

Ethical aspects of clinical research in CIS countries: capacity-building in ethical review



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What is Eastern European Countries ?

Point of view - common status

- 23 countries with varying degrees of political and economical stability (“established”; “emerging”; “poor”)
- Population >500M (normally, well educated)
- Estimated Parma Sales Market > \$30Bn
(“QUINTILES”)

What are Eastern European Countries ?

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- Bulgaria
 - Croatia
 - Czech Republic
 - Estonia
 - Hungary
 - Latvia
 - Lithuania
 - Romania
 - Poland
 - Slovakia
 - Slovenia
 - Yugoslavia

CIS:

- Armenia
- Azerbaijan
- Byelorussia
- Georgia
- Kazakhstan
- Kirghizia
- Moldova
- Russia
- Tajikistan
- Ukraine
- Uzbekistan

What is the CIS?

from the point of view of self-preservation the following public processes are critical; IPA CIS (report, second part of 90s)

- **depopulation of the nation by decreasing average lifespan, increasing total mortality and able-bodied mortality, "rejuvenation" of some diseases, spread of alcoholism and drug addiction**
- **change in consumption of genetically habitual food products, decrease in food calorie content, protein and vitamin insufficiency, that limit physical conditions and capacity for work**
- **reduced accessibility of social services in conditions of miserable budgetary financing, avalanche of privatization, large-scale commercialization of establishments, which negatively influences the quality of human resources**
- **stratification of the society by income when 10% of the most well-to-do population obtain incomes more than 15 times higher than 10% of the least successful people**
- **total population in the CIS has decreased by more than 3 mil.**

What are Eastern European Countries ?

Point of view - biomedical research

- Large and compliant patient pool
- Recruitment rate is higher than in WE
- Naïve patients
- Good quality of data
- Low number of mistakes in CRF
- Adherence to study protocol/sponsors requirements
- Investigators are more motivated than their Western colleagues
- Patients are keep to participate in clinical trials more than in WE

What are Eastern European Countries?

Point of view - biomedical research

Investigators:

- High qualification
- Interest for international CT (resources, publicity, education)
- Devote more time to the trials
- Fluent in English
- National pride
- Science and innovation
- Publications

Patients:

- Confidence in doctor's recommendation
- Belief that new drug will help
- Getting a new drug free
- No money for the drug if refuse to participate
- Better medical care/attention
- Better understanding of the disease
- Better everyday life
- Altruism (to help other people)

What are Eastern European Countries ?

Point of view - biomedical research

- **“Meanwhile, the contribution of Eastern Europe to international drug development represents perhaps 100,000 CRFs per year, i.e. possibly one tenth of the world CRF production. Eastern Europe's contribution could triple until 2008 to 300,000 CRFs annually, assuming a compound annual growth of 20%. This would accelerate drug development on this planet very significantly, by shortening the enrolment period of international studies. If all studies on the critical path in a drug program would include the most productive countries in Eastern Europe, the overall duration of the program could be shortened by at least 25%. This represents an average saving of 2.5 years, or almost 1,000 days. At USD 1 million/d, the shortening of the cumulative enrolment periods of all studies on the critical path represents a saving of USD 1 billion”.**

Ethical Issues with Clinical Trials in Eastern Europe

J-P. Tassignon, EF GCP, PSI Pharma Support Inc, Belgium ,

Conference FECCIS, Almata, Kazakhstan, 26.09.2002

What are Eastern European Countries ?

Point of view - bioethics: stages of medical ethics



- **Hippocratic Ethics:** two principles of duties and behavior of doctors towards their patients: “do no harm” and “do good”, and this was **the code of professional behavior** as created by physicians themselves
- **Nuremberg Code of Medical Ethics + Declaration of Helsinki Ethics:**
compulsory ethical requirements to all scientific studies on human beings

What are Eastern European Countries ?

Point of view - bioethics



- “Are we positive that each patient really receives the aid of a quality that Europe can potentially afford and provide on the basis of up-to-date technology?” (WHO, 1980)
- “Ethical requirements are the **alpha and omega** of all 38 main objectives for the countries of the region to achieve the Health for All status”.
- “By 2000 the difference of health between countries and groups of people within a country must be reduced to at least 25 % by improving health of currently unsuccessful nations and groups.”
- “By 2000 all countries should develop mechanisms for enhancement of ethical aspect in decision-making regarding health of individuals, communities and population (ob.38)

What are Eastern European Countries ?

Point of view - bioethics



- **IMA Declaration on Promotions of Patient's Rights in Europe":** it has declared the necessity for available adequate medical and sanitary aid as one of universal human rights, and that effective and available for all economically and socially acceptable healthcare services provide a basis of public policy in this field. It was also stressed that principles of bioethics include specific liabilities of international organizations, governments, providers of healthcare services, professional associations and the whole society, and although ethical values and principles can be significantly different in various nations there are global fundamental principles of promotion of human rights and well-being.

What are Eastern European Countries ?

Point of view - bioethics

- **Ethics relaxes the inflexible law structure that can not predict and regulate all possible situations and variants in a diversity of relations within "eternal" problems of childbirth, death, disease, and suffering**
- **It is the same with medical ethics, that develops and changes with progress of medical science and practice, with the course of society's life and change of social setting. Healthcare systems and medical practices, as well as medical law and ethics have always combined two aspects. One of them reflects common features of current medicine: level of knowledge, methods of diagnostics and treatment, psychology and psychotherapy. The other responds to details of political and economical structure of the society, social status and inequality of people, regulations of payments for medical aid, etc. But if the first aspect is an all-human value and is inherited from one epoch to another, from country to country, the second one develops as a result of controversial struggle of political ideas and social doctrines**



Setting up of Ethics Committees in EE

- **Ethics without Ethics Committees**
- **Ethics Committees**
- **Ethics Committees with Ethics**



Establishment of Ethics Committees in EE (influence and features)

- Before ICH GCP
- ICH GCP
- WHO, CIOMS
- Nordic Council on Medicine
- European Forum for Good Clinical Practice
- Council of Europe
- Influence of the EU Directive 2001/20/EC
- Strategic Initiative for Developing Capacity in Ethical Review (SIDCER)



Establishment of Ethics Committees in EE

Before ICH GCP: (by cause)

- Local ethics committees (in research with volunteers)
- “Decorative” local ethics committees for pharmaceutical company's requirements



Establishment of Ethics Committees in EE

ICH GCP (in compliance with GCP):

- Local EC in international CT
- Training courses (in sites) initiated by the Pharmaceutical Industry
- Adaptation ICH GCP in countries

*Example: Double standard inside the countries
for domestic and foreign products*



Establishment of Ethics Committees in EE

WHO, CIOMS:

- Contribution from theoretical p.v
- Education for specialist in ethics
- Guidelines, requirements
- International discussion

*Example: no translation in Russian
before 1997*



Establishment of Ethics Committees in EE

Nordic Council on Medicine:

- **Regional training-education courses**
- **Establishment the national system of ethical evaluation in Baltic States**
- **Setting up of NEC in Baltic States**

Example: every year training courses for members of EC from BS and NWR , scholarships, beginning 1990s, Congress GCP in Russia and BS, 1997, first regional workshop for members of EC in Russia and BS, 1998, together with the EFGCP



Establishment Ethics Committees in EE

European Forum for Good Clinical Practice

- Involving the representatives from EE in European process from theoretical and practical p.v.
- Systematic approach (ethics in GCP)
- Systematic approach (education, training, evaluation, discussion, analysis)
- Professional approach

Example: first agreement for establishment the system for EC and ethical evaluation, signed with NEC of RMA in 1998, Congress GCP in Russia and BS, 1997, first regional workshop for members of EC in Russia and BS.1998, together with NCM



Establishment of Ethics Committees in EE

Council of Europe

- **Intergovernmental discussion**
- **Interparliamentary discussion**
- **Legal influence**

*Example: ratification of the Council of Europe's
Convention on Human Rights and Biomedicine.
The document becomes a part of national
legislation, e.g., Georgia*



Establishment of Ethical Review Systems in EE

Strategic Initiative for Developing Capacity in Ethical Review (SIDCER)

- International network with regional actions
- Globalization
- SOPs for the establishment of international, national, regional, and local ECs
- Combination the values of ethics and the establishment of ethical review systems

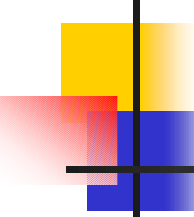
Examples: FECCIS, FERCAP, PABIN, FLACEIS, FOCUS

Why We Needed the Harmonization of Ethical Review in the CIS



- interest and ability CIS's health-care system to participate in international clinical trials (CT)
- interest and motivation of European researchers and drug industry to involve CIS's health-care system in multi-centre CTs
- closed collaboration and integration inside of CIS's health-care system
- community of legal and regulatory procedures
- social and psychological community
- absence of ethical review system in some CIS

Example: FECCIS



Why We Needed the Harmonization of Ethical Review Systems in the CIS

- absence of ECs in some institutions conducting research
- heterogeneity in EC systems and procedures
- heterogeneity in composition of ECs
- lack of transparency and independence
- lack of resources
- lack of monitoring/follow-up systems
- lack of archiving system
- problems with informed consent
- inadequate training of EC members

Example: FECCIS



INTRODUCTION of FECCIS

- *The Forum for Members of Ethics Committees in the CIS (FECCIS) was established at a Workshop on Ethical Review in Russia & the CIS held on 19-21 March 2001 in St. Petersburg, Russia.*
- *Representatives from 11 CIS's states participated in this Workshop.*
- *The practical work of the Forum is formed according to several objectives*

Example: FECCIS



Objectives of FECCIS - The Strategic Plan

- **Establishment of the System of Ethical Review of Biomedical Research on different levels**
- **Distribution to ERC in the CIS of «The Operational Guidelines for Ethics Committees That Review Biomedical Research » (WHO, Geneva, 2000)**
- **Establishment of the education programm in research ethics**
- **Developing Capacity in National Institutions for Supporting Ethical Review**

Example: FECCIS



Establishment of the System of Ethical Review of Biomedical Research on all levels

- ❖ **International System :**
Registration of Forum in the status of Observer of the Permanent Commission on the Human Rights of the Inter-Parlamentary Assembly of the CIS -IPA CIS and model law of bioethics
- ❖ **National System:**
Support in organisation and creation of the system of the National ERC in the CIS
- ❖ **Regional and Local System:**
Training the members of ERC, collaboration with national ERC.

Example: FECCIS



FECCIS as a Observer to the Permanent Commission on Human Rights of the Inter-Parliamentary Assembly of the CIS

- ❖ To guarantee the protection of human rights in healthcare the model laws for the CIS (11 laws currently on healthcare);
- ❖ To create a model law for the protection of human rights in biomedical research

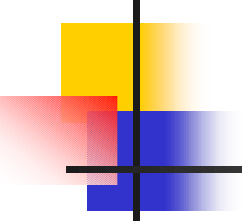
Example: FECCIS

Distribution to ERC in the CIS of « The Operational Guidelines for Ethics Committees that Review Biomedical Research » (WHO, Geneva, 2000)

- **Saint-Petersburg, Russia**
18-20 March 2001 **x**
- **Kyiv, Ukraine**
20-21 September 2001 **x**
- **Almata, Kazakhstan**
26-28 September 2002 **x**
- **Minsk, Byelorussia, planned for 2003-2004**

Example: FECCIS





Distribution to ERC in the CIS «The Guideline for Surveying and Evaluating Ethical Review Practices» (WHO, Geneva, 2002)

- Translation the guideline -08.2002
- Introduce & distribute for CIS representatives on workshop in Alma-Ata, Kazakhstan, 26-28.09 2002;
- Education course «The Guideline for Surveying and Evaluating Ethical Review Practices» in 2003

Example: FECCIS



Collaboration between FORA

To participate in the **international and regional discussions** on research ethics and in the development and harmonization of research ethics guidelines and procedures

To establish **communications networks** among and between various fora that foster collaborative interactions in order to provide a framework for mutual learning and understanding

Examples: FECCIS, FERCAP, PABIN, FLACEIS, FOCUS



Collaboration between FORA

Promoting the highest ethical and scientific standards for biomedical and behavioral research for all people all over the world

Ensuring the quality and effectiveness of ethical review worldwide following the understanding and respect for cultural, regional and national differences

Examples: FECCIS, FERCAP, PABIN, FLACEIS, FOCUS



Collaboration between West and East Europe

- *A European contribution to capacity-building in ethical review*
- Strengthening, **carrying out surveys of opinion of research subjects**, visitations of the research sites, education and training of researchers and ethics committees' members as well as education of the general public could be regarded as the most important areas of activity in the field of ethical supervision of biomedical research
- Promoted development and systematization in XXI century the main principles of bioethics which included not only such principle as "do no harm", "do good", but also the principles of equality, freedom, justice, duty, goodness, humanity



PARTNERSHIP BETWEEN ECs in EUROPE

Ethical values are global principles for the promotion of the dignity, human rights, and well-being of persons.

PARTNERSHIP in Ethics must be Fruitful

West Europe

East Europe

