CLINICAL TRIALS
ADMINISTRATOR
An essential resource for managers of clinical trials

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Information technologies can improve clinical trial quality and efficiency

Expert offers look at some systems that work well

The need for less expensive and more efficient clinical trials has increased in recent years with drug discovery occurring at an explosive rate, and yet the clinical trials process has changed very little over the past decade, an information technologies expert says.

"You have a huge bottleneck with clinical trials, and this is a cost driver that is increasing the social cost of health care and threatening, at some point, to make new compounds unattainable," says **Russell J. Clark**, JD, president of Cancer Technology Applications of Atlanta. The company consults with institutions to put together the right suite of applications to facilitate clinical trials from the recruitment stage to data capture.

"Cancer is an example of where certain new treatment regiments cost $100,000 per patient per year," he says. "Where you can save money is in the clinical trials process, which is primed for dollar savings."

For example, the clinical trials process could use re-engineering and technology applications to reduce the overall time and cost of clinical trials, Clark notes.

"Seventy percent of the total cost of drug development is spent during the clinical trial process," he reports. "The average cancer drug takes 10 years to get through the drug development process."

A recent study found that the average cost to develop a new drug is $900 million for a pharmaceutical company, but another study estimated the cost to be closer to $1.7 billion, Clark contends.

"So it's a lot of money; and my point is that a huge percentage of that cost is wrapped up in clinical trials," he says. "I've spent a significant amount of time in the last five years helping to re-engineer and develop better processes."

From his research into new technologies, Clark offers this brief guide to what will work in making the clinical trial process more efficient and cost-effective while maintaining or improving quality:

• **Patient recruitment:** "When you look at the critical path for clinical trials, the first big choke point that we've identified is patient recruitment," he says. "According to one study, 80% of all clinical trials are

behind schedule because of patient recruitment."

One of the challenges is to match the potential clinical trials subject and physician, especially for cancer trials, he notes.

"You will never get the patient on the trial without the physician being there to educate the patient about what the trial is about," Clark says. "A person can go on a web site to find a trial, but unless it matches back to the treating physician, there isn't much value to finding someone that way."

So he has worked on identifying systems and technologies that will match potential subjects with physicians.

"You need a sophisticated data mining operation that searches structured and unstructured data," Clark explains. "To match the characteristics of a patient with a trial, you need to dig deeper than demographics."

For example, it's possible to match patients using structured data, such as demographics, ICD-9 codes, physician identifiers, and PCT codes, but this method would produce a lot of false positives, and most physicians would not be interested in this method, he says.

"Physicians want more accuracy, and an unstructured data mining tool would allow you to go into the physician's notes and do a much finer search," Clark says.

Here's how challenging the unstructured data mining can be without the help of technology: "In Florida, one customer [gave] me an example of where she'd gotten a request from a pharmaceutical company to find 50 patients for a cardiovascular study, and she and three of her employees went through 30,000 paper charts," he recalls. "Out of that, they found 40 patients."

The other old-fashioned way patient recruitment works is for clinical trials administrators to invite physicians to lunch and then ask them if they have any patients or to give out business cards to physicians who have a high volume of patients who potentially will meet the study's criteria, Clark says.

"So we haven't applied technology effectively in terms of patient recruitment," he says. "And I believe there are tools out there that will do that effectively."

One such tool is PolyAnalysis, sold by Evrika in Aliso Viejo, CA, Clark reports.

"PolyAnalysis will allow a user to go into a research site that has patient data in electronic format, including patient information, ICD-9 codes, structured data, lab results, and transcribed unstructured notes," Clark says. "Most hospitals have these components in electronic format, and you would need to import the data from the system and import data from any electronic program and do a search by eligibility requirements."

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Editorial Questions

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The output is a report that identifies each patient who meets eligibility requirements and the patient's identification number, he adds.

Then, all a clinical trials administrator would need to do is contact the physician and let him or her know that there's a clinical trial for which this patient's identification number appears to fit the trial, Clark says.

"You could attempt recruitment and enrollment through that means," he says.

There are many web sites that offer to do this type of search, but most do not appear to do an adequate job of matching the provider and patient, Clark notes.

And while the American Cancer Society is working on a web site matching program, it's not yet public, he says.

Going digital

• **Data capture:** Once a patient is recruited and enrolled and the protocol and investigator are ready to begin, the challenge is capturing the data that begin with the first patient visit, Clark says.

Most clinical trials continue to use paper forms, he notes. "So the patient visit data are captured relative to the visit recorded in the source document," Clark says. These data include patient history, lab testing, physical exam, and patient charts.

The clinical trials administrator then takes the source document and patient chart and transcribes these into a case report form using the relevant information.

"This is highly inefficient and error-prone, but that's the way we do it," Clark explains. "There have been 60 little companies sprung up in the last 10 years to address this issue; a number of them have failed and gone out of business."

Pharmaceutical companies have continued to be extremely conservative in terms of changing this practice, he adds.

"A few have developed systems, but many of the others march down the paper trail," Clark says.

"I think we'll see some dramatic changes in the near term," he predicts. "There's a stability, proven track record, and proven technology capabilities with the big players who've entered the field, so I think we'll see a major paradigm change there."

Besides being slower, the paper process has more chances for someone to make a mistake with data.

"What happens with paper is the facts are mailed to a central data site and double-entered into an electronic database," Clark explains. "There are two people entering the data under the theory that they won't both make the same mistake; so data is reviewed to see if there's a difference between data entry person one and two, and if there's a discrepancy, it needs to be resolved."

To resolve a difference, the clinical trials administrator is called to clarify the discrepancy before the data officially are entered into the database, he points out.

"That can take weeks from the time of the visit to when the data is entered and queries resolved, and it finally goes into the research database," Clark says. "Juxtapose that with an electronic system in which the data goes in and has its own logic so it won't let you enter, for instance, a 2-foot-tall man into the data site, and it can't make that kind of mistake."

This sends data to the research base quickly, and if there are any discrepancies when it's monitored, these are electronically taken back to the site and resolved, he notes.

"Adverse events can be tracked immediately; and if a trial is going in a bad direction, they can stop it," Clark reports. "Most of the money is spent by trials that go on and on and should be stopped because they're not showing efficacy."

With an electronic data process, a clinical trials administrator will be able to look at the data more quickly and make smarter and faster decisions, saving money, he adds.

Then taking electronic data collection to the next level, there is an electronic medical record that flows and populates the field in the case report form with no double entry, Clark says.

"There's a lot of work on that right now, with a lot of industry leaders and private-public consortiums that have adopted standards so various clinical trial data systems will talk to each other," he says. "There's a push from a number of major players to develop interfaces and integration between clinics and electronic data capture systems."

For example, Microsoft Corp. of Redmond, WA, is entering the field, and Siemens Medical Systems Inc. of Issaquah, WA, is in the business and is the most advanced in terms of integration with other systems in terms of electronic data capture, Clark reports.

• **General efficiency:** "Another big choke point in the process has to do with the IRB, and part of that is the document management function," he says. "So much paper floats around in today's world, the better process is to scan."

It's more efficient to make PDF files of regulatory

documents and e-mail these to IRB members, rather than to mail thick packages of paper, Clark notes.

Most multicenter studies have a separate IRB reviewing the same protocol conducted at the different institutions, and this might mean that a clinical trial will take many months to complete the IRB approval process, he says.

"A better process we've been working on with a number of sponsors is a centralized IRB, where there may be 10 sites and one IRB," Clark says. "This is one of those dinosaurs that dies hard."

Protocol training could be improved through the use of a web-based education format, he says.

It would save travel costs, investigator, and clinical trials staff time because they could learn about the protocol at a time that is convenient for them rather than attending one big meeting, Clark adds.

And the web-based program could test participants to make certain they understand the protocol, so this would meet all regulatory requirements, he says. ■

Improve workflow, avoid bottlenecks

Best practices save time, money

As every clinical trials administrator knows, it's difficult to predict every problem and extra cost that might occur during a lengthy trial process.

"There always seems to be more work done on a project than what gets captured in the budget," says **Bruce Steinert**, PhD, CCRA, director of clinical trials administration at Children's Mercy Hospital in Kansas City, MO.

But with experience and following best practice guidelines, an administrator may find that all goes as well as planned. He offers these suggestions for how to improve the clinical trials process and promote best practices in managing trials:

• **Use consistent contract language.**

"We route contracts through legal and compliance and between investigators and sponsors," Steinert reports. "Whenever possible we use language that's similar to what the investigators use."

The institution developed consistent language over time, and it has worked well with some sponsors, he notes.

"Others will change it and renegotiate the whole thing from scratch, even if it was approved last week," Steinert says. "Whenever possible, we try to use things we already negotiated to avoid having to travel the same path twice."

• **Develop a pricing list.**

Children's Mercy Hospital has a pricing list that was developed for its own projects, as well as for federally sponsored projects, he says.

The price list confirms the best price for laboratory tests, facility charges, and other routine costs.

"We know what it costs to use an examination room for an hour or two hours," Steinert explains. "Our accounting department assembles those costs so we don't get bias from investigators and others."

This pricing list is the starting point in the budgeting process, he adds.

• **Make certain protocol fits with budget.**

"We have two contract specialists who work with [study] coordinators because the principal investigators are too busy for the initial budgeting go-rounds," Steinert says. "Together, the specialists and coordinators make a grid summary of what happens on which visits, who does what, which department will be involved, whether there will be radiology or lab tests, and then we make a base budget."

The base budget then is compared with what the sponsor offers, and the sponsor's study spreadsheet of scheduled activities is compared to the protocol's language, he notes.

"Sponsors will make an initial offer of X amount per patient; we'll see if that fits into our budget, and we're usually in the ballpark," Steinert explains. "Sponsors try to undershoot, but we make sure our costs are met, including IRB costs, pharmacy set-up fees, and our expenses for labor, so the hospital doesn't lose money."

The biggest budgeting problem is labor, he notes.

"As we go through and develop the budget, we estimate what the PI's time will be for various functions and break it down to a per patient charge to figure the cost reimbursement," Steinert explains.

But there's the challenge of capturing time when a PI may be working on several studies at the same time. While he's waiting for a printout on one, he makes a phone call on another, he says.

The institution builds a small cushion in the budget to cover indirect costs; so if there is any additional funds at the close of a study, the money will be used to offset unanticipated labor costs, Steinert says.

Once a contract is in place, the institution charges for its start-up costs as nonrefundable, so

if there are problems with enrollment, the institution will not lose the money invested in attempting to enroll the required patient population, he adds.

• **Anticipate enrollment problems.**

Enrollment problems are common, Steinert notes.

"You can't coerce subjects to go into a study, and there are some studies where a PI thinks it's really important and the hospital thinks so, but patients don't want to try it," he says. "You see that more in a pediatric hospital."

"If there's difficulty in enrolling patients, but you have been screening patients, then you generally will get paid by the number of patients who complete or partially complete the trial," Steinert says. "If an investigator knows there will be some difficulty in enrolling patients, they will screen a lot of patients."

For instance, there may be cases where patients make it all the way through the screening process, but then a final medical test excludes them from the study's criteria, he says.

"We make a good-faith effort to get them into the project, and we build some screen failures in the budgeting process, as well," Steinert says.

"In some protocols, it's difficult to enroll patients, and the sponsors understand that, so they'll put more into the budget on their end," he adds.

The way to anticipate for these problems is to bill screen failures as contingent costs and to anticipate a certain amount of these contingent costs, depending on the study and how difficult the PI thinks it will be to enroll patients, Steinert says.

A second method is to prorate the costs based on actual enrollment, collecting enough per enrolled patient to cover two or three screen failures, he says.

"If we don't enroll anybody for the study, then we eat the costs on that method," Steinert says.

"If a sponsor is having trouble with enrollment at other sites, then they're more receptive to other screening charges, and we can renegotiate if we're having trouble, too," he reports. "If they're meeting enrollment at other sites, and it's just our population that's not meeting it, then they're less receptive."

A good study selection is half the battle, says Steinert.

As studies come into his office, Steinert find out who in the hospital might be interested and then send them copies to assess.

If the physician answers that he or she doesn't have the population or is too busy and can't take on another study, then the institution turns down the study, he explains.

"It's worse to accept the study and do a bad job on it," Steinert says. "It makes us look better to know it's not a good study for us."

• **Negotiate costs that may be duplicated.**

It's becoming more common for sponsors to use central facilities to read EKGs and other types of testing procedures, Steinert says.

This eliminates some evaluator bias, but it creates problems for a hospital where patients also are clinical trials subjects, he notes.

"For our purposes, the hospital is not comfortable taking EKG results and sending these off-site without having it evaluated here because if something turns up then the hospital will need to address it," Steinert explains.

"So we go to the sponsor and say, 'We need to evaluate it here, even if we send the results off, and we need to get that charge covered here,'" he says. "And sometimes, the sponsor will do it and sometimes not."

Therefore, the hospital will have to make a business decision about whether the hospital will donate the time and incur the costs to avoid having the patient suffer from something that the hospital has not discovered, Steinert says.

"We go to the investigator and coordinator and try to get that information [about central facilities] as early in the budgeting process as possible," he says. "Sometimes, it's not available until the investigator needs the test because the sponsor hasn't decided whether to use a central site."

• **Know codes and charges.**

"Our preference is for the hospital's charge code to be included in the budgeting so we know exactly what's budgeted and what the charge code is," Steinert says. "And if they've used it before, we can look it up in the database, and this saves the trouble of sending it back to accounting."

If study coordinators know the codes then the budgeting process moves very quickly, he says.

Coders rely on what was charged and the level of billing that supports it so they won't overcharge a payer or sponsor, Steinert says.

When there's a question about what the charge and code should be, the accounting department will call in coders as well as talk to investigators and the floor nurse, he adds.

"This is all done ahead of time because once the study starts we know the confidentiality requirement is done, the budget is done, everything is approved, and signing the final contract is the last piece on our end," Steinert says. ■

Clinical trials training program wins award

Coordinators, investigators offered different tracks

It started with the research nurses but soon other staff involved in clinical trials wanted to take part in the comprehensive training program being offered at The University of Texas M.D. Anderson Cancer Center in Houston. Last year, the clinical research training program received the 2003 award of excellence for best practice from the Bethesda, MD-based Health Improvement Institute.

"We did surveys and had good feedback about the education, and the question people asked was, 'Why not the faculty?'" says **Kristin Bialobok**, RN, CCRC, CCRA, director of clinical research compliance at the center. Therefore, the center proposed a faculty education program that would require people to sit in a class setting for five two-hour modules, she says.

The lecture sessions were kept small with no more than 50 people, and the educators are clinical research compliance staff, nurses, clinical trials monitors, and trials auditors, Bialobok reports.

"Each module has a competency test of 20 questions; in order to pass the module, you have to get 85% or better on the competency test," she explains. The investigator training consists of five two-hour modules, which are as follows:

- **Module 1:** Research ethics, history of the IRB, and conflict of interest.
- **Module 2:** Responsibilities of the investigator, the M.D. Anderson review and approval process.
- **Module 3:** Informed consent process, institutional research databases, and compassionate use of drugs.
- **Module 4:** FDA inspections, institutional audit process, investigational new drug (IND), and federal regulations on IND policy.
- **Module 5:** Tips for writing a protocol, source documentation, and adverse events.

More than 800 faculty members and fellows have completed the program, Bialobok notes.

The cancer center has made it a policy that new faculty members and fellows are not permitted to participate in research activities until they have documentation that they have completed their courses, she says.

"We have flags in place so if a researcher submits a protocol, and the training isn't listed as completed, then the protocol cannot go through the process," Bialobok adds.

The M.D. Anderson Cancer Center educational program has an option for investigators who think they know all the information and should not have to sit in the classroom, she says.

PIs can take a computerized version of the education session tests without attending classes, Bialobok says.

"We have the test set up so a person couldn't access any other information and either knows the answers or doesn't," she explains. "If a person chooses to take the test, but doesn't score at least 85%, then the person has to go back and take the class that corresponds to the module he or she failed."

"People who failed had to come back, and then we do one session with them, review the information they missed, and they take the test again," Bialobok says.

Since the cancer center started faculty training in September 2002, requiring all faculty to complete the test within one year or before beginning research in the case of new hires, very few have opted out by taking the test, she reports.

Future plans may include ongoing education sessions, Bialobok notes.

"We're assessing that right now," Bialobok says. "We have focus groups and needs assessment projects to see where we need to go from here: What do we perceive as the faculty's needs, and what do they perceive as their needs?"

Eventually, there probably will be an annual refresher course, but it's yet to be determined how this will work, she says.

More in-depth study available

Clinical staff training is more detailed than what the investigators receive and includes seven modules lasting a half-day each. These are broken down into the following topics:

- **Day 1:** Overview of clinical research compliance department, research team roles and responsibilities, elements of a protocol, and clinical research design.
- **Day 2:** Research ethics and history of the IRB, scientific integrity, conflict of interest, informed consent, responsibilities of the investigator, and M.D. Anderson protocol review and approval process.
- **Day 3:** Tips for writing a protocol, adverse events, compassionate use of drugs, FDA inspections, institutional audit process, FDA regulations, and INDs.

• **Day 4:** Institutional research databases, including what they are and how to use them; how to submit electronic documents, and source documentation.

• **Day 5:** Community oncology program, studies sponsored by the National Cancer Institute (NCI), differences in sponsor requirements, and tour of the investigational pharmacy.

• **Day 6:** Overview of statistics, monitors and sponsors, Clinical and Translational Research Center (CTRC), which is a place where investigational drugs are administered and which is set up to deal with protocols; chart manager system, which explains how to order charts in the institution's system; research nurse development model training, including a look at the career ladder and how it works.

• **Day 7:** Study management, research charge ticket, protocol cost analysis, contract budgets, and outpatient documentation.

Since word has spread of the cancer center's comprehensive training program, there have been calls from institutions around the world to learn more about it, Bialobok notes.

"We've had people from Japan and China who were here and wanted to know how to set up programs similar to what we have at M.D. Anderson Cancer Center," she says. ■

The trickledown theory works here

Coordinators train investigators

Research program administrators often find that it's difficult to convince investigators to attend voluntary education courses, but this doesn't mean that institutions should give up on educating researchers. At least one institution has found a way to indirectly teach and update investigators about clinical trials rules, regulations, and processes.

The research training and education program at Baylor Research Institute in Dallas focuses on teaching clinical trials coordinators, who are then expected to go back to their studies and use their new knowledge to better inform their principal investigators.

"I think that many sites, including ours, struggled with how to get investigators to these training programs," says **Betsy Stein**, CCRC, director of clinical research. "I realized this year that the most effective tool we have in educating our investigators and doing quality research here is by investing in our research coordinators."

After coordinators attend the classes, they'll talk about it with investigators, and because research coordinators and investigators form a close team, this is an efficient and effective way to teach investigators, she adds.

"By investing in coordinators we ultimately are investing in our investigators," Stein explains. "They pass the information on in a way that ultimately teaches our investigators without their having to sit in a class."

The research coordinators are the ones who may have the greatest affect on research quality, she notes.

When the Baylor program began, it offered a two-day good clinical practice (GCP) course twice a year, Stein notes.

"The first time we offered it we taught the fundamentals, and that was meant to be applicable to new coordinators and experienced staff," she explains. "The next year, we offered a GCP course that takes it to the next level, building on the education we're providing."

Now that the institute is in its third year of the revamped education program, there is a fundamentals course offered in the fall and an advanced GCP course in the spring, Stein reports.

Course topics include guidance on developing study budgets and research billing compliance, and there is a monthly research coordinator meeting, she adds.

A new goal is to offer shorter programs that can be held in the morning or at lunch-time or in the afternoon, so if a clinical coordinator is busy doing rounds in the morning, he or she will have a more convenient time available for attending a class, says **Elizabeth Cothran**, MS, CIP, director of the office of research subjects protection.

The educational courses also offer continuing education credits so licensed staff may use these to maintain their licenses and certifications, Stein notes. "The offering of educational credits is a big incentive and it's very appreciated, especially since some programs are fairly long," she says.

In all, coordinators attend three coordinator meetings in one quarter, averaging about eight hours, Stein says.

Staff feedback evaluations confirm that participants feel the GCP training is the most important educational program provided by the institution, she says.

Professional medical trial trainers teach the courses, and this gives the program credibility in the eyes of experienced study coordinators, Stein adds.

"The people we have teach a course like that have been research nurses in the past and have worked as a monitor, and they bring a rounded experience with them that coordinators relate to," she says.

Boning up on AE reporting

"One of the most popular sessions is on adverse event [AE] reporting," Cothran says.

The adverse event reporting session covers reporting requirements, evaluating AEs, timelines for reporting, the role of monitors and sponsors, and how AE reporting impacts drug labels, she explains.

"In the drug approval process, the labeling that shows up as possible side effects in the *Physician's Desk Reference* come from adverse event reports made during the clinical trial, including things reported as possibly and probably related to the drug," Cothran says. "It's important for investigators to really evaluate the event and relationship to the study drug because that will have long-term implications for labeling on a product."

The AE session stresses how principal investigators are chosen by the sponsor for their expertise, including their judgment about whether a particular symptom is related or not to a study drug, Stein says.

"If you write down that everything is possibly related, then that kicks into a 'Yes,' and that can result in some bizarre things being attributed to a side effect," she notes. "One example we use in class is how a drug label says a drug causes menstrual cramps when it really doesn't."

While it's the PI's responsibility to make certain AE reporting is fair and accurate, it's the research nurses' responsibility to complete the case report forms as clearly and accurately as possible, Stein adds.

Several times a year, the institute offers a budget writing course as either a refresher or training session that is conducted with the manager of the grants and contracts department, she reports.

The two-hour class includes a presentation piece that discusses the kinds of items that need to be taken into account during the creation of a study budget, including hidden costs. The class also offers research coordinators a look at tools that are available for developing a budget and the in-class use of a budget template for practice, Stein says.

"We have an Excel spreadsheet custom-designed for our site, and we have a sample budget with numbers they can put into the budget template," Stein explains. "They learn how to move through the template and enter data."

A separate course on research billing compliance covers best practices to ensure correct and

accurate billing so that all items included in the study budget are done only for research purposes and are appropriately billed only to the research study and not to the patient's insurer, Stein says.

"This is a complicated process that require special training for coordinators with special forms," she says.

The institution's central billing staff assist in teaching this session, which helps study coordinators learn how the day-to-day handling of billing works and provides them an opportunity to put a face with a name, since they'll be dealing with the billing staff on a regular basis, Stein adds.

One of the new programs for study coordinators involves how to successfully complete IRB forms, Cothran says.

"This class goes through all of the IRB forms, the purpose for them, what the IRB is looking for, things we've seen that are good and bad, and what's important," she says. "I've had a lot of requests for this topic and decided to put it together as a small class, held four times before the end of the year."

So far the class has been booked each time and has received positive feedback, Cothran says.

Besides the class sessions, the institution also provides on-line training that's available at any time for investigators to receive their credentials and a CD-ROM education on topics such as shipping blood samples, Stein says.

"We try to provide a variety of educational approaches and not just classroom teaching," she says. "This is an important part of the program." ■

Software Update

Clinical trial coordinators find MIT software useful

Goal is to make software easy to integrate

[Editor's note: Clinical Trials Administrator *continues the series on clinical trials software, looking at its use, potential, and availability. The software featured in this issue is COEUS, created by the Massachusetts Institute of Technology (MIT) in Boston.]*

The nine years that have gone into developing COEUS have resulted in software that research institutions may use, modify, and improve as they seek greater efficiency in data collection for research.

"COEUS brings core data from the study proposal and starts the set-up from the award process," says **Stephen D. Dowdy**, assistant director of MIT's Office of Sponsored Programs, where COEUS was developed.

"For example, if you have a program project grant, and you need five investigators to have their own accounts to spend out of, COEUS has an award hierarchy concept that allows you to create structures and distribute money to multiple investigators and departments, and it holds it all together for you," he says.

MIT's original intent was to create COEUS for its own use, and so the first module was the awards module, Dowdy explains.

But as the module was upgraded and enhanced, word got out, and research officials from other institutions began to ask if they could purchase a license to use COEUS, he says.

MIT charges $500 for the software, which gives the user all upgrades for free, and COEUS has been licensed to about 100 institutions, Dowdy says. "We're not out to make money on it," he notes. "We're more into setting a national standard or best practice."

Since MIT has no clinical trials program, COEUS does not have a clinical trials management module but it does have about everything else an institution would need to manage research, including proposal development, an award module, an IRB module, a conflicts of interest module, a subcontract module, and a negotiation module, Dowdy reports.

The awards module includes terms, conditions, contracts and report deliverables, and the proposal development module offers assistance with creating proposals, budgeting, system interface with the grants office, and routing research through the institution for signatures, he says.

The next step is to reach an agreement with one of the largest financial software vendors to integrate COEUS with that system so institutions that already have the other system could easily meld the two products' strengths, Dowdy explains. "COEUS is not a financial system," he says. "When we get to that fine line, we say pre-award up through award management, but one of our driving principles is to not create a shadow financial system."

Research institutions that choose to use COEUS for some of their modules will need technical support, particularly if they're new to Oracle, since the COEUS database is Oracle-specific, Dowdy says.

MIT will send information technology consultants to a site if requested at a charge ranging from $90-$150 per hour, he says.

"Some schools have a really good set of technical resources available, and we can generally handle it with phone calls and e-mails when they have trouble," Dowdy says. "And some schools want a SWAT team to set it all up and running and to have the skills to maintain it afterward."

Depending on how much data need to be migrated into COEUS, the start-up time could take a week or months, he adds.

Here's a brief look at the features each module offers:

• **Proposal development:** Multiple people can access this paperless system, and if a person in another department is needed for developing a budget, this assistance can be provided interactively on-line, Dowdy says.

"Most schools have a paper routing sheet for signatures, and that's a linear, sequential process," he says. "With our routing system, the signing can all be done simultaneously if needed."

Also with the grants feature, the system will automatically send the proposal to the central office of the institution and to the granting agency when the proposal has been completed, Dowdy says.

"When you get to the end and it's approved at the central office, then it's automatically going into the federal government's computer system," he explains. "There's no re-keying of data and information."

• **Award module:** Once the proposal is funded, COEUS brings its core data to the award process.

The proposal will have all terms and conditions loaded into the system, including data on who is the sponsor's intellectual program officer, Dowdy notes.

"It also has a template; so when we get a routine NIH award, all routine research proposals have the same basic terms and conditions, so we select the NIH template and standard report with terms and conditions that are repopulated into that system for that one award," he says. "And occasionally, the sponsor may throw in an extra term requirement on one award so the template brings in the standard conditions, and you go to the screen with overrides and add in the extra requirement."

The award module also tracks all of the reports, including fiscal reports, intellectual property reports, and technical reports, listing when they're due, Dowdy says.

"If you have a final technical report due 90 days after expiration, NIH and authorities allow us to give ourselves a no-cost extension so you don't need to update all deliverables," he reports. "When you say, 'I've expanded my award for six months,' they calculate all deliverables and reporting requirements automatically."

The system also tracks cost sharing and shows the approved equipment and approved travel.

• **Subcontract module:** When the NIH awards an institution for a study, there maybe some portion of that study that the institution will farm out to another university, Dowdy says.

"So if I farm out a portion of the award to Harvard, then I become Harvard's sponsor at that point in time," he says.

The subcontract module tracks who the subcontractors are, who the principal investigator is, and the administrative contact at the other institution, Dowdy notes.

"It shows how much money we have farmed out and how much money we anticipate farming out," he says.

• **Conflict of interest module:** Institutions subject to conflict of interest regulations or their own conflict of interest rules will be able to see with this module what all relevant financial interests are for research faculty and investigators, Dowdy says.

"COEUS allows them to make disclosure and track financial entities that they are disclosing and notify appropriate people at an institution when disclosure is made, so the necessary reviews can take place to make sure there is no conflict," he says.

• **IRB module:** MIT designed this module after holding several two-day conferences in which officials with other countries participated in the design.

The module has protocols logged in and assigned to committee schedules, putting them on the agenda, Dowdy says.

After the committee meets, it will record all voting and action the committee took, generate minutes and from those it automatically generates all letters to principal investigators, including approval letters and revision letters, he says.

"It keeps track of the historic record of all correspondence generated," Dowdy says. "It handles amendments, renewals, and sends out a reminder letter automatically of 'Don't forget the protocol is going to expire next month, and you need to start the renewal process.'"

One new direction COEUS may take is into clinical trials management, but this will require funding outside of MIT, he notes.

Institutions interested in seeing COEUS improved may join a consortium in which they have input over new software design and changes to existing modules, Dowdy says.

These institutions will pay $25,000 to $50,000 for this privilege, but this seed money would be enough, possibly, to result in a clinical trials module, he says.

"Schools are becoming so heavily invested in COEUS that they want to participate at a higher level in the future," Dowdy says. "If you can only afford $500, that's great; but for $25,000 — when I hold focus sessions — you get to voice your institution's opinions, and that helps us understand how much more flexible the software has to be to be tailored to meet other schools' needs." ■

IDSA urges federal measures to spur antibiotic development

To avert a looming public health crisis with a unique set of underlying causes, Congress and the Administration, including federal public health agencies, must act quickly to reinvigorate pharmaceutical investment in antibiotic research and development (R&D). Otherwise, doctors won't have drugs to protect Americans against antibiotic-resistant infections — a rapidly growing and often-deadly problem. That is the key message of a recent report by the Infectious Diseases Society of America (IDSA). The IDSA recently presented its findings and recommendations to Congress and federal policy-makers.

While the number of drug-resistant infections continues to rise, the number of new antibiotics in the pipeline to treat these infections is drastically declining. Major pharmaceutical companies have abandoned or drastically cut back their antibiotic development efforts because of the unique challenges to making antibiotics profitable. For example, antibiotics produce a weak return on investment for manufacturers because they work so well and fast. Highlights of proposed policy and administrative actions in the report include the following:

• Establish an independent Commission to Prioritize Antimicrobial Discovery. This commission would decide which infectious pathogens to target using legislative incentives and administrative solutions.

• Create a new type of "wild-card" patent extension. A company that develops and receives approval for a priority antibiotic could extend the market exclusivity period of another FDA-approved drug as long as the company commits to invest a portion of the profits derived during the extension period back into antibiotic R&D.

• Provide tax incentives for R&D of priority antibiotics.

• Establish measured liability protections similar to those that exist for childhood vaccines.

Copies of the report *Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates A Public Health Crisis Brews* can be accessed and downloaded from the IDSA home page (www.idsociety.org). ▼

NIH to make federally funded research public

Researchers financed with government money soon will be required to provide the National Institutes of Health copies of all final version manuscripts upon acceptance for publication in scientific or medical journals.

NIH will make the manuscripts available six months after publication (or sooner if the publisher agrees) on PubMed Central (PMC), the institute's digital repository for biomedical research.

Manuscripts are defined as the author's version following modifications resulting from the peer-review process, a statement from the NIH said. That proposal applies to research funded in whole or in part by the NIH. Specifically, it

COMING IN FUTURE MONTHS

- Measuring staff productivity
- Case report form best practices
- Improve IRB submission process
- Momentum building for public clinical trials registry
- Fixing staffing problems

would include all research grants, cooperative agreements, contracts, and as well as National Research Service Award fellowships.

Since it's a proposed policy change, the NIH will accept comments for 60 days. Comments should be directed to the NIH web site: http://grants1.nih.gov/index.htm or to publicaccess@nih.gov.

The full proposal can be viewed on the *Federal Register* or the NIH web site at www.nih.gov. ■

CE/CME objectives

The CE/CME objectives for *Clinical Trials Administrator* are to help physicians and nurses be able to:

- review pertinent regulatory mandates;
- develop practical clinical trial oversight strategies;
- review best practices shared by facilities that successfully conduct clinical trials. ■

CE/CME *questions*

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

13. Studies reveal that _____ is responsible for a majority of cases where trials are behind schedule.
A. IRB review
B. Subjects enrollment
C. Data management
D. None of the above

14. Recent studies found that the average cost to develop a new drug is between:
A. $100 million to $400 million
B. $500 million to $800 million
C. $900 million to $1.7 billion
D. None of the above

15. Based on the education program developed by M.D. Anderson Cancer, which of the following are course topics that could be taught to clinical research coordinators but omitted from the classes that are mandatory for investigators?
A. Institutional research databases, including what they are and how to use them, how to submit electronic documents, and source documentation.
B. Community oncology program, studies sponsored by the National Cancer Institute, differences in sponsor requirements, and tour of the investigational pharmacy
C. Overview of statistics, monitors and sponsors, Clinical and Translational Research Center; chart manager system; research nurse development model training
D. All of the above

16. According to Bruce Steinert, PhD, CCRA, which of the following are best practices that can improve trial management?
A. Anticipating enrollment problems
B. Developing a pricing list
C. Knowing codes and charges
D. All of the above

Answers: 13-B; 14-C; 15-D; 16-D.