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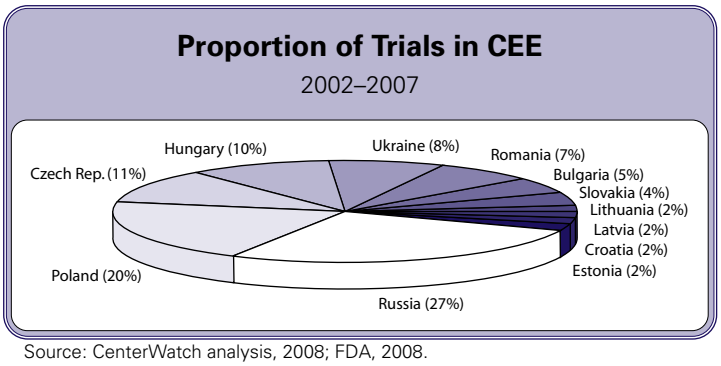
Central and Eastern Europe: Growth Opportunities, Growing Pains

Given the uneven length of global clinical trial experience in CEE countries, many industry insiders consider that the region has both emerging and "emerged" countries. Growth is expected to continue generally in the CEE region, perhaps more quickly in the largest countries, such as Russia and Ukraine.

CRO opportunities are many in Central and Eastern Europe. Global CROs made three major acquisitions between the end of October 2007 and mid April 2008, and that trend should continue. More protocols in the major centers are driving increased competition for sites and clinical research personnel and pushing CROs outside metropolitan research centers to more regional sites.



Source: CenterWatch analysis, 2008; FDA, 2008.

In Part I of CenterWatch's two-part series on Central and Eastern Europe, we discussed some of the advantages, such as patient access, that the region has to offer, as well as the challenges that remain with regard to regulatory and cultural differences. Though costs have been rising, the time savings that CEE countries can offer make the region a major contributor to global clinical development programs.

By this point it should be clear that the Central and Eastern European region cannot be treated as one bloc. Some countries are members of the EU, others are not—although they are trying to harmonize their regulations with the EU's. Cultural norms vary, different languages are spoken and political climates differ. And, as one moves west to east, clinical trial experience decreases.

Some of the CEE countries have more than a decade of global clinical research experience, such as Czech Republic and Poland, and other countries, such as Serbia, have had that history interrupted. Some CEE countries, such as Latvia and Lithuania, are newer to clinical research but offer an established, reliable clinical research environment. Still other countries are relatively new to clinical research but are growing very fast, such as Russia and Ukraine, with the promise of much more growth. Finally, there are countries, such as Belarus and other former Soviet Republics, that are just beginning to enter the clinical research market. Although Georgia, for example, has found that it is not entirely free from Russia's influence.

see CEE on page 7

No Fazing Phase I Growth

Phase I studies have become more complex as drug sponsors want critical data about their compounds to help inform decision-making and avoid expensive late-phase failures.

For CROs that offer early phase services, the future looks good. Demand for outsourced phase I work is increasing at a 13% to 15% rate, slightly higher than the 12% growth rate reported last year.

Many drug sponsors—under pressure to develop new drugs quickly and at the lowest possible cost—have focused on phase I in an effort to get more information about their drug candidates in a shorter period of time.

Phase I studies have become more complex, ask more questions and add patient volunteers earlier than in the past as drug sponsors want critical data about their compounds to help inform decision-making and to potentially avoid an expensive late-phase failure.

see Phase I on page 16

Inside this issue…

Moscow-based CRO **Synergy Research Group** forged an alliance with **Metrics Research**, a five-year-old CRO and site network organization (SMO) based in Karachi, Pakistan. The move falls in line with Synergy's mission to create an international CRO alliance network to compete with the large global CROs. Metrics, a subsidiary of the People Group of Companies, has a second office in Edmonton, Canada, and also performs ICH-GCP studies there. The company stated it is the first CRO/SMO to operate in Pakistan and works as a partner with top 10 global CROs as well as various research foundations in Canada and Italy. Synergy's alliances also include companies from the U.S., Europe, India and Ukraine.

Quintiles has teamed up with Falls Church, Va.-based **DynPort Vaccine Company** (DVC) to establish a new phase I unit in Frederick, Md.—within DVC's headquarters. Construction of the new unit stems from DynPort receiving a seven-year, $32.3 million contract from the National Institute of Allergy and Infectious Disease (NIAID) to research therapies in infectious disease. DVC will be providing the overall management and clinical operations for the trials, with Quintiles providing concurrent early stage and support services at its existing 150-bed unit in Kansas, launched in May 2007.

eClinical

Adding to **etrials**' ongoing financial woes and its recent flurry of senior management changes, Eugene "Chip" Jennings, chief executive officer (CEO) at the Morrisville, N.C.-based eClinical company unexpectedly resigned his post in July, citing family reasons. Jennings was CEO for a little more than a year, replacing John Cline, founder and former CEO, who resigned in May 2007. etrials chose its vice president of technology, Chuck Piccirillo, to temporarily replace Jennings as it goes on a "national search" for a new leader. Jennings has agreed to consult during the transition. The news follows the recent departure of James Clark, who resigned as secretary, treasurer and chief financial officer (CFO) on May 31, 2008. etrials numbers also took a hit in the second quarter, with August's Q2 earnings report showing a net loss of $2.2 million, versus a net loss of $1.3 million in the second quarter of 2007.

Homecare Management Networks

Illinois-based homecare management network company **Clinical Resource Network** (CRN) is expanding internationally into 16 European countries and Israel. The company's services have just begun to be available in some of the countries but will be available in all by the end of this year. CRN offers an in-home nursing service model to sponsors conducting clinical research. Clinicians go to the subject's home, workplace or travel destination to conduct protocol visits, making it more convenient for them to participate in a clinical trial. CRN is expanding into Austria, Bulgaria, Czech Republic, Denmark, Estonia, Germany, Hungary, Israel, Italy, Latvia, Lithuania, Poland, Romania, Slovakia, Spain, Sweden and Switzerland. The company already had a presence in the UK.

CRAcademy Offers New CRA Training Model in Europe

As most industry insiders will acknowledge, the clinical research employment market has undergone a shift—on a global scale—from being employer-driven to candidate-driven. Difficulties finding and keeping qualified clinical trials personnel in Europe and elsewhere have grown. Observers agree that the available workforce simply isn't large enough to meet staffing needs. Experienced and inexperienced professionals alike are capitalizing on the clinical research industry's staffing shortfalls.

Kieran Canisius-Engels, European Director of Clinical Research Academy (CRAcademy) headquartered in Amsterdam, The Netherlands, recognized that some of the talent shortage was being perpetuated by the industry itself.

"I realized that in order to overcome the difficulties in finding qualified staff we had to increase the flow of starters into the industry such as college graduates, nurses, etc. However, we found the training across Europe varied greatly, and most graduates were not even aware of opportunities in clinical research. Many companies did not have a developed in-house training program in clinical research as the cost and amount of time required to train junior staff was seen as a long-term investment, and, therefore, a more attractive option was to poach staff from competitors," Canisius-Engels said.

CRAcademy grew out of the training and educational department of the staffing company DOCS International and was

see CRAcademy on page 6

CRAcademy

continued from page 5

established in 2005. A year before CRAcademy officially opened its doors, Canisius-Engels was on a mission to investigate which direction the market was headed in so that DOCS International would be ready to respond.

"Seeing that there was a shortage coming up, we wanted to provide a service where we, together with the pharmaceutical or biotech company or CRO, would train and develop starters with the right competencies and the right building blocks to become a CRA," said Canisius-Engels. In 2007, DOCS International was acquired by ICON, a top 10 global CRO headquartered in Dublin, Ireland.

Along with her colleagues, Canisius-Engels established CRAcademy's CRA Traineeship Program, which offers a unique opportunity for pharma, biotech and CRO clients to train existing or newly recruited staff in the required knowledge for their role as a CRA. The Traineeship Program offers four weeks of classroom training, during which trainees learn through simulations, lectures, assignments, workshops and role-playing the complete role of a junior CRA. Incorporated in the classroom training is the Core Knowledge Assessment, created by the Association of Clinical Research Professionals (ACRP). In order to receive a "Qualified CRA" status from CRAcademy and the ACRP, the trainee must pass all requirements and receive a passing grade on the qualification examination.

"Our training program creates the highest level of basic knowledge that trainees can get without actually carrying out the clinical research work themselves. The training is done in a safe environment where trainees can learn how to carry out the necessary tasks required without endangering people or equipment. We began to develop this particular program a year ago," Canisius-Engels said.

Since 2005, CRAcademy has partnered with the Institute of Clinical Research (ICR), which is involved in providing modules of the Traineeship.

Once trainees have completed the four-week training, and pass the Core Knowledge Assessment and Interim examination, they move on to a minimum of two-month on-the-job training program. All trainees start or return to their respective sponsor or CRO where they are coached on competency development for a minimum of 27 hours.

They then must complete the CRAcademy CRA Traineeship Workbook and undergo 20 hours of skill training, including a qualification exam review. All trainees take the qualification exam, and every successful trainee who passes the exam receives qualified CRA status from ACRP and CRAcademy. The qualified CRA will generally have the same theoretical knowledge as a certified CRA; however, the certified CRA has extensive practical experience that the qualified CRA does not. CRAcademy is one of only two companies worldwide offering an accredited CRA Traineeship program.

"My goal was to create a standard that ensured that people coming out of this program would be qualified to do the job. When you have a huge need coupled with a shortage of employees, the first response of companies tends to be to hire people and put them onto studies with limited amount of training. This poses a threat to the quality of the study and can cause risk to the safety of patients. Both quality and safety are essential in the CRA role. I am adamant that CRAcademy's name would and will always stand for high quality and global standards," Canisius-Engels said.

Lack of standards is a difficulty that Canisius runs up against in her work with DOCS International when trying to place CRAs with sponsors and CROs. There is no set criteria of knowledge and skills for the title CRA throughout the industry, which leads to problems when hiring and placing staff.

"We have many pharmaceutical and non-pharmaceutical clients who request someone with '12 months experience' irrespective of how that experience was gained, i.e., whether they've been doing data entry under the name CRA, or if they've only been working with Trial Master File for this period and have never actually been to sites," Canisius-Engels said. "They tend to rely on the CV [curriculum vitae] and the number of months worked, and they seem of the opinion that as long as they have the title CRA, they have more knowledge than that of someone with two, three or four months of experience. With our program, we can clearly specify how much knowledge they have before coming in the door and this is generally substantially more than most when they begin."

Canisius-Engels is quick to point out that, in addition to training in technical skills, the CRAcademy coaches potential CRAs in soft skills during the on-the-job portion of its traineeship program. "When we speak about 'what makes a CRA,' the feedback we receive from the industry is always related to technical skills—e.g., have they been to sites, have they done this or that? When you look at successful CRAs, it's not always the person who has the strongest scientific background but is the person who is able to communicate and motivate. I'm proud of the amount of time and energy we spend on the soft skills and on the competency side of the training because I think that it is every bit as important as the technical and the skill side."

CRAcademy has ambitious plans for growth. It has just completed a project for DOCS International with Canisius-Engels

hiring 20 trainees who went through the four-week program and were selected for clients prior to starting their on-the-job portion of the training. DOCS want to do more of this type of work to substantially increase the pool of qualified CRAs across Europe.

In addition, CRAcademy is in discussions with various clients about their CRA needs as they open offices in different countries. "Their requirements go from zero to needing a substantial team yesterday. At the moment, the amount of experience and knowledge a CRA with two years experience has can vary greatly, so it's more comforting for a client to know exactly the extent of knowledge and skill set a CRA has. We are discussing the use of CRAcademy traineeships with various clients in order to create a project team of CRAs who are also trained in client SOPs, indication areas and protocol-specific training," Canisius-Engels said.

The Qualified CRA status denotes a minimum standard of knowledge, but CRAcademy also offers a full service to companies who may wish to add training, such as more company visits or more knowledge on a specific topic or indication.

Up until recently, CRAcademy offered its training programs primarily in Europe. Becoming part of ICON allowed the expansion of the staffing division into the U.S. and provides the opportunity to offer the CRAcademy training model to the U.S. as well.

"Whilst local laws vary from one country to another, the traineeship is standardized. This is a transferable program because I believe that the qualification and the skills for the CRA role should be of a high minimum standard in every country. The standardization of CRA training is a goal which we strive for, but we still have a way to go," Canisius-Engels said,

—Sara Gambrill

CEE

continued from page 1

With so many countries, the CEE region as a whole is impossible to put into one category that encompasses all its variations. It is perhaps because the biopharmaceutical company sponsors and contract research organizations (CROs) have recognized this fact that CEE participation in clinical trials has been able to grow as much as it has.

Given that experience with global clinical research is much longer in countries that border Western Europe than those that are farther east, is it correct to consider every country in the Central and Eastern European region as emerging? The answer from industry insiders from both the West and the East is an emphatic "no."

"Although we think of CEE as one region for obvious reasons, there are differences within the region and in particular, Poland now is, to me, much closer to Western Europe than emerging. Poland has now well and truly emerged. It's not emerging anymore, whilst Ukraine, for example, is still very much an emerging geography," said Nermeen Varawalla, M.D., DPhil (Oxon), MBA, vice president Scientific and Medical Affairs, PRA International. "Having said that, I would say there are parts of the region, in particular Poland, to some extent Czech Republic, which have got highly experienced sites, highly experienced investigators, they have the issue of competitive clinical trials, the cost advantage is becoming small and in a way looking incredibly similar to Western Europe. But their advantage, of course, is that these are sites and investigators with experience as well as patient access … Central and Eastern Europe has been a great success in terms of going to an emerging region and developing clinical trial capabilities there and over the years accumulating high quality clinical data."

Most companies agreed that Poland and Czech Republic had many of the advantages typically associated with the West—investigators and sites with global clinical trial expertise and experience, predictable regulatory timelines, quality data—as well as advantages typically associated with emerging markets such as patient access and enthusiastic investigators. But opinions diverge somewhat from there.

"Definitely countries like the Baltics, Poland, Hungary and Czech Republic can pretty much be excluded from the definition emerging. I would rather use the definition of still being highly productive regions, but saying it's an emerging region after 15 years of good clinical research is a bit too much. Then, of course, if we want to keep talking about emerging regions, I would definitely include Bulgaria, Romania, Serbia and some of the other former Yugoslavian countries, and Ukraine. Ukraine has a lot more to give. And then, of course, the more east you go after that, it is still definitely an emerging region," said Daniel Spasic, chief executive officer of TFS Trial Form Support International.

Alexandra Zaichenko, business development manager of Outsourcing Clinical Trials (OCT), does not see Russia as an emerging country. "There's still lots of space and there are still lots of treatment-naïve patients and still lots of sites to open and lots of investigators to teach and there

see CEE on page 8