trials Regulation — set to take effect in 2020 — in light of the GDPR’s requirements.

The board recommends EU drug regulators revise their recently published guidance document, “Questions and Answers on the Interplay Between the Clinical Trials Regulation and the General Data Protection Regulation,” to more clearly define the legal basis for using personal data under GDPR and explain the types of data usage allowed in clinical trials with or without subjects’ explicit informed consent.

Sites, researchers and sponsors should be able to collect and use patients’ data in a trial, the board says, if they can demonstrate that the data usage is “carried out in the public interest” or “purely for research purposes.”

Read the board’s opinion here: https://bit.ly/2SwlTtW.
CDER Report
continued from page 1

people of racial and ethnic minority groups, has become of greater interest to the general public," CDER director Janet Woodcock said.

The trend for participants aged 65 and older was generally upwards, with a spike in 2017 to 32 percent, but dropping off last year to just 15 percent representation. The spike may have been the result of several trials that were focused toward geriatric patients, such as Portola Pharmaceuticals' Bevyxxa (betrixaban) for prevention of thromboembolism.

CDER approved 59 novel drugs last year — either new molecular entities or biologics — ranging from oncology drugs to preventive migraine drug to treatments for bacterial skin infections, smallpox disease and epilepsy, among others.

The report includes data on the ethnicities, age and sex of participants in each approved novel drug trial. Some trials differed significantly in terms of their demographics. For example, participants in the pivotal trial for Amicus Therapeutics' Fabrys disease treatment Galafold (migalastat) were nearly all white (97 percent) and more than half were female (64 percent).

On the other hand, the key trial for Theratechnologies' Trogarzo (ibalizumab-uiyk), an HIV-1 treatment, was more evenly distributed, with whites, black or African Americans, Asians and Hispanics accounting for 55 percent, 33 percent, 10 percent and 25 percent of the participants, respectively, with a 15 percent female makeup.

Read the report here: https://bit.ly/2DXLzHU.

Clinical studies – especially those for cancer drugs – don’t need as many people as they used to.

— Mark Summers, president, patient engagement, WCG Clinical

ICH GCP E6 R2 Meeting CRO-Vendor Oversight Requirements
An Interactive Workshop Presented by CenterWatch and Wool Consulting Group

MARCH 27
March 27-28, 2019
Marriott Raleigh Crabtree Valley • Raleigh, NC

Through presentations, discussion, class activities and handouts you'll learn how to implement ICH GCP E6 R2 requirements in your organization. Join us for two days of networking and face-to-face interaction with a nationally recognized CRO-vendor expert.

ORDER TODAY! Visit store.centerwatch.com. Register by March 1 and SAVE $200.

The Revised Common Rule
New Requirements for Clinical Trials

After much discussion and repeated postponements, the updated Common Rule finally took effect on January 21, 2019.

In The Revised Common Rule report two prominent healthcare attorneys sift through the new rule to mark out every deletion—highlight every addition—interpret every rewording—that clinical research professionals and institutions will need to understand to be ready to comply.
Investigator’s Brochure
continued from page 1

Investigators often struggle with keeping IB updates clear and concise, balancing the need to provide all the relevant information with the need to produce a document that an IRB can quickly and easily digest.”

—Tiffany Guckin, associate director of regulatory affairs, Invicro

Keep your certification up to date

Earn up to 18 contact hours accepted by ACRP, SoCRA and CCIP organizations

Download a sample issue! www.centerwatch.com/promotion

» Learn critical and practical strategies
» More effectively manage and execute clinical trials
» Maintain nursing certification
» Subscriptions start at $197 a year

SUBSCRIBE TODAY! store.centerwatch.com sales@centerwatch.com (617) 948-5100

Compliance for Sponsors

The SOP for Good Clinical Practice by Sponsors of Clinical Trials ensures safe, effective and successful clinical trials and is a comprehensive customizable and easy-to-use SOP.

Read the full journal and then go to: http://store.centerwatch.com/t-exams.aspx

If you have any questions, feel free to email sales@centerwatch.com

SOP Highlights include:
• FDA guidance documents
• Risk-based monitoring templates
• CAPA plan information and forms
• Site selection and feasibility procedures
• Site initiation visit and training guidelines

ORDER TODAY

REGULATORY UPDATE

1. What did the plaintiffs mention in this clinical trial?
   a. False
   b. True
   c. Nurse coordinator
   d. All of the above

2. Discuss the concept of individual liability in IRB activities.
   a. False
   b. True
   c. IRB members may have individual liability in the case of
      a. A, B, and C
      b. An adverse event
      c. Nurse coordinator
      d. All of the above

3. Explain the importance of proper documentation of IRB liability
   a. False
   b. True
   c. IRB meeting documentation has
      a. Minutes
      b. 56
      c. 312
      d. All of the above

4. Discuss the future of patient engagement in clinical trials.
   a. False
   b. True
   c. A, B, and C

5. Identify the elements of or incorrect risk determination.
   a. False
   b. True
   c. IRB meeting documentation has
      a. Minutes
      b. 56
      c. 312
      d. All of the above

6. For medical device clinical trials, the regulatory authority publishes its
   a. False
   b. True
   c. IRB members may have individual liability in the case of
      a. A, B, and C
      b. An adverse event
      c. Nurse coordinator
      d. All of the above

7. For studies involving children, the IRB failed to assure the
   a. False
   b. True
   c. IRB members may have individual liability in the case of
      a. A, B, and C
      b. An adverse event
      c. Nurse coordinator
      d. All of the above

8. Patient engagement
   a. False
   b. True
   c. A, B, and C

9. Discuss the importance of proper documentation of IRB liability
   a. False
   b. True
   c. IRB meeting documentation has
      a. Minutes
      b. 56
      c. 312
      d. All of the above

10. Discuss the future of patient engagement in clinical trials.
    a. False
    b. True
    c. A, B, and C

11. Explain the importance of proper documentation of IRB liability
    a. False
    b. True
    c. IRB meeting documentation has
       a. Minutes
       b. 56
       c. 312
       d. All of the above

12. Identify the elements of or incorrect risk determination.
    a. False
    b. True
    c. IRB members may have individual liability in the case of
       a. A, B, and C
       b. An adverse event
       c. Nurse coordinator
       d. All of the above

13. For medical device clinical trials, the regulatory authority publishes its
    a. False
    b. True
    c. IRB members may have individual liability in the case of
       a. A, B, and C
       b. An adverse event
       c. Nurse coordinator
       d. All of the above

14. Discuss the future of patient engagement in clinical trials.
    a. False
    b. True
    c. A, B, and C

15. Explain the importance of proper documentation of IRB liability
    a. False
    b. True
    c. IRB meeting documentation has
       a. Minutes
       b. 56
       c. 312
       d. All of the above

16. Identify the elements of or incorrect risk determination.
    a. False
    b. True
    c. IRB members may have individual liability in the case of
       a. A, B, and C
       b. An adverse event
       c. Nurse coordinator
       d. All of the above

17. Discuss the concept of individual liability in IRB activities.
    a. False
    b. True
    c. A, B, and C

18. Discuss the future of patient engagement in clinical trials.
    a. False
    b. True
    c. A, B, and C

19. Explain the importance of proper documentation of IRB liability
    a. False
    b. True
    c. IRB meeting documentation has
       a. Minutes
       b. 56
       c. 312
       d. All of the above

20. Identify the elements of or incorrect risk determination.
    a. False
    b. True
    c. IRB members may have individual liability in the case of
       a. A, B, and C
       b. An adverse event
       c. Nurse coordinator
       d. All of the above

21. Discuss the concept of individual liability in IRB activities.
    a. False
    b. True
    c. A, B, and C

22. Discuss the future of patient engagement in clinical trials.
    a. False
    b. True
    c. A, B, and C

23. Explain the importance of proper documentation of IRB liability
    a. False
    b. True
    c. IRB meeting documentation has
       a. Minutes
       b. 56
       c. 312
       d. All of the above

24. Identify the elements of or incorrect risk determination.
    a. False
    b. True
    c. IRB members may have individual liability in the case of
       a. A, B, and C
       b. An adverse event
       c. Nurse coordinator
       d. All of the above

25. Discuss the concept of individual liability in IRB activities.
    a. False
    b. True
    c. A, B, and C

26. Discuss the future of patient engagement in clinical trials.
    a. False
    b. True
    c. A, B, and C

27. Explain the importance of proper documentation of IRB liability
    a. False
    b. True
    c. IRB meeting documentation has
       a. Minutes
       b. 56
       c. 312
       d. All of the above

28. Identify the elements of or incorrect risk determination.
    a. False
    b. True
    c. IRB members may have individual liability in the case of
       a. A, B, and C
       b. An adverse event
       c. Nurse coordinator
       d. All of the above

29. Discuss the concept of individual liability in IRB activities.
    a. False
    b. True
    c. A, B, and C

30. Discuss the future of patient engagement in clinical trials.
    a. False
    b. True
    c. A, B, and C

31. Explain the importance of proper documentation of IRB liability
    a. False
    b. True
    c. IRB meeting documentation has
       a. Minutes
       b. 56
       c. 312
       d. All of the above

32. Identify the elements of or incorrect risk determination.
    a. False
    b. True
    c. IRB members may have individual liability in the case of
       a. A, B, and C
       b. An adverse event
       c. Nurse coordinator
       d. All of the above
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>AtriCure, Inc.</td>
<td>cryoICE Ablation System</td>
<td>atrial fibrillation (Afib)</td>
<td>Phase I trial initiated enrolling up to 150 subjects at up to 20 centers in the U.S. with persistent and long-standing persistent atrial fibrillation undergoing cardiac surgical procedure(s) for heart valve repair or replacement and/or coronary artery bypass procedures</td>
<td>atricure.com</td>
</tr>
<tr>
<td>Verseon</td>
<td>VE-1902</td>
<td>coronary artery disease</td>
<td>Phase I trial initiated enrolling 100-120 healthy volunteers</td>
<td>verseon.com</td>
</tr>
<tr>
<td>Actinium Pharmaceuticals, Inc.</td>
<td>Actimab-A and venetoclax</td>
<td>Acute Myeloid Leukemia (AML)</td>
<td>Phase I/II trial initiated enrolling subjects with relapsed or refractory AML that have been previously treated with venetoclax and subjects that have never received venetoclax</td>
<td>actiniumpharma.com</td>
</tr>
<tr>
<td>Orphan Technologies</td>
<td>OT-58</td>
<td>classical homocystinuria</td>
<td>Phase II trial initiated enrolling up to 20 subjects</td>
<td>orphantechnologies.com</td>
</tr>
<tr>
<td>Neurana Pharmaceuticals</td>
<td>tolperisone</td>
<td>acute muscle spasms of the back</td>
<td>Phase II trial initiated enrolling 400 subjects</td>
<td>neuranapharma.com</td>
</tr>
<tr>
<td>BioLineRx Ltd.</td>
<td>BL-8040</td>
<td>pancreatic cancer</td>
<td>Orphan Drug Designation granted by the FDA</td>
<td>biolinerx.com</td>
</tr>
<tr>
<td>REGENXBIO, Inc.</td>
<td>RGX-181</td>
<td>late-infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease</td>
<td>Rare Pediatric Disease Designation granted by the FDA</td>
<td>regenxbio.com</td>
</tr>
<tr>
<td>Pharnext SA</td>
<td>PXT3003</td>
<td>Charcot-Marie-Tooth disease Type 1A (CMT1A)</td>
<td>Fast Track Designation granted by the FDA</td>
<td>pharnext.com</td>
</tr>
<tr>
<td>Teleflex Incorporated</td>
<td>MANTA Vascular Closure Device</td>
<td>large bore femoral arterial access site closure</td>
<td>PMA granted by the FDA</td>
<td>teleflex.com</td>
</tr>
<tr>
<td>Flowonix Medical, Inc.</td>
<td>Flowonix Maestro Software for Clinician Programmers used to program Prometra Pump Systems</td>
<td>intrathecal infusion of drug therapy</td>
<td>Approval granted by the FDA</td>
<td>flowonix.com</td>
</tr>
<tr>
<td>Cook Medical</td>
<td>Zenith Dissection Endovascular System</td>
<td>Type B dissections of the descending thoracic aorta</td>
<td>Approval granted by the FDA</td>
<td>aortic.cookmedical.com</td>
</tr>
<tr>
<td>Mylan N.V.</td>
<td>generic Advair Diskus (fluticasone propionate and salmeterol inhalation powder)</td>
<td>twice-daily treatment of asthma in patients aged four years and older and maintenance treatment of airflow obstruction and reducing exacerbations in patients with chronic obstructive pulmonary disease (COPD)</td>
<td>Approval granted by the FDA</td>
<td>mylan.com</td>
</tr>
</tbody>
</table>
## Research Center Spotlight

Research Center Spotlight is a monthly selection of clinical research centers who have Research Center 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 expertise and services in conducting and managing clinical studies.

To learn more about becoming a Research Center Profile page subscriber, contact Sales at (617) 948-5100 or sales@centerwatch.com.

### Axiom Clinical Research of Florida
Tampa, FL  
(813) 353-9613  
kcarlson.axiom@verizon.net

Axiom Clinical Research of Florida has been completing neurology studies in an outpatient setting since 1993. It has EDC capabilities and a regulatory submission turnaround time of three days.

### Care Access Research
Santa Clarita, CA  
(617) 841-7406  
trials@careaccessresearch.com

Care Access Research, Santa Clarita, is a multi-specialty, independent research center specializing in Phase II-IV clinical trials. It staffs four certified PIs and four certified CRCs.

### Carolina Institute for Clinical Research
Fayetteville, NC  
(910) 302-8151  
vgomez@wakeresearch.com

Carolina Institute for Clinical Research is a multi-disciplinary clinical research site that effectively combines strategic accelerated volunteer recruitment and retention with high-quality clinical trial conduct practices.

### The Clinical Research Center, LLC
St. Louis, MO  
(314) 514-8509  
generalmailbox@clinicalresearchcenter.com

A dedicated clinical research center, The Clinical Research Center specializes in pharmaceutical research involving respiratory illnesses such as asthma, allergies, COPD and the study of inhaled devices.

### Clinical Research of Central Florida, Inc.
Winter Haven, FL  
(866) 308-3271  
t.knight@clinicalresearchcf.com

Clinical Research of Central Florida conducts clinical Phase II through IV trials in all areas except pediatric and oncology.

### Clinical Research Partners, LLC
Richmond, VA  
(804) 477-3045  
ab@crpllc.info

Since 1998, CRP has successfully conducted over 120 Phase II-IV clinical trials. CRP employs eight full-time coordinators and has a 600+ local and regional physician referral base.

### Family Care Research
Boise, ID  
(208) 621-2501  
jill@injurycareresearch.com

Family Care Research is a dedicated research clinic that assists pharmaceutical and device companies to find new therapies to help patients better manage their healthcare.

### Rapid Medical Research, Inc. (RMR)
Cleveland, OH  
(216) 682-0320 x242  
lisa.hoagland@rapidmedicalresearch.com

RMR has conducted trials in over 70 therapeutic areas since 1997. Its on-site recruitment department recruits participants utilizing its database of over 15,000 potential research subjects.

### Spartanburg Medical Research
Spartanburg, SC  
(864) 583-1556  
jturner@medresearch.com

Spartanburg Medical Research is a dedicated Phase I-IV research site conducting trials since 1990, SMR has completed over 400 studies with a regulatory turnaround time of one day.

### Western States Clinical Research, Inc.
Wheat Ridge, CO  
(303) 940-9773  
research@wscrinc.com

WSCR's research subject database currently includes 1,750 potential study participants. Involved in research since 1991, it has conducted 280 studies.