STANDARD SUMMARY PROJECT FICHE - TRANSITION FACILITY

1. Basic Information
   1.1 CRIS Number: 2005/017/518.02.05
   1.2 Title: Strengthening of expert capacity in the State Institute for Drug Control (SUKL)
   1.3 Sector: Internal Market
   1.4 Location: Czech Republic

2. Objectives
   2.1 Overall Objective(s):
      Ability to assume the full scope of obligations of EU membership in the area of evaluation of human
      medicinal products and surveillance of medical devices and human tissues and cells; implementation of
      new/revised Community legislation related to the regulation of medicinal products for human use, human
      cells and tissues and medical devices.
   2.2 Project purpose:
      Building of sufficient in-house expert capacity and network of co-operating experts to enable SUKL
      play an active role in the EU regulatory system in full compliance with acquis communautaire,
      including ability to provide experts to the European network and act in line with planned regulatory
      activities of EMEA (Road map) and competent authorities of other MS and set up the infrastructure for
      surveillance in the area of tissues and cells and medical devices.
   2.3 Justification:
      The need to complete preparation for application of both the centralised and decentralised authorisation
      procedures for medicinal products has been identified in CMR 2003 (Chapter 1. Free movement of
      goods, pp16-17: “In the area of pharmaceuticals, the Czech Republic has not yet completed the revision
      of marketing authorisations nor preparations for the application of EU centralised procedure and mutual
      recognition of national authorisations. The Czech Republic is carrying out improvements to
      implementation on a continuous basis, but particular attention should be paid to medicinal products and
      cosmetics.”)
      The recommendation to strengthen in-house capacity for clinical assessment in order to comply with the
      tight timelines demanded by the EU regulatory system is one of the outcomes of the twinning project
      no. CZ01/IB/OT-03 (CZ01.04.03) “Strengthening market surveillance of medicinal products for human
      use, including alignment of authorisation conditions with EU practice”. (Final Report Chapter 5
      Evaluation - Peer review: The lack of dedicated clinical assessor team in house was identified as a
      weakness, although it was noted that there are already experienced clinically qualified people currently
      in house who could take over some of these duties if their current work could be offloaded to
      administrative “case managers”; Final Report Chapter 6 – Conclusion and Recommendations,
      Component 1 (Marketing Authorisations): “The proposed re-organisation of the Registration Branch
      should be implemented as soon as is practical upon recruitment of replacement personnel for those who
      have resigned. Consideration should be given to conducting clinical assessments in-house, particularly
      for bioequivalence and variations.”)
      There is insufficient expertise available in the Czech Republic to implement Directive 2004/23/EC on
      human tissues and cells, which is being transposed into the national legislation, and to build the
      appropriate regulatory and monitoring infrastructure.
      Growing importance of protection of public health and accent on development of new health
      technologies justify the need of additional expertise and training in vigilance and clinical trials of
      medical devices.
      Apart from the acquis communautaire listed in Annex 4 it is also necessary to take into account the
      application of the Treaty provisions on free movement of goods as interpreted by the European Court of
      Justice (ECJ). In the non-harmonised area, the case-law of the ECJ plays an important role and although
      the Czech Republic has not been involved in any case concerning medicinal products, the ECJ rulings
      relevant for all three areas covered by the project must be studied and reflected in SUKL decisions.
      Therefore, information on most relevant and recent cases referred to the ECJ is highly desirable.

3. Description
3.1 Background and justification:

After accession, the State Institute for Drug Control (SUKL) became part of the European network of National Competent Authorities (NCAs) responsible for regulation of medicinal products for human use. The regulation of medicines is included in the acquis communautaire (Directive 2001/83/EC – substantially amended during the year 2004 by the directives 2004/24/EC and 2004/27/EC, Regulation (EC) No 726/2004 etc., please see Annex 4), covering regulation at both the European and national level. Transposition and implementation of the relevant parts of the acquis, along with harmonised regulatory practice and mutual confidence in the regulatory authorities of the Member States, are essential to ensuring a satisfactory level of public health protection and free movement of medicinal products.

The State Institute for Drug Control (SUKL) is an authority of the Czech Ministry of Health and has the responsibility for regulation of human medicinal products from the point of view of quality, safety and efficacy, including market surveillance and issuing relevant authorizations/certificates. Its obligations within the EU include among others scientific evaluation performed within all kinds of marketing authorisation procedures and post-authorisation maintenance, participation in work of scientific committees of the European Medicines Agency (EMEA), surveillance of national market involving both medicines and medical devices, transposition of relevant EU legislation into national legislation and cooperation in many respects with the EMEA and NCA of other MS. Its effective operation is crucial to the successful inclusion of the Czech Republic into the EU regulatory network.

a) Strengthening expert capacity in pre-clinical and clinical assessment:
Currently, the process of granting and maintenance of marketing authorisations is hindered by lack of expert capacity for clinical assessment; this part of the assessment procedure is to a large extent ensured by external clinical experts whose work is coordinated by SUKL staff. Following the recommendation of the Twinning Project CZ01/IB/OT-03 - Final Report Chapter 6 – Conclusion and Recommendations: Component 1 (Marketing Authorisations) point 2: “A review of processes to ensure maximum efficiency should be undertaken with a view to delegating tasks to the most appropriately qualified level of staff, not necessarily the highest level of qualified staff.” - SUKL is taking steps to reorganise operations of its Marketing Authorisation Branch and recruit new staff. This should happen in order to assemble and stabilise cadre of internal clinical experts and closely cooperating external experts, which will be able to complete the necessary assessment work within the tight timelines demanded by the European Regulatory System while respecting standards defined by the EU regulations, guidelines and practices. To achieve this aim, this pool of experts will need appropriate training and mentoring by experienced trainers, similar to that provided to pharmaceutical assessors within the previous twinning project.

b) Competent supervision of quality and safety of human tissues and cells:
In April 2004, a new EU directive setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells came into force (Directive 2004/23/EC). Obligations imposed on Member States by this directive include namely setting up a system for accreditation and surveillance over establishments where procurement, processing, preservation, storage and distribution of human cells and tissues are undertaken, over preparation processes and cells and tissues vigilance. Only part of the area covered by Directive 2004/23/EC is currently subject to regulation in the Czech Republic and there is insufficient expertise available to build the necessary regulatory infrastructure. In order to meet the requirements laid down by this directive it is necessary to review the existing situation in the Czech Republic, concerning legislation and the actual state of management of human tissues and cells and tissue establishments as defined by the Directive. All aspects of quality and safety of human tissues and cells should be considered and appropriate training for inspectors, assessors and other staff involved in regulation should be provided.

c) Operation of vigilance system for medical devices and monitoring of clinical trials of medical devices:
In the area of medical devices, SUKL is responsible for investigation of adverse incidents and where necessary for taking actions, supervision of clinical trials from the point of view of compliance with relevant regulations. In order to act fully in line with EU regulatory requirements laid down by Council Directive 93/42/EEC etc. (see Annex 4) and practices these activities require review of compliance with the EU system and appropriate training to bridge the gaps identified.
3.2 Linked activities:

In 2002-2004 the State Institute for Drug Control was involved in the Twinning project no. CZ01/IB/OT-03 (CZ01.04.03) “Strengthening market surveillance of medicinal products for human use, including alignment of authorisation conditions with EU practice”.

This twinning project covered a number of areas related to the marketing authorisation process, inspection, pharmacovigilance, human resources and quality management. The current proposal is aimed to build on the outcomes of the twinning project in the area of preclinical and clinical assessment of dossiers and pharmacovigilance taking into account its recommendation to build an in-house expert capacity particularly for bioequivalency and marketing authorisation variations (Final Report, Chapter 6 – Conclusion and Recommendations: Component 1 points 1 to 4). It is also intended to reinforce and consolidate the training already delivered to SUKL staff and collaborating experts to enable the Czech Republic participate actively in the EU marketing authorisation procedures (as specified in Directive 2001/83/EC Title III, Chapter 4 Mutual recognition of authorisations, Regulation (EC) No. 726/2004, see Annex 4).

The other two parts of the proposed project cover areas that were not included in the previous project and their importance has become apparent with development of new technologies, new safety standards and adoption of new EU legislation (Directive 2004/23/EC on human tissues and cells). The achievements and outcomes of the previous twinning project justify the intention to use this instrument for strengthening SUKL expertise in the area of medical devices and human tissues and cells.

3.3 Results:

**Clinical assessment:**
- Sufficient number of assessors (internal and external) producing preclinical and clinical assessment reports compliant to the EU regulatory requirements available for the most relevant groups of medicinal products.
- Effective system enabling to train newly recruited staff the basic evaluation skills in place.
- SUKL involved in the process of creating EU guidelines and writing assessment reports to support EU evaluation procedures (e.g. “scientific advice”, referral procedure, co-rapporteurship for centralized procedure).

**Tissues and Cells:**
- Sufficient expertise available to exercise supervision over tissue establishments.
- Functional regulatory system in the area of human tissues and cells incorporated into the Institute’s QMS.
- Tissue establishments informed on legal requirements and standards of good working practices.
- Compliance of all tissue establishments in the Czech Republic as defined by Directive 2004/23/EC with requirements of the directive verified.

**Medical Devices:**
- Functional system of vigilance of medical devices in place:
  - Compliance of SUKL internal procedures and guidance documents with MEDDEV guidelines (EC guidelines for medical devices)
  - Recommendations for maintaining database of adverse incidents in format enabling information and data exchange with EU authorities incl. its compatibility with EUDAMED (European database of medical devices)
- Functional system of monitoring of clinical trials of medical devices in place.

3.4 Activities:

(1) Twinning (0,500 M €)

**RTA (Residence Twinning Advisor)**
The RTA located in SUKL for the period of 12 months, preferably an experienced assessor who will have some experience from project management; his/her responsibilities will include co-ordinating the work of short-term experts involved in the different parts of the project and delivery of training in his/her area of expertise. He/she should have experience from a similar institution in an EU
Member State, should be fluent in English (written and oral) and experienced in assessment of preclinical and clinical part of the dossier (working experience of at least five years within the partner agency), knowledgeable of EU authorisation procedures and capable of resolving logistic and management issues

**STEs (Short Term Experts)** - overall requirement apx.. 250 man-days (specified below)

Approx. 25 to 30 STE who will provide expertise in the areas specified in Logframe Matrix. With regard to the reasons specified below (3.5 Lessons learned), the beneficiary prefers short-term secondments of experts (up to 10 working days); in some cases repeated visits of one expert should be considered.

**Study trips** – 7 study trips (1 person/approx. 5 days each) – see the specification below

**Training** of the staff

**Clinical assessment:**
- Review of evaluations performed by SUKL assessors and analysis of working practices to identify areas for improvement: approx. 150 man-days will be delivered, covering both theoretical and practical parts;
- **3 study visits** (1 person/5 days each) directed at obtaining experience with daily practices of a working assessment team in the partner authority (work shadowing), esp. understanding of the management of evaluation process involving both internal and external expertise, opportunity to observe working meetings where practical issues related to various dossier assessment are discussed in order to understand the way of solving scientific problems. The number of visits reflects the need to provide training to 3 different assessors evaluating different categories of medicinal products, e.g. chemical based medicines, biological products and herbal medicines.
- Development of internal system for training and mentoring.
- Development of mechanisms for internal peer review system for assessment reports.
- Training on the application of the EC law in the non-harmonised area and study of recent rulings of the European Court of Justice (ECJ) relevant for the area of evaluation of medicinal products

**Tissues and cells**
- Review of current Czech legislation from the point of view of compatibility with EU directive 2004/23/EC. Analysis of the case law of the ECJ in the area of human tissues and cells.
- Training of 2 inspectors by means of workshops and joint inspections in CR and observed inspections/study stay in MS. Two **study visits**;
  - First visit - 1 person/5 days – observed inspection of 1-2 tissue establishments to get experience with standards of work of a well established tissue/cell facility (e.g. bone marrow and/or eye bank) and understand the way how compliance with the directive is achieved and get experience with inspection techniques
  - Second study visit – 1 person/5 days - directed at understanding of organisation of the supervision system in MS and the quality system of national competence authority.
- Setting up a system for control and accreditation of tissue establishments, drafting of internal procedures and SOPs (Standard operating procedures).

**Medical devices**

In the area of vigilance of medical devices

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1 MEDDEV 2.12-1 rev.4, Guidelines on a medical devices vigilance system: The purpose of the vigilance system is to improve protection of health and safety of patients, users and others by reducing the likelihood of the same type of adverse incidents being repeated in different places at different times. This is to be achieved by evaluation of reported adverse incidents and, where appropriate, dissemination of information, which could be used to prevent such repetitions or to alleviate the consequences of such incidents.
• Review of current Czech legislation in force from the point of view of compatibility with EU legislation. Review of the EC legislation in the non-harmonised area and analyses of the impact of the ECJ rulings in the area of medical devices and study of most relevant recent cases.
• Review of current SUKL internal procedures and working practices and recommendations for improvement.
• Review of 10-20 cases of adverse incidents investigated by SUKL staff.
• Training of staff (approx. 5 people) in approx. 10 workshops and joint inspections
• 1 study visit (1 person/5 days), to obtain practical experience with daily working practices in the partner authority directed at understanding the MD (Medical Device) vigilance system and in-site investigation of adverse incidents.
• Analysing of the existing databases of medical devices and adverse incidents taking account of experience of other Member States and providing recommendations for improvement.

In the area of monitoring of Clinical Trials:
• Review of current Czech legislation for clinical trials (Act no. 123/2000 Coll., and implementation regulations) from the point of view of compatibility with Directive 93/42/EEC. Impact of the ECJ rulings in the area of clinical trials of medical devices and study of most relevant recent cases
• Training of 2 inspectors in the area of control of clinical trials of medical devices in the CR
• 1 study visit (1 person/5 days), to obtain practical experience with daily working practices in the partner authority directed at preparation and conduct of inspection at trial site

3.5 Lessons learned:

In the course of the previous twinning project CZ01/IB/OT-03 (CZ01.04.03) “Strengthening market surveillance of medicinal products for human use, including alignment of authorisation conditions with EU practice” it became apparent that the original structure of the Covenant where medium term experts were present for up to 12 weeks would have not achieved all the desired results. The SUKL staff were unable to make the necessary time available for this type of delivery because it would have compromised their ability to maintain the core business. As a consequence, the Covenant had to be revised to increase the number of short-term expert visits (see Final Report Chapter 3 Background and 3rd Q Report Twining Activities point 4.: The additional flexibility introduced into the project by shortening the placement time of MCA Experts in Prague has proved to be effective in managing expert resource both from the point of view of MHRA (Medicines and Health Care Products Regulatory Agency) managers, who have to provide the resource and from the viewpoint of SUKL staff who have to assimilate the training whilst continuing to maintain their core responsibilities).

Therefore, the proposed project relies on the delivery of training in short time periods (one or two-week visits) with a period of consolidation and then further training to reinforce what had been developed, rather than long-term secondments of MTEs which has proved to be an excessive overload both for the beneficiary and the twinning partner. Attention should be paid to careful planning and regular review of what has been achieved, as well as ensuring continuous support from the SUKL top management. Management of training should be adjusted to cover also practical problems the trainees deal with in normal daily activities. From this point of view using mentoring techniques to provide the trainees skills to deal with practical problems and situations is highly desirable.

The role of twinning adviser and regular meetings of the steering committee proved to be very important for the successful completion of the project. Following recommendations of the previous project SUKL has started restructuring of its Marketing Authorisation branch and takes steps to improve quality management and company culture. Together with increasing ability of SUKL (based on new possibility to cover the costs of selected regulatory activities from fees charged to applicants the introduction of which was supported also by the outcomes of the previous project) to improve working conditions and attract highly qualified staff these provisions should help maintain the staff trained during the project and contribute to sustainability of its results.

4. Institutional Framework

The Ministry of Health (MoH) is responsible for the legislation related to the public health. The Act No. 2/1969 on establishment of ministries and central bodies of state administration, § 10, section 1) defines MoH as a central body of state administration in the protection of public health.
The final beneficiary of the project is the **State Institute for Drug Control (SUKL)**, the Czech national authority responsible for regulation of medicinal products for human use. The institutional framework will not change during the project and there is no intention that the project would lead to a change in the institutional framework. No constraints are identified in this respect.

The Steering Committee will be set up in which a CFA representative will participate. The SC will meet every three months to supervise the implementation of the project. Day-to-day running of the project will be managed by the RTA and Czech Project Manager in cooperation with Component Leaders. Regular reports on the project progress will be submitted by the MS and BC Project Leaders to the CFCU. The Czech Project Leader will be Dr Milan Šmíd, PhD, the Director of SUKL.

## 5. Detailed Budget (in M€)

<table>
<thead>
<tr>
<th>€M</th>
<th>Transition Facility support</th>
<th>Co-financing</th>
<th>Total cost (TF plus cofinancing)</th>
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<tr>
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<td>Investment Support</td>
<td>Institution Building</td>
<td>Total Transition Facility (=I+IB)</td>
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<td>year 2005</td>
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<td>Twinning contract</td>
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<tr>
<td>Total</td>
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## 6. Implementation Arrangements

### 6.1 Implementing Agency

The Central Finance and Contracts Unit (CFCU) is the Implementing Agency responsible for administrative and financial implementation of the project (tendering, contracting, disbursement). The contact person is **Mr. Jan Slavíček**, Programme Authoring Officer (PAO), Ministry of Finance, Letenská 15, 118 10 Prague 1, phone +420-2-5704-4550, e-mail: jan.slavicek@mfcr.cz.

The CFA is fully responsible for overall monitoring and evaluation of project implementation. Main Contract – Ms Jana Hendrichová – Director of CFA, Ministry of Finance, Letenská 15, 118 10 Prague 1, phone +420 257 044 59, e-mail: jana.hendrichova@mfcr.cz.

Responsibility for technical aspects related to the preparation, implementation and control will rest with the beneficiary institution the State Institute for Drug Control (SUKL) (for address, see bellow point 6.2.), and will be co-ordinated by the Ministry of Health, MUDr. Katerina Ciharová, SPO, Palackého nám. 4, 128 01 Prague 2, Czech Republic, tel. 224 972 140, e-mail: katerina.ciharova@mzcr.cz.

### 6.2 Twinning

State Institute for Drug Control, Šrobárova 48, 100 41 Prague 10, Czech Republic

Contact person: **Ms Maryna Krenková**, tel. 420 272 185 760, mail to maryna.krenkova@sukl.cz

### 6.3 Non-standard aspects

N/A

### 6.4 Contracts

| Twinning | 0.500 M € |

## 7. Implementation Schedule

7.1. Start of tendering/call for proposals 4Q/2005

7.2. Start of project activity 2Q/2006

7.3. Project Completion 2Q/2007
8. Sustainability

Experience from the previous twinning project, high level of commitment of SUKL management to the project and careful consideration that has been given to recommendations from both internal and external evaluation of the previous project justify expectations of sustainable results.

Sustainability will be ensured by elaborating Standard Operating Procedures, that will be incorporated into the Institute’s Quality Management System, training sufficient number of people who will be able to pass on experience to newly recruited staff and creating mechanisms for coaching and mentoring junior staff. Sustainability of project will be strengthened by consolidation of the network of external experts and growing involvement of both internal and external experts in the Community structures.

9. Conditionality and sequencing

The three parts of the project are not interdependent. Training can run in parallel adhering to the logical sequence of review (gap analysis), delivery, consolidation and reinforcement of knowledge, followed by evaluation of achieved results. For the pre-clinical and clinical part, prior to delivery it is necessary to complete restructuring of the relevant department, consolidate its staff and verify its functioning in practice.

As regards the area of human tissues and cells, the transposition of EU directive into national legislation has to be completed.

As for vigilance and clinical trials of medical devices, sufficient level of co-operation with other institutions participating on medical devices surveillance system (e.g. Ministry of Health) should be ensured.

All the above-mentioned conditions are achievable by the envisaged start of the project.

ANNEXES TO PROJECT FICHE

1. Logframe planning matrix
2. Detailed implementation chart
3. Contracting and disbursement schedule
4. List of relevant Laws and Regulations
## LOGFRAME PLANNING MATRIX

**Project Title:** Strengthening of expert capacity in the State Institute for Drug Control

<table>
<thead>
<tr>
<th>Overall Objective</th>
<th>Objectively verifiable indicators</th>
<th>Sources of verification</th>
</tr>
</thead>
</table>
| Ability to assume the full scope of obligations of EU membership in the area of evaluation of human medicinal products and surveillance in the area of medical devices and human cells and tissues; implementation of new/revised Community legislation related to the regulation of medicinal products for human use, human cells and tissues and medical devices. | Active involvement of SUKL in EU authorisation procedures i.e. commenting of appx. 50% of MA procedures for centralised products, acting as RMS in MRP or as rapporteur/co-rapporteur in referral procedures relevant for CR starting as of 4Q 2006. SUKL among leading NCA from new MSs as far as involvement in EU procedures is concerned. Auditable system to execute the surveillance and fulfil the obligations imposed by the directives on tissues and cells and medical devices in place in 2007. | SUKL Annual Report  
EU benchmarking self-assessment report,  
Community Tracking System  
EMEA homepage |

<table>
<thead>
<tr>
<th>Project Purpose</th>
<th>Objectively verifiable indicators</th>
<th>Sources of verification</th>
<th>Assumptions</th>
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</table>
| Building of sufficient in-house expert capacity and network of co-operating experts to enable SUKL play an active role in the EU regulatory system in full compliance with acquis communautaire, including ability to provide experts to the European network and act fully in line with planned regulatory activities of EMEA (Road Map) and competent authorities of other Member States, and set up the infrastructure for surveillance in the area of tissues and cells and medical devices. | • Availability of appropriately trained staff in defined areas (pre- and clinical assessment, tissues and cells control, vigilance and clinical trials of medical devices) at the end of the project.  
• Generation of assessment reports, which are subject to peer review (4Q 2006)  
• Compliance of tissue establishments with directive 2004/23/EC monitored.  
• Adverse incidents of medical devices systematically monitored | SUKL Annual Report, SUKL website Final Project Report  
Comprehensive report on peer review system and reviewed ARs by STE/RTA  
SUKL report on the status of compliance of tissue establishments with the standards set by Directive 2004/23/EC verified by STE/RTA | Legislative process continues as presumed Co-operation of professional bodies and MoH SUKL human, material and financial resources remain on adequate level |
and communicated to EU NCAs.

- Compliance of medical devices clinical trials systematically monitored.

Audit report prepared by joint audit group composed of STE/RTA and experienced SUKL internal auditor

<table>
<thead>
<tr>
<th>Results</th>
<th>Objectively verifiable indicators</th>
<th>Sources of verification</th>
<th>Assumptions</th>
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<tbody>
<tr>
<td>1.1 Sufficient number of assessors (internal and external) producing preclinical and clinical assessment reports compliant to the EU regulatory requirements available for the most relevant groups of medicinal products</td>
<td>1.1 Pool of 10-15 internal experts and 40 external experts trained in approx. 15 seminars aimed at assessment of preclinical and clinical part of dossier, evaluation of protocols of clinical trials; contracts on cooperation concluded with external experts</td>
<td>Final Report of the project Implementation Status Reports Interim Quarterly Reports Training records of SUKL staff Monitoring reports submitted for discussion by the SMSC twice a year</td>
<td>Staff consolidation Optimal conditions for cooperation with external experts (Equipment, communication system, suitable draft contract) Advanced level of English ensured by tailored language courses financed by the Czech side</td>
</tr>
<tr>
<td>1.2 Effective system enabling to train newly recruited staff the basic evaluation skills in place.</td>
<td>1.2 User-friendly manual for assessors drafted, system of guidance and mentoring junior staff, peer review mechanism.</td>
<td>Interim Quarterly Reports</td>
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<tr>
<td>1.3 SUKL involved in the process of creating EU guidelines and writing assessment reports to support EU evaluation procedures (e.g. “scientific advice”, referral procedure, co-rapporteurship for centralized procedure)</td>
<td>1.3 Pool of 30 internal and external experts trained who can be nominated to serve either as members of the EMEA scientific committees, of the working parties or as part of the scientific assessment teams</td>
<td>SUKL Annual Report</td>
<td></td>
</tr>
<tr>
<td>2.1 Sufficient expertise available to exercise supervision over tissue establishments</td>
<td>2.1 Three SUKL inspectors trained in workshops and observed inspections.</td>
<td>Training records, inspection reports, regular reports on project progress SUKL internal documents Implementation Status Reports Interim Quarterly Reports</td>
<td>Directive 2004/23/EC transposed into national legislation</td>
</tr>
<tr>
<td>2.2 Functional regulatory system in the area of human tissues and cells incorporated into the Institute’s QMS.</td>
<td>2.2 Proposals for improvement of working practices, SOP (Standard Operating Procedure) on inspection of tissue establishments.</td>
<td>Public information released by SUKL in SUKL Bulletin and on website</td>
<td></td>
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<tr>
<td>2.3 Tissue establishments informed on</td>
<td>2.3 Guidance document available to</td>
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</table>
### 2.4 Compliance of all tissue establishments in CR as defined by Directive 2004/23/EC, with requirements of the directive verified.

3.1 Functional system of vigilance of medical devices in place:
- Compliance of SUKL internal procedures and guidance documents with MEDDEV guidelines
- Recommendations for maintaining database of adverse incidents in format enabling information and data exchange with EU authorities incl. its compatibility with EUDAMED

3.2 Functional system of monitoring of clinical trials of medical devices in place

### Activities

<table>
<thead>
<tr>
<th>Activities</th>
<th>Means</th>
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| Clinical assessment | 1 Twinning Contract (approx. 0.500 M €)  
RTA seconded to SUKL for 12 months – 0,150 M €  
STEs – approx. 250 man-days (see below) – appr. 0,250 M €  
7 Study trips – appr. 0,010 M € (altogether)  
**Training** of the staff |

<table>
<thead>
<tr>
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<th>ASSUMPTIONS</th>
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<tr>
<td></td>
<td>Knowledge of English improved in language courses financed by the Czech side</td>
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</table>
| Objective | Clinical assessment - approx. 10-15 STEs (appr. 150 man-days) covering areas of clinical and preclinical assessment, writing Assessment Reports, evaluation of bioequivalence and risk/benefit ratio. They will cover both theoretical and practical training and development of the internal systems for training and peer review of assessment reports.  
3 study visits (1 person/appr. 5 days each) to obtain practical experience from MS daily evaluation practices for medicinal products in three therapeutic areas. |
| --- | --- |
| 1.2 Development of internal system for training and mentoring | Tissues and cells – appr. 40 man-days of STEs:  
1 STE experienced in EU legislation on human tissues and cells (appr. 5 days)  
2 STE experienced in practical aspects of human tissues and cell regulation including assessment of procedures and vigilance (appr. 20 man-days)  
2 STE experienced in inspections (10 man-days)  
1 STE who will provide advice on drafting inspection procedures (5-10 man-days)  
2 study visits, (1 person/5 days each) observed inspections of tissue establishments and understanding the organisation of supervision system and quality system in MS, |
| 1.3 Development of mechanisms for internal peer review system for assessment reports | Restructuring of registration branch completed  
Strengthening personal capacity of inspectorate (recruitment of one new inspector)  
Co-operation with relevant EU authorities  
Support from the Ministry of Health  
Cooperation with UZIS |
<table>
<thead>
<tr>
<th>Medical devices</th>
<th>Medical devices</th>
<th>Staff consolidation</th>
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<tbody>
<tr>
<td><strong>3.1 Vigilance of medical devices</strong></td>
<td><strong>3.2 Monitoring of Clinical Trials</strong></td>
<td>Ability to absorb training while maintaining core business Knowledge of English improved through tailored language courses and self-study</td>
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<tr>
<td>- Review of current Czech legislation in force from the point of view of compatibility with EU regulations. Review of the EC legislation in the non-harmonised area and analyses of the impact of the ECJ rulings in the area of medical devices and study of most relevant recent cases.</td>
<td>- Review of current Czech legislation for clinical trials from the point of view of compatibility with Directive 93/42/EEC</td>
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<td>- Review of current SUKL internal procedures and working practices and recommendations for improvement</td>
<td>- Training of 2 inspectors in the area of control of clinical trials of medical devices</td>
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<td>- Review of 10-20 cases of adverse incidents investigated by SUKL staff</td>
<td>- 1 STE experienced in developing medical devices vigilance system</td>
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<tr>
<td>- Training of staff in workshops and joint inspections, 2 study visits to get experience on working practices in partner authority</td>
<td>- 2-3 STE experienced in monitoring of clinical trials of medical devices</td>
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<tr>
<td>- Analysis of the existing databases of medical devices and adverse incidents taking account of experience of other Member States and providing recommendations for improvement</td>
<td>- 2 study visits – 1 person/5 days each, one visit aimed at obtaining practical experience from work in the partner authority and understanding the MD vigilance system and on-site investigation of adverse incidents, second study visit directed at preparation and observing an inspection at MD trial site</td>
<td></td>
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<tr>
<td><strong>3.2 Monitoring of Clinical Trials</strong></td>
<td></td>
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<tr>
<td>- Review of current Czech legislation for clinical trials from the point of view of compatibility with Directive 93/42/EEC</td>
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<tr>
<td>- Training of 2 inspectors in the area of control of clinical trials of medical devices</td>
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### Medical Devices (in the CR)

<table>
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<th>PRECONDITIONS</th>
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<table>
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<th>List of abbreviations</th>
<th>NCA</th>
<th>National Competent Authority</th>
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<tr>
<td>AR assessment report</td>
<td>QMS</td>
<td>quality management system</td>
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<tr>
<td>ECJ European Court of Justice</td>
<td>RMS</td>
<td>Reference Member State</td>
</tr>
<tr>
<td>EMEA European Medicines Agency</td>
<td>SUKL State Institute for Drug Control</td>
<td></td>
</tr>
<tr>
<td>MoH Ministry of Health</td>
<td>SOP</td>
<td>Standard Operating Procedure</td>
</tr>
<tr>
<td>MD medical devices</td>
<td>UZIS</td>
<td>Institute of Health Information and Statistics of the Czech Republic</td>
</tr>
<tr>
<td>MS Member State</td>
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<tr>
<td>MRP Mutual Recognition Procedure</td>
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**DETAILED IMPLEMENTATION CHART**

Project Title: Strengthening of expert capacity in the State Institute for Drug Control

<table>
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<tr>
<th>Year Action</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
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<td>Start of project activity</td>
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<td>Project completion</td>
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## ANNEX 3

### CONTRACTING AND DISBURSEMENT SCHEDULE

#### Cumulative Quarterly Contracting Schedule (mil. €)

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<thead>
<tr>
<th>Project Title</th>
<th>1Q/05</th>
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<th>3Q/05</th>
<th>4Q/05</th>
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<th>3Q/07</th>
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#### Cumulative Quarterly Disbursement Schedule (mil. €)

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LIST OF RELEVANT LAWS AND REGULATIONS


**Commission Regulation (EC) No 1085/2003** of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products falling within the scope of Council Regulation (EEC) No 2309/93

**Directive 2001/20/EC** of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use


**Commission Regulation (EC) No 847/2000** of 27 April 2000, laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts ‘similar medicinal product’ and ‘clinical superiority’


**MEDDEV 2.12/1 rev.4** (April 2001) Guidelines on a medical devices vigilance system

Case-law of the European Court of Justice relevant for areas covered by the project