1. **Basic Information**

1.1 CRIS Number: **2003/004-979-02.01**

1.2 **Twinning number: LV/2003/IB/EC-01**

1.3 Title: **Medicinal Products Market Surveillance and Pharmacovigilance**

1.4 Sector: Internal Market / Free Movement of Goods

1.5 Location: Republic of Latvia

   Leading institution: Ministry of Health  
   25 Baznicas iela, Riga, LV-1010

   Involved institutions:  
   State Agency of Medicines  
   15 Jersikas iela, Riga, LV-1003

   State Pharmaceutical Inspection  
   15 Jersikas iela, Riga, LV-1003

   Hospital ”Gailezers”  
   2 Hipokrata iela, Riga, LV-1038

2. **Objectives**

2.1 Overall Objective(s):

   Ensure quality, safety and efficacy of medicinal products

2.2 Project purpose:

   Development of market surveillance and pharmacovigilance system for human and veterinary medicinal products

2.3. Accession Partnership and NPAA priority

   **Accession Partnership:**

   Free movement of goods
   - Complete the process of transposition and implementation of all New Approach and sectoral legislation with the acquis; in particular as concerns food legislation, fertilisers, and the renewal of existing marketing authorisations for pharmaceuticals.
   - Reinforce national accreditation system; upgrade the national metrology system; complete the reform of the market surveillance system; designate the appropriate bodies regarding notification procedure and ensure their functioning.

   Consumers and health protection
   - Ensure the effectiveness of administrative structures involved in market surveillance.

   **NPAA:**

   LA-007 – Provide people with high-quality, effective and safe medicinal products.
   LA-032 – Complete alignment of legislation on quality, safety and hygiene of veterinary, phytosanitary, agricultural products and food and EU standards.

3. **Description**

3.1 Background and justification
The Position Paper of the Republic of Latvia (Chapter 1: "Free Movement of Goods") defines the implementation of *acquis communautaire* and institution building as the main requirements in sector of medicinal products for human use and veterinary medicinal products.

Law “On Pharmaceutical Activities” introduces the main requirements of EU Directives (2001/83/EC, 89/105/EEC, 91/356/EEC and other relevant) in the area of medicinal products for human use to the Latvian legislation. Additionally there are the relevant Regulations of the Cabinet of Ministers in Latvia (see Annex 5). The process of approximation of directives is carried out according to schedule set up by the National Integration Program into European Union.

In veterinary medicinal products field the Law "On Pharmaceutical Activities" and the Law "On Veterinary Medicine" define the main responsibilities, but there are not detailed regulations on manufacturing, marketing authorisation, labelling, and distribution of veterinary medicinal products and other relating issues.

According to conception "On Establishment of the Unitary Surveillance System for Human and Veterinary Medicinal Products” of June 17, 2002 the functions of the market surveillance of veterinary medicinal products has been transferred from the Ministry of Agriculture to the Ministry of Health and its subordinated institutions (see the division of responsibilities between the ministries in Annex 7).

The structural reorganisation in the area of medicinal products for human use has been completed and there are no problems of administrative means. In general in the sector of medicinal products for administration of medicinal products market the all-necessary institutions are established under supervision of the Ministry of Health (until February 2003 the Ministry of Welfare) and operating in Latvia:

- State Agency of Medicines (SAM) ensures the evaluation of medicinal products and drugs, their registration, monitoring, control and distribution management within the country as well as maintains the vigilance monitoring system;
- State Pharmaceutical Inspection (SPI) implements the state surveillance function and controls manufacturing and distribution of qualitative, safe and effective medicinal products and prevents potential risks related to the pharmaceutical activities;
- Drug Pricing and Reimbursement Agency (DPRA) ensures the enforcement and the establishment of the reimbursement system of medicines and medical devices.

However, taking into account the additional functions relating supervision of veterinary medicinal products, the market surveillance institutions should be strengthened. There are 901 pharmacies, 58 wholesalers, and 17 manufacturers operating in Latvia. More than 8300 health professionals prescribe drugs and there are approx. 4500 medicinal products on the market. Additionally there are 152 veterinary pharmacies, 22 veterinary wholesalers and 9 veterinary manufacturers in Latvia.

Under supervision of the Ministry of Health the work is under way in all involved institutions to elaborate the Strategy of the Further Development of the Latvian Market Surveillance and Vigilance System for Medicinal Products in compatibility with the European market surveillance and pharmacovigilance systems (EudraVigilance). The Strategy will be based on the National legislation on medicinal products in Latvia, which is harmonised to the EU requirements.

Phare project will give significant support for implementation of the above mentioned Strategy and development of the unitary market surveillance and pharmacovigilance system for human and veterinary medicinal products in Latvia by:

- development and implementation of unitary information system in pharmaceutical sector;
- strengthening of the capacity of the medicinal products market surveillance and vigilance monitoring institutions;
- encouragement of the health professionals to take active part into the adverse drug reactions surveillance.

The planed project activities have been discussed with the Latvian Pharmacists’ Society and attained its obvious ideas support.

**Component 1 – Development and implementation of unitary information system in order to ensure the effective market surveillance of medicinal products and patient protection**
In order to promote efficient market surveillance system of medicinal products and co-ordination among competent authorities, pharmaceutical enterprises and health care institutions it is planed to establish unitary information system (IS). Potential structure of surveillance information system for pharmaceutical market is shown in the Annex 7. The IS will consolidate following components:

- medicines utilisation monitoring IS,
- adverse drug reactions monitoring IS,
- medicines batch monitoring IS,
- medicines ads monitoring IS,
- Drug database (already existing and should be reengineered taking into account future European database on medicinal products ("EudraPharm") which is under development).

This unitary system as an effective tool of the state competent authorities for pharmaceutical market surveillance will promote:

- rapid emergency plan for withdrawal of non-qualitative pharmaceuticals;
- the possibility to obtain and handle information about pharmaceuticals consumption in human and veterinary field;
- effective reimbursement system of medicines;
- rapid and reasonable decision-making process.

Latvian institutions lack necessary experience regarding requirements of electronic data exchange between member states and EU regulatory bodies on medicinal products market surveillance and vigilance, therefore external expertise is needed on following questions:

1) evaluation of existing information system;
2) evaluation of main functions of State Agency of Medicines which must be supported by information systems;
3) recommendations on further necessary developments of information exchange between SAM and EU regulatory bodies;
4) develop recommendations for further IT system of the SAM.

Component 2 – Strengthening of the capacity of the medicinal products market surveillance and vigilance monitoring institutions

In 2001 the Adverse Drug Reactions Monitoring Department (ADRMD) was founded as SAM structural unit. The main functions of ADRMD are to collect and analyse spontaneous reports by Latvian physicians about serious and unexpected adverse reactions, as well as expedited reports by marketing authorisation and holders of medicinal products authorised in Latvia. For strengthening of the pharmacovigilance capacity it is necessary to have the twinning expert facility (on Pharmacovigilance System, including Rapid Alert System) and possibility to visit the relevant competent authorities.

The Medicines Testing Laboratory (MTL) of the State Agency of Medicines is responsible for quality control of medicinal products intended for human as well as for veterinary use according to EU requirements. As already mentioned the workload of market surveillance is increasing. The MTL is equipped with facilities for performing physical and physically chemical analysis, as well as with devices for pharmacotechnical testing of tablets and capsules dissolution and disintegration, tablets hardness and size, and for counting particles in solutions. Nevertheless the MTL needs additional specific laboratory facilities (see detailed list of equipment in Annex 8).

Due to more and more intensive flow of different types of documents related with authorisation of medicinal products, with all other activities provided by the SAM, rational and effective management of them is one of the core issues to fulfil the service obligations (timeframe for evaluating of dossiers, response to customers claims or requests, confidentiality and et cetera). For that reason State Agency of Medicines needs equipment (see Annex 8) for storage and turnover tens of thousands dossiers and plenty of all other documents.

According to the additional functions the responsibility of the State Pharmaceutical Inspection is widened by supervision of the veterinary medicinal products. It is planed that from 2003 the State Pharmaceutical Inspection will take on the supervision of the distribution of medical devices and blood
products too. Taking into account all these additional functions, the professional and technological capacity of the SPI have to be considerably strengthened by training of staff and updating of IT capacity.

**Component 3 - Encouragement of the health professionals to take active part into the adverse drug reactions surveillance**

Encouragement of the health professionals to take more active part into the adverse drug reactions (ADR) surveillance system plays essential role in development of the pharmacovigilance system. In this reason the project covers practical field too.

The main problems are following:
- Health professionals don’t have enough knowledge and experience in reporting of adverse reactions.
- The ADR monitoring is ineffective due to the low reporting activity from physicians and pharmacists.
- Health professionals are not enough encouraged for reporting.

The implementation of this project component will give substantial support for establishment of ADR surveillance system in Latvia according to EU requirements by such means:
- Implementation of the pilot project in hospital "Gailezers" (one of the largest hospitals of Latvia) for approbation of the ADR monitoring and Reporting System;
- Practical training of the health professionals;
- Support to the encouraging activities to involve health professionals into the ADR surveillance;
- Publication of informative materials On Pharmacovigilance Issues.

The Toxicological Centre with Poisons Information Centre is the structural unit of the hospital "Gailezers”. The Toxicological Centre has significant impact on the pharmacovigilance development by its fulfilled functions and the pilot-project implementation, particularly taking into account that it is located at the hospital’s "Gailezers” territory. It is planed that the Toxicological Centre (TC) staff will take active part at the pilot pharmacovigilance investigation, which will take place in the hospital "Gailezers”. For further strengthening of the TC’s capacity the complex data bases on drug monitoring should be needed.

3.2. Linked activities:

Phare project "Technical Assistance to Support Restructuring of the Pharmaceutical Sector in Latvia” in human medicinal products field (LE 96-0951) was finished on 04/12/1998. Three competent authorities under supervision of the Ministry of Welfare - State Agency of Medicines, State Pharmaceutical Inspection and Medicines’ Pricing and Reimbursement Agency - were established by support of this project. The strengthening of the supervise capacity of these institutions is planned by the implementation of this project.

MATRA Pre-accession Co-operation Programme’s financed by the Netherlands government project ”Support to the Development and Implementation of Good Clinical Practice, Good Manufacturing Practice and Good Distribution Practice for Medicinal Products” (MAT01/LV/9/1) is in implementation from 01.01.2002. to 30.06.2003.

3.3. Results:

**Component 1 – Development and implementation of unitary information system in order to ensure the effective market surveillance of medicinal products and patient protection**

- Unitary medicinal products market surveillance information system established including:
  - Medicines utilisation monitoring IS;
  - Medicines ads monitoring IS;
  - Medicines batch monitoring IS;
  - Adverse drug reactions (ADR) monitoring IS;
  - Existing Drug database has been reengineered and existing data are transferred;
  - Network hardware facilities, cabling and software licences in place.
Twinning should achieve the following guaranteed results:

- The Strategy of the Further Development of the Market Surveillance System for Medicinal Products in Latvia is assessed and completed;
- Recommendations about existing IT system evaluation and further system development according to the standards in European Agency for the Evaluation of Medicinal Products (EMEA) and EU agencies;
- System administrators are trained in administration of the relevant IT system by experience of the EU institutions.

**Component 2 – Strengthening of the capacity of the medicinal products market surveillance and vigilance monitoring institutions**

- The capacity of the Medicines Testing Laboratory strengthened for testing medicines for human and veterinary use;
- The capacity of the State Agency of Medicines strengthened with necessary equipment for storage and turnover dossiers of medicines register;
- The IT facilities of the State Pharmaceutical Inspection have been upgraded.

Twinning should achieve the following guaranteed results:

- Effective and rapid system of non-qualitative medicines withdrawal has been developed;
- Pharmacovigilance staff of the State Agency of Medicines is trained on Adverse drug reactions (ADR) monitoring by taking experience in the relevant institutions of EU countries;
- The inspectors of SPI are trained on surveillance of veterinary medicinal products.

**Component 3 - Encouragement of the health professionals to take active part into the adverse drug reactions surveillance**

- Informative materials “On Pharmacovigilance Issues” and “Pilot – project implementation results” have been published
- The IT capacity of the State Toxicological Centre has been improved.

Twinning should achieve the following guaranteed results:

- Pharmacovigilance pilot project at the hospital ”Gailezers” has been implemented;
- Health professionals are trained in pharmacovigilance basis knowledge and adverse drug reactions manifestations in different organ systems;
- Pilot pharmacovigilance investigation has been carried out at the hospital ”Gailezers”.

3.4. Activities:

Division of project activities between Twinning instrument and Technical assistance for this particular project is based on the following principles:

Twinning instrument is optimal for the adoption of acquis and provision of best policy practice, training and consultations during day-to-day co-operation with Candidate state authorities.

Technical assistance is optimal for activities, which need more technically time-consuming individual preparatory work and involvement of large number of similar experts during implementation (e.g. databases).

**Component 1 – Development and implementation of unitary information system in order to ensure the effective market surveillance of medicinal products and patient protection**
Twinning activities:
- Supervision of project implementation and evaluation and compiling of the Strategy of the Further Development of the Market Surveillance System for Medicinal Products in Latvia
- Elaboration of existing IT system recommendations for further system development according the standards in the European Agency for the Evaluation of Medicinal Products (EMEA) and EU agencies, which includes:
  - evaluation of the existing information system;
  - evaluation of the main functions of State Agency of Medicines (SAM) which must be supported by information systems;
  - recommendations for the further necessary developments of information exchange between SAM and EU regulatory bodies;
  - recommendations for the further SAM system evolution;
  - evaluation of the information system specifications elaborated by local specialists.
- Training for IT system administrators in administration of the relevant IT system by experience at the EU institutions.

Main beneficiary institution will be the State Agency of Medicines. The State Pharmaceutical Inspection will be partner in implementation of the Strategy of the Further Development of the Market Surveillance System for Medicinal Products in Latvia.

Twinning means:
- PAA, (see profile and detailed tasks of PAA below), 12 man months;
- Short term twinning expert (2 man months)
- 2 one-week study visits for IT system administrators (2 persons from the State Agency of Medicines).

Short term expert profile
The assignee should have at least 5 years professional experience and the following expertise in the executing team:
- knowledge on the pharmaceutical sector in EU Member States;
- knowledge on computerised information systems used to support functions in authorities in pharmaceutical sector;
- knowledge on standards for electronically data exchange to be used for data exchange between EU Member States authorities in pharmaceutical sector;
- theoretical understanding and practical implementation knowledge of the information systems development in the pharmaceutical sector;
- knowledge of specifications for information system development evaluation;
- language skills – English;
- communication skills.

Technical assistance activities:
- Development of Medicines utilisation monitoring IS;
- Development of Medicines ads monitoring IS;
- Development of Adverse Drug Reactions monitoring IS;
- Development of Medicines batch monitoring IS;
- Reengineering of existing Drug database;
- Transfer of existing data.

Technical assistance means:
Service contract (Contract 2).

Supplies activities:
- Strengthening of the unitary information system by provision of network hardware facilities, cabling and software licensing (see the detailed description in Annex 8).

Supplies means:
Supply contract (Contract 4).
Component 2 – Strengthening of the capacity of the medicinal products market surveillance and vigilance monitoring institutions

Twinning activities:
- Elaboration of pharmacovigilance procedures including Rapid Alert System;
- Training for pharmacovigilance staff of State Agency of Medicines on Adverse drug reactions (ADR) monitoring by taking experience in the relevant institutions of EU countries;
- Training for State Pharmaceutical Inspection’ staff on market surveillance of veterinary medicinal products and blood products.

Twinning means:
- PAA (see profile and detailed tasks of PAA below), 12 man months;
- Short term twinning expert on pharmacovigilance procedures (0.5 man month);
- 2 one-week study visits for SAM pharmacovigilance staff on Adverse drug reactions (ADR) monitoring (2 persons);
- 2 one-week study visits for SPI staff on market surveillance of veterinary medicinal products and blood products (4 persons).

Short term expert profile:
- at least 5 years professional experience in pharmacovigilance procedures;
- knowledge in EU building pharmacovigilance system;
- language skills – English;
- communication skills.

Supplies activities:
- Strengthening of the capacity of the Medicines Testing Laboratory for testing human and veterinary medicinal products (see the detailed description in Annex 8);
- Strengthening of the State Agency of Medicines medicaments register archive facilities (see the detailed description in Annex 8);
- Strengthening of the State Pharmaceutical Inspection IT facilities.

Supplies means:
Supply contracts (Contract 3 and Contract 4).

Component 3 - Encouragement of the health professionals to take active part into the adverse drug reactions surveillance

Twinning activities:
- Pilot Project implementation at the hospital "Gailezers"
  - 1 seminar on basic knowledge in pharmacovigilance (30 persons from Latvian leading hospitals);
  - 2 seminars on knowledge in adverse drug reaction manifestations in different organ systems and 9 sub-seminars on clinical manifestations and mechanisms of adverse drug reactions (30 persons from Latvian leading hospitals):
    - Cardiovascular reactions;
    - Dermatological reactions;
    - Neurological reactions;
    - Reactions of the renal system;
    - Blood disorders;
    - Liver disorders;
    - Gastro-intestinal system reactions;
    - Respiratory system reactions;
    - Impact of genetic and interethnic differences.
  - Pilot pharmacovigilance investigation at the hospital "Gailezers”.
- Final conference with participation of representatives from health care institutions of Riga and regions for presentation of results of the pilot – project and exchange of experience (100 persons).
Twinning means:
- PAA (see profile and detailed tasks of PAA below), 12 man months;
- 12 training seminars on pharmacovigilance (5 days) by 5 – 6 lecturers, depends on the expanse of competence;
- supervision of pilot pharmacovigilance investigation at the hospital “Gailezers” (1 month) by supervision of the twinning expert.

Lectors profile:
- at least 5 years professional experience in pharmacovigilance;
- academical (lector) experience;
- knowledge in adverse drug reaction manifestations in different organ systems, particularly:
  - Cardiovascular reactions;
  - Dermatological reactions;
  - Neurological reactions;
  - Reactions of the renal system;
  - Blood disorders;
  - Liver disorders;
  - Gastro-intestinal system reactions;
  - Respiratory system reactions;
  - Impact of genetic and interethnic differences;
- language skills – English.

Short term expert profile:
- at least 5 years professional experience in pharmacovigilance;
- knowledge and practical experience in design and carry out of the clinical investigations;
- language skills – English;
- communication skills.

Supplies activities:
- Strengthening of the IT capacity of the Toxicological Centre by the software licences complex for drug monitoring;
- Publication of informative materials on pharmacovigilance and pilot – project results.

Supplies means:
Supply contract (Contract 4 and Contract 5).

Twinning arrangements for the project:
The significance of the project as well as the ambitious goals set therein call for involvement of the Pre-accession Advisor for the whole duration of the project 12 months to:
- be the head of the all the project’s experts and activities, being the leading EU counterpart of the beneficiary
- assist responsible structures for capacity building activities,
- be responsible for management and co-ordination of all the components of the project to ensure that the project proceeds, as planned, in an efficient and orderly fashion
- advice the Project Steering Committee (PSC) on ways to improve design, planning and implementation framework of the project components
- upon request from the head of the PSC, deliver general advisory support to the Ministry of Health, other involved institutions
- ensure successful correlation and collaboration of all the institutions engaged in the project activities as far as it is necessary to achieve the project objectives
- follow up on the activities carried out during short-term missions of the expert pool in all the components proposing the PSC any further measures needed to ensure the sustainability of the project
The PAA profile should comprise:

- at least 10 years professional experience from working in private or public administration and a good grounding in the fields of:
  - laying down structures and strategic developments in market surveillance;
  - institutional building and medicinal products market surveillance procedures;
  - planning of pharmaceutical system and pharmacovigilance development;
  - organisation of market surveillance data processing activities;
  - assistance to governmental bodies and their subordinate institutions for preparation those to their future role in EU;
- experience of working with senior politicians and officials in an advisory role;
- management and communication skills;
- language skills - English.

3.5. Lessons learned

According to the Final Report of the previous Phare project "Technical Assistance to Support Restructuring of the Pharmaceutical Sector in Latvia" in human medicinal products field (LE 96-0951), "the further development of the pharmaceutical monitoring system will significantly increase knowledge of the real consumption and use of medicinal products in Latvia, which is a vital step towards the needed changes to obtain more correct use of medicinal products, both from the therapeutic / preventive aspect, and from the economic / cost–effectiveness aspect”.

4. Institutional Framework

The leading institution for implementation of the project will be the Ministry of Health (Regulation of the Cabinet of Ministers No.20 adopted 14 January 2003 “Statutes of the Ministry of Health”). Involved institutions in the implementation of the project will be:
- State Agency of Medicines (ensures the evaluation of medicinal products and drugs, their registration, monitoring, control and distribution management within the country as well as maintains the vigilance monitoring system);
- State Pharmaceutical Inspection (implements the state surveillance function and controls manufacturing and distribution of qualitative, safe and effective medicinal products and prevents potential risks related to the pharmaceutical activities);
- Hospital "Gailezers" (one of the largest Latvian hospitals). The Toxicological Centre with Poisons Information Centre is the structural unit of the hospital "Gailezers"

The detailed descriptions of functions see in Annex 6.

Project steering committee will be established to oversee project implementation. The Steering Committee will comprise representatives from the European Commission Delegation, Ministry of Health, Ministry of Finance (NAC office), State Agency of Medicines and State Pharmaceutical Inspection.

5. Detailed Budget

(In Euro)

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* Parallel co-financing. Parallel co-financing will be applied for covering of office costs for experts, infrastructure facilities and travel costs for national counterparts.

**Joint co-financing, excluding all taxes and duties.

6. Implementation Arrangements

6.1. Implementing Agency

Implementing agency of the project will be the CFCU, PAO Valentina Andrejeva, State Secretary of Ministry of Finance. CFCU will be responsible for the financial and administrative management of the project in accordance with EDIS procurement rules, regulations and procedures.

Programme Authorising Officer - V. Andrejeva, State Secretary of the Ministry of Finance.
1, Smilsu str., LV-1919, Riga, Latvia
Ph. 371-7212726;
Fax. 371-7095413.

Central Finance and Contracting Unit - A. Eberhards, Director,
1, Smilsu str., LV-1919
Ph. 371-7094342;
Fax. 371-7094348.

Ms. Ruta Zilvere, Deputy State Secretary of the Ministry of Welfare (28 Skolas str., Riga, LV 1331, Latvia; ph. 371 7021605, fax 371 7276445) is the Senior Programme Officer and responsible for the technical implementation of the project until nomination of the Senior Programme Officer of the Ministry of Health.

The State Agency of Medicines as subordinated body of the Ministry of Health will carry out technical implementation of the project. In implementation of the project State Pharmaceutical Inspection will be involved actively as well.

Beneficiary institutions and contact person:
Ministry of Health (MoH)
Department of Pharmacy
Mr. Juris Bundulis
Director of Department
Tel.: +371 7021608
Fax: +371 7021691
E-mail: Juris_Bundulis@vm.gov.lv
Address: 25 Baznicas str., Riga, LV- 1010
6.2. Twinning

The PAA will be situated in the State Agency of Medicines. Mr. Janis Ozolinš, Director General of the State Agency of Medicines will be the Latvian counterpart of the PAA.

Project leader and counterpart for the PAA

Mr. Janis Ozolinš  
Director General of the State Agency of Medicines  
Tel.: +371 7078400  
Fax: +371 7078428  
E-mail: Janis.Ozolins@vza.gov.lv  
Address: 15 Jersikas str., Riga, LV-1003

6.3. Non-standard aspects

There will be no non-standard aspects regarding implementation of the project. Standard procedures of the Commission in accordance with Practical Guide to PHARE, ISPA and SAPARD contract procedures as well as Twinning manual will be followed under Extended Decentralised Implementation System. Prior to EDIS accreditation, DIS will be followed. EDIS will apply from the date of accession at latest.

Ratio: if during project implementation the project cost for some reasons will decrease, the Phare financing will also decrease proportionally.

6.4. Contracts

- Contract No. 1: Twinning covenant - 283 100 euro (parallel co-financing);
- Contract No. 2: Service (TA) contract - 298 200 euro (joint co-financing, excluding all taxes and duties)
- Contract No. 3: Supply contract – 389 400 euro (joint co-financing, excluding all taxes and duties)
- Contract No. 4: Supply contract – 340 700 euro (joint co-financing, excluding all taxes and duties)
- Contract No. 5: Supply contract - 40 000 euro
(joint co-financing, excluding all taxes and duties)

7. **Implementation Schedule**

Contract No. 1: Twinning covenant (283 100 euro)
- Start of tendering/call for proposals - 4 Quarter 2003
- Start of project activity – 1 Quarter 2004 (duration 12 months)
- Project Completion – 4 Quarter 2004

Contract No. 2: Service (TA) contract (298 200 euro)
- Start of tendering/call for proposals - 4 Quarter 2003
- Start of project activity – 2 Quarter 2004 (duration 4 months)
- Project Completion – 3 Quarter 2004

Contract No. 3: Supply contract (389 400 euro)
- Start of tendering/call for proposals - 3 Quarter 2003
- Start of project activity – 1 Quarter 2004 (duration 5 months)
- Project Completion – 2 Quarter 2004

Contract No. 4: Supply contract (340 700 euro)
- Start of tendering/call for proposals - 3 Quarter 2003
- Start of project activity – 1 Quarter 2004 (duration 6 months)
- Project Completion – 3 Quarter 2004

Contract No. 5: Supply contract (40 000 euro)
- Start of tendering/call for proposals - 1 Quarter 2004
- Start of project activity – 2 Quarter 2004 (duration 3 months)
- Project Completion – 3 Quarter 2004

8. **Equal Opportunity**

Participation in the project will require professional qualifications and competence in the particular area and will allow an equal opportunity for women and men to participate in implementation of the project.

9. **Environment**

No environmental impact to be expected

10. **Rates of return**

N/A

11. **Investment criteria**

N/A

12. **Conditionality and sequencing**

- The Strategy of the Further Development of the Market Surveillance System for Medicinal Products and Medical Devices in Latvia elaborated
- Adequate staffing in the recipient institutions has to be in place for implementation and monitoring of project activities before the start of the project
- Co-financing via national budget ensured

**ANNEXES TO PROJECT FICHE**

1. Logical framework matrix in standard format
2. Detailed implementation chart
3. Contracting and disbursement schedule by quarter for full duration of programme (including disbursement period)
4. List of relevant Laws and Regulations
5. Institutional framework related to the project
6. Dividing of the functions between the Ministry of Health and the Ministry of Agriculture related to the medicinal products
7. Potential IT add-on
8. Organisational Structure of the State Pharmaceutical Inspection (current and planned)
# Logical Framework Matrix

## LOGFRAME PLANNING MATRIX FOR

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<td>Medicinal Products Market Surveillance and Pharmacovigilance</td>
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## Overall objective

- Ensure quality, safety and efficacy of medicinal products

## Objectively verifiable indicators

- Developed efficient functioning and transparent unitary market surveillance system for human and veterinary medicinal products

## Sources of Verification

- Regular Progress Report
- Information form Latvian health care institutions
- Official publications
- Reports of State Agency of Medicines

## Project purpose

- Development of market surveillance and pharmacovigilance system for human and veterinary medicinal products

## Objectively verifiable indicators

- Unitary medicinal products market surveillance information system functional inline with EU requirements;
- The pharmacovigilance system functional

## Sources of Verification

- Project Final Report;
- Reports of the project involved institutions;
- Training missions’ reports;
- Spontaneous Adverse Drug Reactions (ADR) reports

## Results

### Component 1

- The Strategy of the Further Development of the Market Surveillance System for Medicinal Products in Latvia is assessed and completed;
- Recommendations about existing IT system evaluation and further system development according to the standards in European Agency for the Evaluation of Medicinal Products (EMEA) and EU agencies;
- System administrators are trained in the relevant IT system administration;

## Objectively verifiable indicators

- Software packages;
- Drug database;
- Veterinary medicinal products are tested at the Medicines Testing Laboratory;
- Number of report on Adverse Drug Reactions;
- Effective and rapid system of non-qualitative medicine withdrawal operational

## Sources of Verification

- Project reports;
- Reports of the project involved institutions;
- Training missions’ reports;
- Spontaneous ADR reports;
- Monitoring Reports

## Assumptions

- Pharmaceutical market surveillance institutions are willing to implement efficient market surveillance system
- The high efficient information exchange between pharmaceutical market institutions optimises the surveillance procedure
- Precise and modern process of the testing of medicinal products is framed
• Unitary medicinal products market surveillance information system established.

Component 2
• Effective and rapid system of non-qualitative medicine withdrawal has been developed;
• Pharmacovigilance staff of the State Agency of Medicines (SAM) are trained in Adverse drug reactions monitoring;
• The inspectors of State Pharmaceutical Inspection (SPI) are trained on surveillance of veterinary medicinal products;
• The capacity of the Medicines Testing Laboratory has been strengthened for testing medicines for human and veterinary use;
• The capacity of the SAM strengthened with necessary equipment for storage and turnover dossiers of medicines register;
• The IT facilities of SPI have been upgraded.

Component 3
• Pharmacovigilance pilot project at the hospital "Gailezers" is implemented;
• The IT capacity of the State Toxicological Centre has been improved;
• Informative materials on pharmacovigilance and pilot project results have been published;
• Health professionals are trained in pharmacovigilance basis knowledge, adverse reactions manifestations in different organ systems;
• Pilot pharmacovigilance investigation has been carried out at the hospital "Gailezers".

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<tr>
<th>Activities</th>
<th>Means</th>
<th>Assumptions</th>
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<tr>
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<td>Supervision of project implementation and evaluation and compiling of the Strategy of the Further Development of the Market Surveillance System for Medicinal Products in Latvia</td>
<td>• pre-accession advisor (PAA), 12 m/m;</td>
<td>• All involved institutions have sufficient labour capacity for implementation this project</td>
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<td>Elaboration of existing IT system recommendations for further system development according the standards in EMEA and EU agencies;</td>
<td>• 1 short term expert for elaboration of IT systems, 2 m/m;</td>
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<td>Training for IT system administrators;</td>
<td>• 1 short term expert on pharmacovigilance procedures, 0,5 m/m;</td>
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<tr>
<td></td>
<td>• 2 one-week study visits for IT system</td>
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</tbody>
</table>

- Inspectors of SPI are able to perform surveillance of veterinary medicinal products
- Pharmacovigilance staff SAM is able to perform Adverse drug reactions monitoring
- Equipment and hardware supplied and installed
- Informative material available
### Rapid Alert System:
- Training for pharmacovigilance staff of SAM;
- Pilot Project implementation at the hospital “Gailezers”;
- Training for SPI staff on market surveillance of veterinary medicinal products and blood products.

### Service:
- Development of Medicines utilisation monitoring IS;
- Development of Medicines ads monitoring IS;
- Development of Adverse Drug Reactions monitoring IS;
- Development of Medicines batch monitoring IS;
- Reengineering of existing Drug database and migration of existing data.

### Supply:
- Purchase of Network hardware facilities, cabling and pharmaceutical software licensing;
- Equipping of the Medicines Testing Laboratory with specific laboratory equipment for testing human and veterinary medicinal products;
- Installation of the cold room in the Medicines Testing Laboratory;
- Equipping of the Medicines Testing Laboratory with up-to-date laboratory furniture;
- Strengthening of the IT capacity of the Toxicological Centre;
- Publication of informative materials on pharmacovigilance.

### Rapid Alert System:
- 2 one-week study visits for SPI staff on market surveillance of veterinary medicinal products and blood products (4 persons);
- 2 one-week study visits for the SAM pharmacovigilance staff (2 persons);
- 12 training seminars on pharmacovigilance (5 days), (30 persons from the leading Latvian hospitals);
- Final conference of the pilot – project in the hospital “Gailezers” (100 persons).

### Service:
- Long term expert facility and development of software;
- Reengineering of existing Drug database.

### Supply:
- Purchase of equipment;
- Production of informative materials.

### Preconditions
- Development of the network system strategy between involved institutions by work group
- The Strategy of the Further Development of the Market Surveillance System for Medicinal Products and Medical Devices in Latvia elaborated
- Adequate staffing in the recipient institutions has to be in place for implementation and monitoring of project activities before the start of the project
- Co-financing via national budget ensured
IMPLEMENTATION CHART

Project N°:
Project Title: Medicinal Products Market Surveillance and Pharmacovigilance

<table>
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<th>Twinning Covenant (Contract 1)</th>
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<td>Elaboration of pharmacovigilance procedures including Rapid Alert System (0.5 man-month)</td>
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<td>Final conference with participation of representatives from health care institutions of Riga and regions</td>
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Service (TA) Contract (Contract 2)
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<td>Reengineering of existing Drug database and transfer of existing data</td>
<td>X</td>
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**Supply Contract (Contract 3)**

- Equipping of the Medicines Testing Laboratory with refrigerating chambers, up-to-date laboratory furniture and specific laboratory equipment for testing human and veterinary medicinal products (see the detailed description in Annex 6)
- Equipping of the State Agency of Medicines with specific equipment for dossiers and other documents storage (see the detailed description in Annex 6)

**Supply Contract (Contract 4)**

- Network hardware facilities, cabling and software licensing for the State Agency of Medicines
- Equipping of the State Pharmaceutical Inspection with hardware (5 computers) and network facilities
- Complex of the software licences for the State Toxicological Centre for monitoring of adverse drug reactions

**Supply Contract (Contract 5)**

- Publication of informative materials on pharmacovigilance
## CUMULATIVE CONTRACTING and DISBURSEMENT SCHEDULE (by quarters)

### Contract 1, Twinning Covenant*

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* Parallel co-financing

** Joint co-financing, excluding all taxes and duties
### List of relevant Laws and Regulations

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<th>Relevant Law and Regulations</th>
<th>EU Directives</th>
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<tr>
<td>Regulations <strong>138</strong> of the Cabinet of Ministers of 20 March 2001 On Classification of Medicinal Products for Human Use</td>
<td><strong>2001/83/EC</strong></td>
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<td>Regulations <strong>104</strong> of the Cabinet of Ministers of 6 March 2001 On Pharmacovigilance of Medicinal Products for Human Use</td>
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<td>December 2000</td>
<td>On Manufacturing and Control of Medicinal Products for Human Use</td>
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<td>On Marketing Authorisation of Medicinal Products for Human Use</td>
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<td>September 2000</td>
<td>On Clinical Trials of Medicinal Products for Human Use</td>
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<td>Regulations 234</td>
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<tr>
<td>June 1998</td>
<td>On Labelling of Medicinal Products for Human Use</td>
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Institutional framework related to the project

The main responsibility of the **Ministry of Health** in field of pharmaceuticals is the pharmaceutical policy making and supervision, and the most important directions of this policy are following:

- give patients better access to qualitative, safe and efficient medicines;
- give better access to pharmaceutical care and ensure rational development of pharmaceutical enterprises;
- development of legislative acts in compliance with EU requirements and international agreements;
- supervision and monitoring of medicines’ (including narcotic and psychotropic medicines) trade;
- dealing with questions of the pharmacoconomics;
- monitoring of the distribution of pharmaceutical information;
- encourage rational use of medicines;
- regular information exchange between involved institutions with clearly defined requirements for information flow;
- analysis of pharmaceutical activities and prognosis of the development of pharmaceutical sector;
- analysis of investments and finance needed in pharmaceutical area.

The aim of **State Agency of Medicines** (SAM) and the main performance directions are evaluation of medicinal products and drugs, their registration, monitoring, control and distribution management within the country. The SAM fulfils the following activities:

- issues clinical trial performance licenses and monitors the process of the clinical trials and summaries their results;
- gathers, summaries and distributes the information on the current events regarding the topics as to the quality control of the medicinal products and drugs;
- organises the co-operation with other international organisations at to the medicines quality control and quality control of pharmaceutical products;
- co-operates with international pharmaceutical and medical organisations;
- according to the legislative regulations, issues the importing and exporting, transit and distribution certificates of the medicines and drugs;
- prepares and submits the proposals to the Ministry of Health on the laboratories, institutes and other institution to be included in the list of the organisations licensed to give official evaluations on the quality of medicines and drugs.

State Agency of Medicines issues the Drug Register - an official publication, where all the medicinal products registered in Latvia are listed.

The present structure (see Annex 10) of the SAM has been developed at the result of 5 years operation, which ensures efficacy and quality of the agency’s work. At the same time the prospective progress related to new, planned functions and responsibilities that would increase the
extent of the SAM functions from 2003 must be taken into account. To improve the transparency of medicines authorisation and to decrease bureaucratic obstacles in co-operation with the clients – medicines manufacturers – merging of Pharmacology and Pharmacopoeia Departments and establishing Human Medicines Authorisation Department is planned. In the prospect it is planned to establish Veterinary Medicines Authorisation Department and Law Department. The Law Department would take over licensing of pharmaceutical companies from the Ministry of Health, is anticipated as shown in Annex 10, too.

**State Pharmaceutical Inspection** (SPI) exercises direct oversight and control over the market for medicinal products to ensure that the manufacturing and distribution of high quality, safe and effective medicinal products eliminate any possible pharmaceutical risk factor. The main tasks of the State Pharmaceutical Inspection:

- control of the process of manufacturing of medicinal product in accordance with Good Manufacturing Practice requirements;
- control of the process of distribution of medicinal product in accordance with Good Distribution Practice requirements;
- inspection of the pharmaceutical enterprises and health care institutions in respect of distribution of medicinal products;
- control of the process of implementation the legislative requirements in practice;
- control of the advertising of medicinal products.

As new functions on supervision of the veterinary medicinal products and medical devices are assigned to the State Pharmaceutical Inspection, there will have to be a review of its existing structure (see Annex 11). The current structure was established in August 2002, adding a deputy director for pharmaceutical affairs. This structure helps to ensure the quality of the Inspection’s work, but in future it requires the additional review of structure (see planed structure in Annex 11) for successfully fulfil new functions.

The **Toxicological Centre** with **Poisons Information Centre** is the structural unit of the hospital **"Gailezers"**. Toxicological Center has the following functional tasks and responsibilities:

**Toxicological Center** (treatment facility for poisoned patients):

- provide specialized treatment for poisoned patients;
- provide consultative and practical clinical management of chemical disasters victims;
- practical training in toxicology of the health professionals involved with the care of poisoned patients;
- cooperation with Poisons Information Center in order to minimize the risk of poisoning and to prevent the cases of poisoning.

**Poisons Information Center**: 

- provide recommendations for the management of poisoning to both healthcare professionals and general public;
- collection of epidemiological data of poisonings;
- toxicosurveillance for the emergence of new public health risks;
• provision of assistance to state agencies (including public health agencies) involved with hazardous materials;
• cooperation with Toxicological Center in order to minimize the risk of poisoning and to prevent the cases of poisoning;
• training in toxicology of the health professionals involved with the care of poisoned patients;
• education of general public how to prevent poisoning and what to do after poisoning.
### ANNEX 6

**Dividing of the functions between the Ministry of Health and the Ministry of Agriculture related to medicinal products**

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<td>Institutions after reorganisation</td>
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<tr>
<td>Marketing authorisation of medicinal products</td>
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<td>MoH</td>
</tr>
<tr>
<td>1) human medicinal products</td>
<td>1) MoH</td>
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<td>2) veterinary medicinal products</td>
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<tr>
<td>1) human medicinal products</td>
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<tr>
<td>2) veterinary medicinal products</td>
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<tr>
<td>Supervision of narcotic and psychotropic drugs issues</td>
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<tr>
<td>1) human medicinal products</td>
<td>1) MoH</td>
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<td>2) veterinary medicinal products</td>
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<tr>
<td>Supervision of clinical trials</td>
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<td>1) human medicinal products</td>
<td>1) MoH</td>
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<td>2) veterinary medicinal products</td>
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<tr>
<td>Supervision of advertising of medicinal products</td>
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<td>Reimbursement system for medicinal products</td>
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<tr>
<td>Restrictions of using of medicinal products for animals</td>
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<td>MoA</td>
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<tr>
<td>Designation and control of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin</td>
<td>MoA</td>
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<tr>
<td>Control of distribution of the nutriments and additives for animals</td>
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</table>

Abbreviations:
MoH – Ministry of Health
MoA – Ministry of Agriculture
ANNEX 7

Potential IT add-on

Drug registration process
SAM

Monitoring of circulation of medicines
SAM

Monitoring of narcotics
SAM

Monitoring of medicines included in reimbursement system
DPRA

Monitoring of members of pharmaceutical market
DPh

Adverse drug reactions monitoring
SAM

Clinical trials
SAM

Inspections monitoring
SPI

DRUG DATABASE
Latvian Drug register
SAM

DPh – Department of Pharmacy of the Ministry of Health
SAM – State Agency of Medicines
SPI – State Pharmaceutical Inspection
DPRA – Drug Pricing and Reimbursement Agency
State Pharmaceutical Inspection
Current organizational structure

State Pharmaceutical Inspection

Internal audit department (1)

Head

Deputy, Pharmaceutical subjects

Medical establishment control department (2)

Medicines manufacturers control department (2)

Deputy, Juridical subjects

Accounting department (1)

Household department (1)

Secretariat

Pharmacy and wholesalers control department (4)
Planned Organisational Structure of the State Pharmaceutical Inspection

- **Director**
  - **Deputy, Pharmaceutical Affairs**
    - Human and Vet. Medic. Manufac. and Wholesaler Control Dept. (3)
    - Medical Devices Control Department (3)
  - **Deputy, Legal Affairs**
    - Medicine Pricing Control Department (1)
    - Housekeeping Department (1)
    - Secretariat (1)
  - **Internal Audit Department** (2)
  - **Public Relations Department** (1)
  - **Accounting Department** (2)
  - **Personnel Dept.**

**Department director**
- Human and Veterinary Pharmacy Control Department (10)
- Human and Veterinary Medical Establishment Control Department (4)
- Medicine Advertising Control Department (2)