

# CLINICAL TRIALS *Advisor*<sup>®</sup>

Vol. 11, No. 18  
Sept. 21, 2006

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## **Patent Infringement Suits Hit EDC Industry**

Two leading electronic data capture (EDC) providers have settled patent infringement lawsuits with a little-known Maryland firm, in one case for a multimillion-dollar amount. Datasci, the triumphant plaintiff, is now suing three other firms.

Datasci's patent (U.S. Patent No. 6,496,827, dated Dec. 16, 2002) covers "methods and apparatus for the centralized collection and validation of geographically distributed clinical study data" via "existing wide area networks, such as the Internet."

Leading EDC provider Phase Forward announced Feb. 16 that it agreed to pay \$8.5 million to Datasci to settle a patent infringement lawsuit filed in June 2004 over three of Phase Forward's products and related services — InForm, Clintrial and Clintrial Integra-

(See **EDC**, Page 2)

## **Device Trial Sponsors Must Be Careful In Wording Trial Agreements**

Sponsors of device trials must word their agreements with investigators and sites even more carefully in certain areas than sponsors of drug trials, according to a speaker at the FDA Clinical Trial Requirements Conference in Minneapolis.

"A lot of the issues that have to be covered in an investigator agreement [in a device trial] are automatically covered by FDA Form 1572 for drugs," Robert Klepinski, an attorney with Fredrikson & Byron, Minneapolis, told *CTA*. That form covers investigators' responsibilities in overseeing clinical drug trials (*CTA*, Aug. 10). "That's not so for device companies, so they must get it into the agreement," he added.

A device trial sponsor must have an agreement with the investigator to satisfy FDA rules, and an agreement with the site to cover payment, indemnification and other matters. However, some sponsors

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## EDC, from Page 1

tion Solution. The lawsuit also named Phase Forward client Quintiles as a defendant.

Phase Forward did not admit any liability when it made the one-time payment, which gave the firm “a fully paid-up, nonexclusive license to the patent on a going-forward basis,” according to a company press release. Phase Forward spokeswoman Gretchen Dock told *CTA* the company is barred from commenting further as part of the settlement.

On Aug. 31, Datasci scored another victory in a lawsuit against DataLabs, which agreed to settle in exchange for “a nonexclusive licensing arrangement on a going-forward basis,” according to a DataLabs press release. Financial terms were not disclosed. “DataLabs’ primary concern was the possibility of our customers being drawn into the suit,” William Maya, CEO of DataLabs, said in a statement. “By quickly settling this pending litigation, each of our valued customers can be assured that all DataLabs products are free of any ... patent issues.”

### Three New Lawsuits

Datasci is now suing three other EDC providers for patent infringement in federal court in Baltimore — Datatrak, etrials and DSG — according to the plaintiff’s attorneys, Mark Wasserman and Stanley Fisher of law firm Reed Smith.

The attorneys disclosed few details about Datasci to *CTA*, declining to discuss whether it is actually engaged in providing EDC services. “They don’t market systems,” Fisher said.

Two people are listed on Datasci’s patent: Mark Kozam and Louis Korman. “Dr. Kozam is the co-inventor on the patent along with another doctor,” said Wasserman. Both doctors are apparently gastroenterologists; Kozam is listed as a committee member of the website editorial board of the American Society for Gastrointestinal Endoscopy. His office referred all questions to his lawyers. Korman is listed as a medical staff member at George Washington University Hospital.

“Datasci’s patent is the pioneer patent in this technology and is way ahead of any of the defendants,” said Wasserman.

The CEO of one of the new defendants begged to differ. Datatrak “has been doing electronic trials since 1993, so it has a fair amount of prior art,” Jeffrey Green told *CTA*, using a technical patent-law term that means his company was using the technology first. “It’s well-known that we are the longest historical company — their patent was issued in 2002,” Green added.

Etrials issued a statement Aug. 8 saying, “the company believes the complaint is without merit and intends to vigorously defend the action.”

“We believe complaints of this nature are just a cost of doing business in our industry,” etrials CEO John Cline said. “We will aggressively defend our right to deliver all elements of our eClinical suite and will work diligently to prevail successfully in this case.” A spokeswoman told *CTA* that the firm cannot comment further.

DSG officials could not be reached for comment by press time.

### Broader Implications

It is somewhat surprising that Phase Forward and DataLabs settled with Datasci, Ed Seguine, CEO of eclinical company Fast Track, told *CTA*. “I would have expected them to fight.”

The patent infringement lawsuits “won’t limit EDC adoption” because it is too far along, Seguine said. However, clinical trial sponsors “will require their EDC vendors to indemnify them so they’re not at risk.” This may have been a major factor driving the settlements, he said.

The fact that Datasci holds a patent for doing EDC over the Internet is controversial in itself. Seguine said it was analogous to Amazon.com’s patent for its “1-click” online shopping system, which was also controversial because of what many saw as the obviousness of the technique. “There is a question about what is patentable as a business process,” he said. — Martin Gidron

## Implementing EDC a Matter of Clear Definitions

The biggest hurdle in switching from paper case report forms to electronic data capture (EDC) in clinical trials “is making sure you’ve clearly defined and documented your processes,” said Linda Staley, vice president of information technology at Dendreon, a Seattle-based firm that develops treatments that harness the immune system to fight cancer.

“We’re a biotechnology company. Our infrastructure was pretty much nonexistent when I came here 18 months ago. There were only one or two people in the IT department then,” Staley recalled.

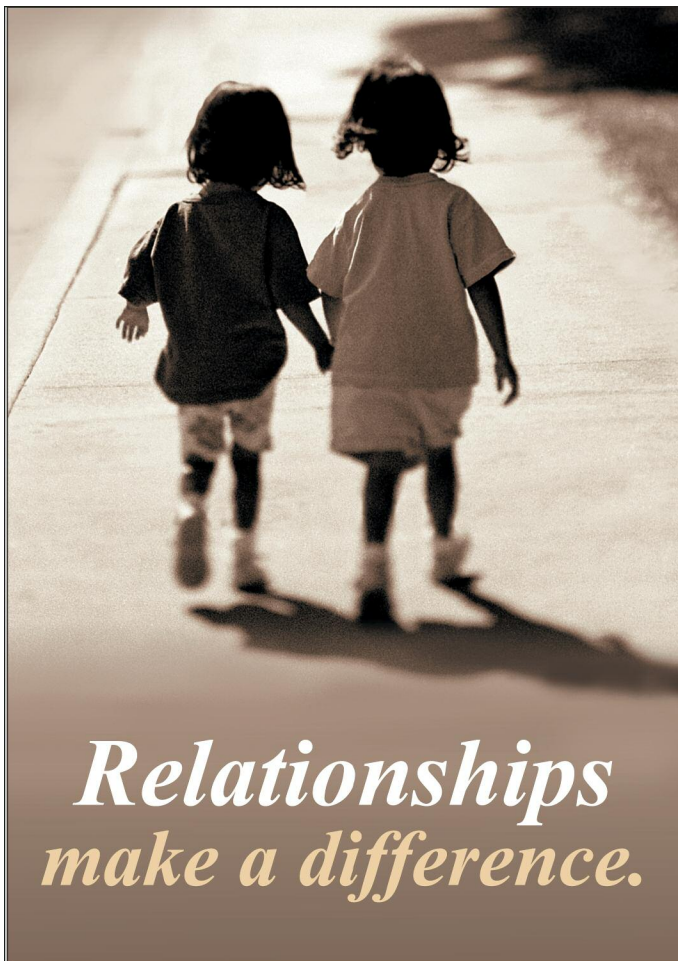
Since then, the company has completed a Phase III clinical trial for Provenge (sipuleucel-T), a new prostate cancer therapy. “We’re preparing for a commercial effort after approval,” Staley said. To that end, the company has chosen Oracle’s “E-Business Suite” applications, including Oracle

Order Management, Oracle Process Manufacturing and Oracle Advanced Supply Chain Planning.

These are meant to help Dendreon determine exactly where each patient-specific dose is in the supply chain at any given time while documenting regulatory compliance and protecting patient data.

Dendreon’s new electronic regime will include the esubmission of its biologic license application (BLA) for Provenge to the FDA, Staley said. The company plans to submit the BLA later this year. The key to successfully converting over to esubmissions is to “keep open communications” with the FDA, Staley said. “We are working with their technical staff to implement this technical and electronic process.”

Dendreon’s IT Department is currently coping with the transition from the clinical trial phase to the commercial phase, which requires mapping out process flows, clinical processes, manufacturing flows, quality control and billing, Staley said. — Martin Gidron



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## CLINICAL SITE BEST PRACTICES

### Are You Ready for an Investigator Audit?

Clinical investigators (CIs) should be prepared for a number of specific criteria FDA inspectors look for in an audit, according to the FDA's Rhonda Mecl.

The best way to prepare is to make sure you are up to date on all the requirements for CIs, which Mecl, a consumer safety supervisor with the FDA's Minneapolis District Office, outlined in a talk at the FDA Clinical Trial Requirements conference in Minneapolis, Aug. 23–24. The conference was sponsored by the Association of Clinical Research Professionals.

Among the things CIs must do, according to Mecl's outline, are:

- Submit FDA Form 1572, the Investigator Statement or Investigator Agreement;
- Personally conduct or supervise the study according to the investigator statement, investigational plan or brochure and regulations;
- Ensure that associates know the obligations of the study;
- Report adverse events and protocol deviations;
- Protect the rights, safety and welfare of all subjects and ensure proper informed consent;
- Ensure initial and continuing approvals from the institutional review board (IRB), including approvals for any changes in the study;
- Control the investigational drug or device by supplying it only to research subjects and maintaining adequate records of its use and disposal; and
- Maintain adequate and accurate case histories of all observations and data on each subject.

The extensive recordkeeping requirements for CIs are a common cause of trouble if not done right. CIs must keep all records or reports, including case report forms, signed and dated informed consent forms, and medical records such as test results, progress notes and hospital charts.

*(See Investigator Audit, Page 5)*

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## Investigator Audit, from Page 4

CI must also permit the FDA to access, copy and verify any or all of these records.

Also on the list of documentation requirements for CIs are progress reports, safety reports of adverse events and financial disclosure reports, all of which go to the sponsor; a final report that the CI prepares “shortly after” completion of the study; reports to the IRB; changes in research activity; and unanticipated problems.

CIs must keep trial records for two years after market approval or the discontinuation of the study. This rule applies to sites as well, said Demetria Lueneburg of the FDA’s Minneapolis office, who prepared Mecl’s presentation. In fact, there is “no separate entity in the regs called ‘site,’” Lueneburg noted. The regulations require sponsors to keep records for two years after completion of the research, and IRBs for three years.

Audits start with an interview between the FDA and the principal investigator, at which credentials and FDA Form 482 are presented. The FDA investigator asks a list of standard questions, including:

- How the CI became involved in the study;
- What the responsibilities of team members are;
- How the results were recorded;
- How patients were recruited;
- What the control and disposition of the drug or device are; and
- How subject randomization was done.

The FDA is looking for several things in these audits, according to Mecl. One is the source of the study subjects: Do they even exist? In at least one notorious case, that of the Southern California Research Institute, the investigator was accused of inventing fictitious subjects (*CTA*, June 29).

The FDA investigator will want to know if the study subjects meet inclusion and exclusion criteria and if the protocol was followed with each subject (*CTA*, Aug. 24). Informed consent,

lab work and tests under the protocol, and agreement of the results with the trial data are also key areas in a CI audit.

The FDA investigator will also want to see reporting of concomitant therapy and will check whether adverse events were reported properly to the IRB and the sponsor and whether the test article’s use and disposition can be traced.

CIs being audited are required to furnish a laundry list of documentation, including the trial protocol and amendments, informed consent documents, IRB approvals including amendments, curricula vitae of primary personnel, any publications from the study, a list of other clinical studies the CI has been involved in going back two years, patient charts, all lab reports, a file of correspondence with the sponsor and the IRB, a monitor visit log, patient recruitment ads with IRB approvals, the names and addresses of all labs used and pharmacy records.

Common deficiencies that FDA inspectors find in CI audits include the following, according to Mecl:

- Failure to follow the protocol;
- Missing source documents;
- Failures in drug or device accountability;
- Changes made to original records without documentation;
- Failure to send serious adverse event reports to the IRB;
- Missing items in the informed consent process; and
- Missing IRB approvals.

At the end of the audit, the FDA investigator issues an FDA Form 483, List of Observations, and holds a “closeout discussion” with the CI and staff. If the FDA inspector has found deficiencies such as those listed above, the agency may take a number of regulatory actions, including barring the data from being used to support the study; sending a warning letter; conducting a sponsor inspection; disqualifying the CI; imposing a consent agreement; seizure and stock recovery in ongoing studies; and even getting injunctions against or prosecuting offenders. — Martin Gidron

## Device Sponsor, from Page 1

“prefer to have one agreement including both the investigator obligations and the deal with the institution [research site],” whereas others “want a separate investigator agreement attached to the institution agreement,” Klepinski said at the conference, which was sponsored by the Association of Clinical Research Professionals, Aug. 23–24.

The most important reason device trial sponsors should have clinical agreements, according to Klepinski, is that “it is a teaching opportunity for explaining all the requirements.” It’s also necessary “to have something to point back at when noncompliant behavior occurs” and for filing a lawsuit in extreme cases.

Whether the agreements with the site and the investigator are in one document or two, sponsors must have the investigators “sign something that satisfies 21 CFR 812.43,” said Klepinski. “Do not let the [site] talk you into just them signing. You need the investigator to buy into all the terms of the institution agreement, such as [intellectual property], unless the investigator is an employee and the institution’s signature also binds the investigator.”

To satisfy federal regulations, device trial sponsors must require that the investigator supply:

- A curriculum vitae;
- A statement that he or she has the necessary experience;
- A statement that he or she has not been terminated from an investigation due to compliance failures;
- A statement of his or her commitment to supervise all testing of the device and ensure that all requirements of informed consent are met, although institutional review board (IRB) approval is necessary before getting informed consent;
- Submission of financial disclosure information and a promise to supplement it as needed; and
- Commitments to conduct the study in accordance with the investigator agreement, investigational plan (which is broader than just the protocol alone) and other FDA and IRB conditions.

Standard terms for a site agreement, according to Klepinski, include payment for research; an intellectual property clause covering patent rights, copyrightable material, publication rights and confidentiality; termination; indemnification; and a subject-injury clause.

The termination clause deserves more attention than it often gets, said Klepinski. You want to be able to terminate at any time, particularly if the investigator is not available or if there is a compliance issue. “This is different from ending the study. You need to be able to tell them to stop enrolling patients when you reach your limit. [But] this is not termination of the agreement,” he said. The termination clause should not be for a fixed period of time, but should run until the study is closed and the sponsor does not need any further work.

Indemnification also needs careful attention. The term means that one party agrees to protect the other and pay for certain costs or risks. Sites ask for indemnification, but sponsors can ask for it in return.

“Limit your indemnification to what you can control,” Klepinski advised. “Indemnify for problems with your device, injuries directly caused by your device or injuries caused by a procedure required by your protocol. Do not broadly indemnify for ‘anything resulting from the study.’ Do not indemnify for risks of normal hospital care that are not part of your protocol.”

Last, insurance for participant injuries resulting from the study has become a knotty problem. “Device companies are not prepared to become health insurers,” Klepinski told *CTA*.

Many are small and “survive on venture capital,” he pointed out. Thus, they must be careful not to put themselves in a position where they become the trial participants’ primary insurer, which is a real risk under recently changed Medicare regulations. A sponsor that agrees to supplement Medicare becomes the primary insurer, and in that case it is actually a violation to submit bills to Medicare.

Klepinski’s advice to sponsors: consult carefully with your attorney, limit what you promise in your plan, check what your insurance and deductible cover and “hope that it will be clarified.”  
— Martin Gidron

## SPONSOR BEST PRACTICES

### Plan Ahead for Successful Patient Recruitment

The increasingly difficult challenge of patient recruitment can be tackled successfully if sponsors adopt the right strategies from the start, say experts in the field.

“Use all of your resources up front. Don’t wait for ‘Plan B’ to happen — use Plan B while Plan A is still running,” said Andra Schemera, manager of clinical sciences, Regeneron Pharmaceuticals.

Such advance preparation is essential because the marketing tools sponsors typically use to recruit patients, such as pamphlets and other advertising, have to be cleared by the institutional review board as well as the company’s own legal and marketing departments, Schemera said. Thus, it’s important to prepare these materials in advance even if you don’t plan on using them right away, so that “if you see enrollment declining, you can just pull them off the shelf.”

#### Marshal Your Resources

Sponsors can turn market conditions and existing resources to their advantage. “Especially these days, patients are really taking charge of their own situation,” Schemera said. Sponsors should reach out to these newly empowered patients through targeted ads on TV and the radio, and in selected periodicals. For example, if you are recruiting for an osteoarthritis study, consider advertising in a local retired persons’ magazine, Schemera said.

Sponsors who properly cultivate principal investigators (PIs) can reap big rewards in patient recruitment, Schemera said. “Some investigators run a lot of clinical trials. You need to get them fully engaged in yours so they will be good to you.” This is especially true in the field of oncology, where “a lot of your work gets farmed out to [contract research organizations].

Some investigators never even get to see the sponsor.”

The solution, said Schemera, is to get the sponsor’s doctors to “engage with the PIs.” Regeneron, which is active in oncology trials, sponsors “mini-dinners” at which the two groups can meet. “Get them interested in your study. If the investigator has bought in, he will pull your binder off the shelf when a patient walks in the door looking for a trial to take part in.”

#### Special Challenges

Certain types of clinical trials pose special patient-recruitment challenges, said Mike Nourie, CEO of Accélère, a patient recruitment firm. In one current clinical trial that his company is working on, patients must be identified, screened and enrolled within 12 hours of their arrival in hospital emergency rooms. Technology helps provide solutions in cases like this. “We are shooting for an increase in enrollment of two to 10 times,” Nourie said.

A somewhat similar set of problems arose in a neurological study of stroke victims. The protocol called for following up with the patients two to four weeks afterward. “These secondary studies are very difficult to recruit for, since the numbers [of patients] are very low and the dollar amounts are very high,” Nourie said. Dedicated software helped ensure that “researchers don’t lose track” of the patients.

A different sort of patient recruitment problem arises when “the population is distributed across a hospital,” Nourie said. As an example, he cited a blood transfusion study that was done at the University of California, San Francisco. Patients’ blood-plasma data had to be correlated with other lab data, and “it is difficult to get to patients while they are being transfused.” The solution his firm came up with, Nourie said, involved using “electronic surveillance to find clinical patients.” — Martin Gidron

## EU CLINICAL TRIALS DIRECTIVE

### Country Profile: Latvia

*The European Union recently implemented the EU Clinical Trials Directive (CTD) to better protect clinical trial participants while streamlining the bureaucracy to make the EU more attractive for clinical research (CTA, Nov. 17). CTA continues its monthly profiles of individual EU member states, detailing where each country stands on implementing the EU directive, as well as the steps sponsors must take to conduct trials. This month, CTA covers Latvia, one of the three Baltic Republics that regained their independence from the former Soviet Union in 1991.*

Clinical trials in Latvia are covered by “Cabinet Regulation No. 172” of Feb. 28, 2006. The language closely follows that of other EU member nations, copying word-for-word the European Commission’s Good Clinical Practice (GCP) Directive to state that, “The rights, safety and well-being of the subject shall prevail over the interests of science and society” (CTA, Aug. 24).

Latvia’s State Agency of Medicines and an ethics committee, the equivalent of an institutional review board, must approve all clinical trials. To get this approval, the sponsor or duly authorized person must submit a lengthy list of documents to the State Agency of Medicines, including the following:

- The European Clinical Trials Database (EudraCT) number;
- The European Commission’s application form for permission to conduct a clinical trial, in both paper and electronic (XML) versions, signed by the sponsor or authorized representative;
- The protocol and amendments, if any, signed by the sponsor and investigator;
- A list of all actual clinical trials involving the investigational medicinal product;
- An investigational medicinal product dossier, which should contain such information as the quality of the test product and placebo, data from nonclinical and clinical studies and a risk-benefit analysis;

- A list of other EU member states where the application has been submitted, and information on authorization status there;
- A copy of the manufacturing license if the investigational medicinal product(s) are manufactured in Latvia or elsewhere in the European Economic Area, or import authorization if not;
- Certification that the product and its active ingredients follow EU good manufacturing practice (GMP);
- The informed consent form developed by the sponsor in the “official language,” with translations for subjects who need them;
- Proof of insurance for subjects injured as a result of the clinical trial, as well as proof of insurance or indemnity against investigator and sponsor liability;
- Documentation of financial compensation plans for trial subjects;
- The investigator’s brochure or a “summary of product characteristics.” The brochure must be a compilation of clinical and nonclinical data on the investigational medicinal product relevant to the study. The information must be presented in a concise, simple, objective, balanced and nonpromotional form so that a doctor or potential investigator can understand it and make an unbiased risk-benefit assessment. The sponsor must validate and update this brochure at least once a year;
- A sample of the product labeling in the official language;
- Curricula vitae of the investigator and any subinvestigators;
- Written affirmation from the investigator that he or she has the proper training, and that the clinical trial will be conducted in accordance with the protocol and any normative acts; and
- A power of attorney, if the documentation is submitted by the sponsor’s authorized representative.

The Latvian State Agency of Medicines has up to 45 days to review a valid application, except when reviewing proposed trials for gene or somatic-cell therapy, or for products containing

(See [EU Directive](#), Page 9)

## EU CLINICAL TRIALS DIRECTIVE

### EU Directive, from Page 8

genetically modified organisms, when it may take up to 180 days. (Gene therapy trials that result in modifications to the subject's germ line genetic identity are banned.) For a trial of "xenogenic cell therapy," the agency may take as long as it likes to review the application.

In all cases, the agency may ask for additional information, pausing the 45-day clock until it gets what it needs. In the case of multisite clinical trials, whether restricted to Latvian territory or carried out in more than one EU country, the State Agency of Medicines is to make a single decision. Sponsors may appeal any denial.

All clinical trials, including bioavailability and bioequivalence studies, must be designed, conducted and reported in accordance with GCP principles. All clinical trial information must be recorded, handled and stored so that it can be accurately reported, interpreted and verified, while protecting patient confidentiality.

### Additional Sponsor or Responsibilities

The sponsor or its legal representative must be registered in the EU. The sponsor may delegate any or all trial-related functions to another physical or legal entity, e.g., a contract research organization, but the sponsor remains responsible for ensuring that the conduct of the trial and the data generated comply with regulations.

It is the sponsor's responsibility to supply and ensure the quality of the investigational medicinal product(s), which must be manufactured and controlled in accordance with GMP. The sponsor must also supply the investigational medicinal product(s) and devices for product infusion (if any) free of charge, and must determine storage conditions, storage times, reconstitution fluids and procedures. The sponsor is to inform everyone involved in the clinical trial of these requirements.

Sponsors are not responsible for a deliberate or accidental injury to a trial subject caused by the investigator or other individuals involved in the clinical trial. The investigator is also responsi-

ble for the accounting and storage of investigational medicinal product(s) at the research site.

The ethics committee in a clinical trial must be an independent body approved by the Minister of Health, and consist of qualified and experienced professionals who are able to review the ethical and scientific aspects of the proposed clinical trial. There must be at least nine members, including at least two who do not have medical educations, and two who are independent of the research site. Both sexes must be represented on the committee.

For a clinical trial to proceed, the ethics committee and the Latvian State Agency of Medicines must determine that the anticipated therapeutic and public health benefits justify the risks. Compliance with this requirement is to be permanently monitored.

The trial subject, or his or her legal representative, must give informed consent. If a volunteer is unable to write, oral consent in the presence of at least one witness is permitted in exceptional cases.

The trial subject, or his or her legal representative, must be given the opportunity, in a prior interview with the investigator or a member of the research team, to understand the objectives, risks and inconveniences involved in the clinical trial and the conditions under which it is to be conducted.

He or she must also be informed of his or her right to withdraw from the clinical trial at any time. Clinical trial subjects have rights to physical and mental integrity, privacy and the protection of personal data.

For minors, there are a number of additional protections. At least one parent or legal representative must give informed consent. Consent represents the minor's "presumed will" and may be revoked at any time, without detriment to the minor; minors who are capable of making up their own minds may withdraw consent themselves. The minor must receive information on the trial "according to its capacity of understanding" from staff experienced in dealing with children. — Martin Gidron

## INDUSTRY NEWS

### Medidata to Provide EDC to Canada's NCIC

Medidata Solutions announced that the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) has chosen Medidata's Rave 5.5 electronic data capture (EDC) system to conduct and analyze its national and international cancer therapy trials. The NCIC CTG plans to conduct at least 30 Phase I, II and III trials using

Medidata Rave in the next five years in Canada, the U.S. and Europe.

NCIC CTG Director Joseph Pater first learned about Rave from Medidata's work with the UK's National Cancer Research Network when he was working on restructuring the latter's cancer clinical trials program.

### Clinical Trials Recruiting Patients

| Recruiting Sponsor: Bayer |   |  |        |  |
|---------------------------|---|--|--------|--|
| ClinicalTrials.gov ID     | Condition   | Intervention   | Pha    | URL  |
| NCT00108953               | Hepatocellular Carcinoma, Liver Cancer  | Drug: BAY 43-9006 (sorafenib)  | II/III | <a href="http://www.clinicaltrials.gov/ct/show/NCT00108953?order=1">www.clinicaltrials.gov/ct/show/NCT00108953?order=1</a>   |
| NCT00110344               | Renal Cell Carcinoma  | Drug: BAY 43-9006 (sorafenib)  | II     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00110344?order=2">www.clinicaltrials.gov/ct/show/NCT00110344?order=2</a>   |
| NCT00119639               | Kidney Diseases   | Drug: BAY 43-9006 (sorafenib)  | I      | <a href="http://www.clinicaltrials.gov/ct/show/NCT00119639?order=3">www.clinicaltrials.gov/ct/show/NCT00119639?order=3</a>   |
| NCT00259129               | Cancer  | Drug: BAY 43-9006 (sorafenib)  | I      | <a href="http://www.clinicaltrials.gov/ct/show/NCT00259129?order=4">www.clinicaltrials.gov/ct/show/NCT00259129?order=4</a>   |
| NCT00300885               | Non-SmallCell Lung Cancer (NSCLC)   | Drug: BAY 43-9006 (sorafenib)  | III    | <a href="http://www.clinicaltrials.gov/ct/show/NCT00300885?order=5">www.clinicaltrials.gov/ct/show/NCT00300885?order=5</a>   |
| NCT00306137               | Transfusion Requirements for Surgery for Lung or Esophageal Cancer  | Drug: BAY a-0128   | III    | <a href="http://www.clinicaltrials.gov/ct/show/NCT00306137?order=6">www.clinicaltrials.gov/ct/show/NCT00306137?order=6</a>   |
| NCT00306150               | To Reduce Transfusion Requirements in Patients With Bladder Cancer Undergoing Radical or Total Cystectomy | Drug: BAY a-0128   | III    | <a href="http://www.clinicaltrials.gov/ct/show/NCT00306150?order=7">www.clinicaltrials.gov/ct/show/NCT00306150?order=7</a>   |
| NCT00327379               | Reduce Transfusion Requirements in Patients Undergoing Elective Spinal                                    | Drug: Aprotinin  | III    | <a href="http://www.clinicaltrials.gov/ct/show/NCT00327379?order=8">www.clinicaltrials.gov/ct/show/NCT00327379?order=8</a>   |
| NCT00329628               | Prevention of Venous Thromboembolism  | Drug: Rivaroxaban (BAY59-7939)   | III    | <a href="http://www.clinicaltrials.gov/ct/show/NCT00329628?order=9">www.clinicaltrials.gov/ct/show/NCT00329628?order=9</a>   |
| NCT00352859               | Cancer, Renal Cell Cancer (RCC)   | Drugs: Nexavar (Sorafenib, BAY43-9006); Gemcitabine; Interferon          | IV     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00352859?order=11">www.clinicaltrials.gov/ct/show/NCT00352859?order=11</a> |
| NCT00107081               | Fever, Neutropenia, Cancer  | Drug: ciprofloxacin and amoxicillin; Procedure: Outpatient management    | III    | <a href="http://www.clinicaltrials.gov/ct/show/NCT00107081?order=14">www.clinicaltrials.gov/ct/show/NCT00107081?order=14</a> |
| NCT00135226               | Diabetes Mellitus   | Drugs: aspirin, Omega-3-acid Ethyl Esters                                | IV     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00135226?order=15">www.clinicaltrials.gov/ct/show/NCT00135226?order=15</a> |
| NCT00137787               | Febrile Neutropenia   | Drugs: ciprofloxacin, cefepime   | III    | <a href="http://www.clinicaltrials.gov/ct/show/NCT00137787?order=16">www.clinicaltrials.gov/ct/show/NCT00137787?order=16</a> |
| NCT00139984               | Hypertension  | Device: 24 hour blood pressure measurement                               | IV     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00139984?order=17">www.clinicaltrials.gov/ct/show/NCT00139984?order=17</a> |
| NCT00144417               | Tuberculosis  | Drug: Moxifloxacin (with rifampin, pyrazinamide, and ethambutol)         | II     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00144417?order=18">www.clinicaltrials.gov/ct/show/NCT00144417?order=18</a> |
| NCT00153062               | Cerebrovascular Accident  | Drugs: extended-release dipyridamole + aspirin; clopidogrel; telmisartan | IV     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00153062?order=19">www.clinicaltrials.gov/ct/show/NCT00153062?order=19</a> |
| NCT00177970               | Clostridium Difficile-Associated Diarrhea (CDAD)  | Drug: intravenous immunoglobulin G (IVIG)                                | IV     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00177970?order=21">www.clinicaltrials.gov/ct/show/NCT00177970?order=21</a> |
| NCT00178464               | Sickle Cell Disease   | Drug: aspirin  | I/II   | <a href="http://www.clinicaltrials.gov/ct/show/NCT00178464?order=22">www.clinicaltrials.gov/ct/show/NCT00178464?order=22</a> |
| NCT00225849               | Hypertension, Hyperlipidemia, Diabetes Mellitus   | Drug: aspirin  | IV     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00225849?order=24">www.clinicaltrials.gov/ct/show/NCT00225849?order=24</a> |
| NCT00259168               | Insulin Resistance, Impaired Fasting Glucose  | Drug: Nateglinide  | IV     | <a href="http://www.clinicaltrials.gov/ct/show/NCT00259168?order=25">www.clinicaltrials.gov/ct/show/NCT00259168?order=25</a> |


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