NEW REGULATORY LANDSCAPE FOR CLINICAL TRIALS IN RUSSIA

Ramil Abdrachitov
Clinical Research Director
Topics to be covered

- Main change
- Previous status
- Organizational changes
- Changed requirements
- Document flow and timelines
- Patients’ insurance
- Changes in import regulations
- Transition period history
- Impact of changes
Main change

Clinical trials in Russia are mandatory for drug registration in the country

Consequence

• Russia must participate at least in phase III international studies
• Registration of drugs with already finished phase III (without Russia) is under the question
• Potential increase of CTs in Russia
Previous status of regulatory bodies

- Ministry of Health Care and Social Development (regulations)
  - Accreditation of medical institutions
  - Supervision of clinical trials
  - Inspections in clinics
  - Approval of clinical trials
  - Information services related to clinical trials
  - Relations with medical community

- National Ethics Committee
  - Ethics supervision of clinical trials

- Federal Service for Supervision in Health Care and Social Sphere
  - Review of study documents

- Scientific Center of Expertise of Medicines and Medical Devices
  - Medical institutions
    - GCP compliance
    - Clinical trials reports
    - Local ethics committees
    - SAE reporting
Current status of regulatory bodies

Ministry of Health Care and Social Development
- Accreditation of medical institutions
- Approval of clinical trials
- Information services related to clinical trials
- Relations with medical community

Federal Service for Supervision in Health Care and Social Sphere
- Supervision of clinical trials
- Inspections in clinics
- Pharmacovigilance

National Ethics Council
- Ethics supervision of clinical trials

Scientific Center of Expertise of Medicines and Medical Devices
- Review of study documents

Medical institutions
- GCP compliance
- Clinical trials reports
- Local ethics committees
- SAE reporting

Clinical Research Region CEEMEA
Requirements to institutions

All institutions doing CTs should undergo accreditation by MoH by 01.09.2011 on following:

- License for medical activity
- Intensive care unit if phase I studies are planned
- Presence of copies of legislative documents regarding CTs
- Compliance with GCP
- Protection of confidential information

Accreditation is valid for 5 years
List of accredited institutions is available in the Internet
Requirements to investigators

- 5-years experience in clinical trials to be a PI
- Specialization is relevant to the field of the trial
- Submitted CV (template is available) should contain following information about CT experience:
  - Protocol ID and title in Russian, phase, timelines
  - Number of regulatory approval of the CT
  - PI’s name if applicant was a co-investigator
  - Document proving participation in the study as co-investigator
- Registry of investigators will be available in the Internet
Previous process of approval

Company

- File III + NEC approval
  - Federal Service for Supervision in Health Care and Social Sphere
  - Result of expertise
  - Scientific Center of Expertise of Medicines and Medical Devices

- File I
  - National Ethics Committee

- File II
  - NEC approval

STUDY APPROVAL
Current process of approval

- Ministry of Health and Social Development
- Scientific Center of Expertise of Medicines and Medical Devices
- National Ethics Council
- Company

Study Approval

Results of expertise

NEC approval
New requirement - electronic application?

- Detailed application form on web-site of MoH
- All submitted documents should be attached
- Electronic application duplicates the paper one
- Currently is requested before the final stage of approval
Declared approval timelines

- **Company**

- **Ministry of Health and Social Development**
  - Results of expertise
  - NEC approval
  - Federal Governmental Budgetary Institution in Charge of Drug Review

- **National Ethics Council**
Patients’ insurance

- Previously – civil liability insurance (patients health, liability of investigators)
- Currently – only health and life insurance of patients
- Insurance tariffs and compensations are defined clearly
- Personalized insurance policy per each patient
- Insurance company should have a list of insured patients containing personal data:
  - Full name
  - Gender
  - Date of birth
  - Passport details
  - Place of living
# Patients’ insurance limits

<table>
<thead>
<tr>
<th>Insurance case</th>
<th>Liability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>~ 67 000 USD</td>
</tr>
<tr>
<td>I status of disability</td>
<td>~ 50 000 USD</td>
</tr>
<tr>
<td>II status of disability</td>
<td>~ 33 000 USD</td>
</tr>
<tr>
<td>III status of disability</td>
<td>~ 16 700 USD</td>
</tr>
<tr>
<td>Damage without disability</td>
<td>~ 10 000 USD</td>
</tr>
</tbody>
</table>
## Patients’ insurance tariffs

<table>
<thead>
<tr>
<th>Study phase</th>
<th>Tariff per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>~ 327 USD</td>
</tr>
<tr>
<td>Phase II</td>
<td>~ 127 USD</td>
</tr>
<tr>
<td>Phase III</td>
<td>~ 65 USD</td>
</tr>
<tr>
<td>Phase IV</td>
<td>~ 48 USD</td>
</tr>
</tbody>
</table>
# Patients’ insurance coefficients

<table>
<thead>
<tr>
<th># of patients enrolled</th>
<th>Tariff coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50</td>
<td>1</td>
</tr>
<tr>
<td>50-100</td>
<td>0.95</td>
</tr>
<tr>
<td>101-200</td>
<td>0.9</td>
</tr>
<tr>
<td>201-400</td>
<td>0.85</td>
</tr>
<tr>
<td>401-600</td>
<td>0.8</td>
</tr>
<tr>
<td>601-800</td>
<td>0.75</td>
</tr>
<tr>
<td>&gt;800</td>
<td>0.7</td>
</tr>
</tbody>
</table>
Price of patient’s insurance

Price = Coefficient * Tariff per pt * # of pts

E.g. for phase II study with 110 pts

Price = 0.9 * 127 * 110 = $12 573
Import of study drug

- Previously import license from Roszdravnadzor was valid for both kinds of study drug (not registered and registered)
- Currently MoH issues import license for not registered drug only
- Registered study drug should be imported on license from Ministry of Industry and Trade
- Result – problems with import of registered drugs for clinical trials
- MoH is initiating the amendment of the Government Decree in order to solve this problem
Transition period history

# of CTs approved

90
80
70
60
50
40
30
20
10
0
Transition period history

- MoH was supposed to issue approvals since 01.09.2010
- First approval from MoH 12.11.2010
- 102 approvals for 5 months, with signs of speeding up
- Refusals on formal reasons requiring submission of additional documents
- Time of paperwork is much higher than declared timelines
Negative results

• Problems with import of study drug registered in Russia
• Increased cost and administrative burden related to insurance of patients
• Potential additional data privacy considerations
• Requirement of 5 years CT experience limits number of potential PIs
• All institutions should be re-accredited by 1 September 2011
Positive results

- Declared approval timelines look very promising
- Applicant interacts only with MoH instead of separate interactions with 3 bodies
- Clear and standardized requirements to insurance of patients
- More information will be publicly available (trials, institutions, investigators)
- Document flow became more transparent
Major areas of risk for 2011

• Unsettled regulations regarding import of study drug
• Decreased quantity of available study sites as a combination of:
  • Accreditation of institutions by 01.09.2011
  • Increased requirements to PI’s experience
Conclusion

- CTs in Russia now are mandatory for drug registration
- Re-organization of RA caused significant drop in number of approved CTs in 2010-11
- Approval process is not settled yet to declared timelines but with positive signs
- Some amendments to the legislation are still to be made