

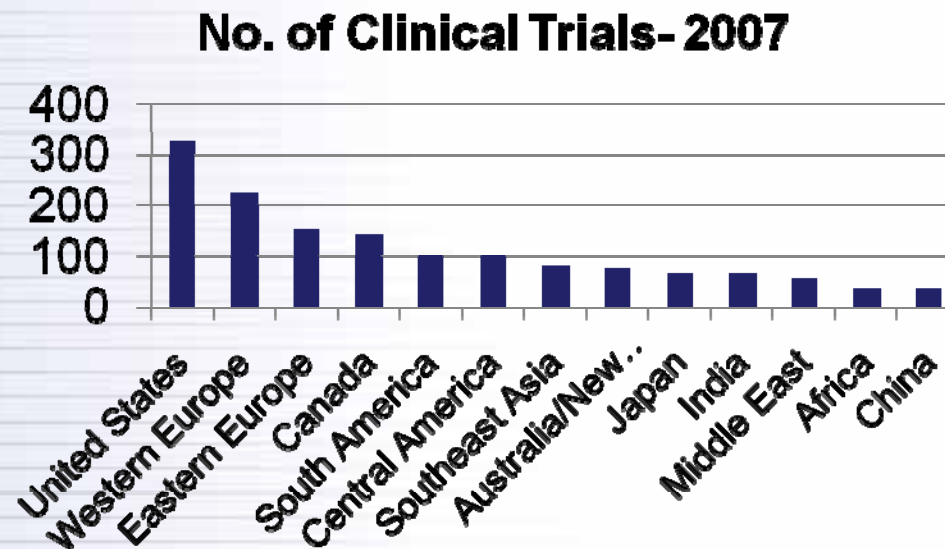
**CURRENT CLINICAL ENVIRONMENT
EASTERN EUROPE AND RUSSIA**

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Where is Development Going



- 65% of all FDA-regulated clinical trials will be conducted outside of the United States in the next three years*



* Tufts Center for the Study of Drug Development , 2010

* Figure 1- The New England Journal of Medicine, November, 2007



Why in Russia and Eastern European Countries



- Russia and Eastern Europe is one of most attractive regions to conduct clinical trials
- There has been steady and significant change in clinical research over the last 10-20 years; investigative sites in Russia and Eastern Europe have become increasingly experienced, often out-performing their European and North American counterparts in terms of enrollment and Quality

Russia	148 mil
Ukraine	49,6 mil
Poland	38,7 mil
Romania	22,3 mil
Czech Republic	10,5 mil
Belarus	10 mil
Bulgaria	7,7 mil
Other EEC	15 mil

Why in Russia and Eastern European Countries



- In general drug laws adhere to Western European standards or ICH-GCP compliance principles incorporated into legislation
- Parallel RA-EC approval
- Time-to-approval is consistent with approval times ranging from 60 to 90 days, depending on the country.
- Clinical trials are performed only in approved and licensed by MoH sites
- Rapid start-up after approval
- Very experienced investigators, practiced at following ICH/GCP guidelines
- Huge pool of subjects in investigators' databases
- High recruitment and low drop-out rate

Number of approved clinical trials in Russia and Eastern European Countries



	2009	2008	2007	2006	2005
Russia	577	615	563	507	447
Ukraine	340	331	254	158	125
Romania	335	408	220	331	402
Czech Republic	269	272	287	278	254
Bulgaria	98	203	29	175	175
Poland	498	486	447	454	443

Advantages to place clinical trials in Russia and Eastern European Countries



- Centralized healthcare system with a developed referral network and a number of private practices. As a result - few sites are needed to get a large number of quality patients.
- Good selection of high-quality investigational sites.
- ICH-GCP compliance principles incorporated into legislation.
- High recruitment rates with low drop-out rates: A patient recruitment rate in the region can be up to 10 times higher than in US and EU, depending on the indication.
- Savings in costs: Average cost per patient in Eastern Europe is 28% lower than in Western Europe and 47% than in the UK. Gives strong incentive to reduce clinical trial expenditure by using local CROs and labs.
- High level of qualification and continuing education of investigators for conducting clinical trials. As a result the quality of clinical trial data is high.
- Logistic issues continue to improve as the growth of clinical research spreads across the region

High Recruitment Rate



- Russia and Eastern European Countries use centralized healthcare system
- Free of charge treatment guaranteed by the different Country constitutions is limited and often not up-to-date
- Insurance system does not reimburse 100% of medications
- Low rate of migration and relocation
- For some diseases a trial will be the only way to get modern diagnostic procedures and potentially effective treatment
- Huge pool of drug naïve patients
- Governmental funded programs for certain types of diseases (e.g., cancer, HIV, tuberculosis, and cystic fibrosis) do not cover the needs of the whole population
- A number of clinical trials includes Post Trials Programs

Approved clinical trials (%) for the last 5 years

Russia



(selected therapeutic areas)

Therapeutic areas	2009	2008	2007	2006	2005
Oncology	18	15	17	19	17
Circulatory System	11	14	17	16	14
CNS and Musculoskeletal system	13, part of them are included in other studies	17, part of them are included in other studies	14	15	17
Infection Diseases	Not exact percentage, as most of them are included in other studies	8	7	9	11
Respiratory System	11	10	6	5	Not exact percentage, as most of them are included in other studies
Gastroenterology	Not exact percentage, as most of them are included in other studies	Not exact percentage, as most of them are included in other studies	5	6	8
Others	35	27	24	22	24

Russia-Challenges



Approvals could be contested and possibly refused for the following:

- Clinical Trials for medical devices and equipment
- Clinical Trials with the aim to evaluate features for the definitive medication
- Clinical Trials with vulnerable groups of patients:
 - Under-aged
 - Military servicemen
 - Convicted subjects
 - Pregnant women

Clinical Trials in Ukraine



- Clinical trials in Ukraine have started since 1996 when GCP standards have been adopted
- Average number of approved by MoH research sites-460
- Number of approved Clinical Trials:
 - year 2009-340
 - year 2006-158
 - year 2005-125
- Strong experience of Clinical Trials in:
 - Oncology
 - Cardiology and Circulatory System
 - Endocrinology
 - Gastroenterology
 - CNS

Ukraine - Challenges



- Immunology – lack of regulations;
- Gene therapy – not limited RA approval process duration, lack of experienced sites;
- Biological medicines – lack of regulations;
- Radiology – lack of regulations, extremely difficult import of the IMP

Russian and Ukraine Audit Excellence

By 2007 the FDA had performed 35 Audits in Russia and 4 Audits in the Ukraine. The results are remarkable since the difference in quality and compliance is so dramatic.

54% - No Action Indicated for Russian and Ukraine Sites

38 % - No action Indicated for US and Western European Sites

7% - Official Action Indicated for US and Western Europe Sites

2% - Official Action Indicated for Russian and Ukraine Sites

“Compared to other non - US sites, Russia is Better.”

Antoine N. El-Hage, PhD, MS - FDA Branch Chief, Good Clinical Practices II

Clinical trials in Romania



- Fourth most populated Eastern European Country
- ICH-GCP recommendations are incorporated into local legislation
- Experienced sites and investigators with GCP training
- Motivated patients

Therapeutic Areas	Registered CTs performed in Romania 1997-2010 (%)
Cancers and Other Neoplasms	12,9
Nutritional and Metabolic Diseases	8,9
Heart and Blood Diseases	7,8
Respiratory Tract (Lung and Bronchial) Diseases	7,3
CNS	7,1
Gastroenterology	4,1
Ophthalmology	0,3
Injuries, Poisonings, and Occupational Conditions	0,8
Mouth and Teeth Diseases	0,3
ENT	0,2

Approved clinical trials (%) for the last 5 years

Bulgaria



(selected therapeutic areas)

	2009	2008	2007	2006	2005
Oncology	29	31	3	16	14
CNS (Neurology and Psychiatry)	29	33	2	17	22
Endocrinology	15	17	7	6	6
Cardiology and Circulatory System	16	23	4	9	5
Gastroenterology	10	15	1	7	5
Rheumatology	13	11	1	3	6
Pulmonology	12	12	1	9	7

Bulgaria - Challenges



- Very restricted legislation for clinical trials with narcotic drugs
- Clinical trials with vulnerable patients
- Clinical trial with stem cells-no regulations
- Clinical trials in immunology
- Clinical trials in radiology

Clinical trials in the Czech Republic



- Conducted from more than 20 years
- Clinical trials are regulated by EU regulation
- Long traditions in medicine
- Experienced investigators

Therapeutic Areas	Number of CTs 2008-2010 <small>Bioequivalence and Phase I studies are not included</small>
Oncology	149
Cardiovascular	77
CNS <small>(neurology and psychiatry)</small>	97
Metabolic Disorders	55
Rheumatology	47
Ophthalmology	9
Surgery	8
Alergology	2
ENT	3
Radiodiagnostics	1

Czech Republic - Challenges

- Saturation of clinical trials in some therapeutic areas
- Clinical trials in Neonatology and Pediatric care- both parents have to sign ICFs
- Clinical trials in ENT, Radiology, Stomatology, Diagnostics-not enough motivation from patients
- Some RA/EC restrictions in approval of Clinical Trials

Clinical trials in Poland



- Good to be performed:
 - Orphan drugs
 - Anti-infective drugs
 - Antiviral drugs
 - Oncology
 - Ambulatory setting
- Some difficulties with:
 - Trials in emergency settings
 - Planned hospitalization
 - Background treatment paid by government and not by Sponsor

Poland - Challenges



- Clinical trials in Emergency setting-Not possible to receive contents in short time (les than hours), as court have to make decision on behalf of Sponsor
- Clinical trial with planned hospitalization-internal hospital organization issues
- Clinical trials in Background treatment paid by government and not by Sponsor

CONCLUSIONS



- Russia and Eastern European Countries are one of the most attractive places to conduct clinical trials
- All hot therapeutic areas are active and growing in the Region
- Gene therapy and biological medicines lack of current regulation across the region makes approval more challenging in certain countries
- ICH-GCP principles are incorporated into local legislations and refreshed at Investigator Meetings
- Well educated and GCP trained investigators
- Experience and dedicated research teams
- Highly motivated and compliant patients
- Excellent quality of data
- Potentially significant savings in cost and time

Thank You



A large, 3D-rendered red question mark is centered in the upper half of the slide. It is surrounded by several smaller, semi-transparent grey question marks of varying sizes and orientations, creating a sense of depth and focus on the central red one.

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