

## Standard Summary Project Fiche – IPA decentralised National programmes

(Project No: TR2009/0301.01)

### **1. Basic information**

**1.1 CRIS Number: TR2009/0301.01**

**1.2 Title: Quality Control Tests for Human Vaccines and Sera**

**1.3 ELARG Statistical code: 1 Free Movement of Goods**

**1.4 Location: Ankara/Turkey**

### **Implementing arrangements:**

#### **1.5 Implementing Agency:**

The CFCU will be the implementing agency and will be responsible for all procedural aspects of the tendering process, contracting matters and financial management including payment of project activities. The Director of the CFCU will act as Programme Authorizing Officer (PAO) of the project.

Mr.Muhsin ALTUN (PAO-CFCU Director)

Central Finance and Contracting UnitCentral Finance and Contracting Unit

Tel: +90 -312- 295 49 00

Fax: +90 -312- 286 70 72

E-mail: [muhsin.altun@cfcu.gov.tr](mailto:muhsin.altun@cfcu.gov.tr)

Adress: Eskişehir Yolu 4. Km. 2 street (Halkbank Kampüsü) NO: 63 C-Blok 06580  
Söğütözü/Ankara Turkey

#### **1.6 Beneficiary:**

The principal beneficiary of the ‘Vaccines and Sera Project’ is Refik Saydam National Public Health Agency (RSNPHA) (Ministry of Health)

Contacts at Refik Saydam National Public Health Agency:

SPO candidate:

Assoc. Prof. Mustafa ERTEK, President

Refik Saydam National Public Health Agency

Tel: + 90 312 458 24 00

Fax : +90 312 458 2408

Email: [mustafa.ertek@saglik.gov.tr](mailto:mustafa.ertek@saglik.gov.tr)

Address: Cemal Gürsel Cad. No: 18

Sıhhiye/ Ankara

Under the responsibility of PAO, SPO shall carry out the following tasks:

- (a) be responsible for the technical aspect of the operations within the line ministries;
- (b) assist the programme authorizing officers in the good and timely preparation and implementation of operations at technical level;
- (c) be in charge of the co-ordination within each priority axis set down in the Beneficiary’s project proposal.

The project will be implemented by the Biological Control and Research Laboratory (BCRL) of Refik Saydam National Public Health Agency (RSNPHA) assisted by the International Relations, EU and Project Department (IREUPD) of the agency. Interim Quarterly Reports will be prepared and discussed at the Steering Committee (SC) meetings to be held on a quarterly basis. The Project Steering Committee will be chaired by the proposed SPO, Assoc. Prof. Mustafa ERTEK, President of RSNPHA and will be composed of:

Dr. Yıldıırım CESARETLİ, Vice President of RSNPHA  
(SPO Delegate candidate)  
Tel: + 90 312 458 24 10  
e-mail: [yildirim.cesaretli@rsh.gov.tr](mailto:yildirim.cesaretli@rsh.gov.tr)

Dr. Serpil ŞENELT, Head of  
International Relations, EU and Project Department of RSNPHA  
(SPO Delegate candidate)  
Tel: + 90 312 458 2455  
e-mail: [serpil.senelt@saglik.gov.tr](mailto:serpil.senelt@saglik.gov.tr)

Dr. Filiz KOÇ, Chief of  
Biological Control and Research Laboratory of RSNPHA  
(SPO Delegate candidate)  
Tel: +90 312 458 2076  
e-mail: [filiz.koc@rsh.gov.tr](mailto:filiz.koc@rsh.gov.tr)

Dr. Mehmet Ali TORUNOĞLU, Deputy Director General  
DG Primary Health Care, MoH  
Tel: +90 312 435 2971  
e-mail: [mehmet.torunoglu@saglik.gov.tr](mailto:mehmet.torunoglu@saglik.gov.tr)

Dr. Saim KERMAN, Deputy Director General  
DG Pharmaceuticals and Pharmacy, MoH  
Tel: +90 312 309 1141  
e-mail: [saim.kerman@saglik.gov.tr](mailto:saim.kerman@saglik.gov.tr)

Representatives of the Delegation, CFCU and EUSG will participate in the SC meetings as observers. Representatives of the General Directorate for Pharmaceuticals and Pharmacy, General Directorate for Primary Healthcare, General Directorate for Mother and Child Health and other related departments of the MoH, other interested parties including academia, the related sector and representatives and non-governmental organizations such as the Infectious Diseases Association of Turkey will be involved in the project activities and meetings that require their involvement.

### **Financing:**

**1.7 Overall cost (VAT excluded)<sup>1</sup>: 3.587.200 €**

**1.8 EU contribution: 3.257.620 €**

---

<sup>1</sup> The total cost of the project should be net of VAT and/or other taxes. Should this not be the case, the amount of VAT and the reasons why it should be considered eligible should be clearly indicated (see Section 7.6)

**1.9 Final date for contracting:** Two years after the signature of the Financing Agreement

**1.10 Final date for execution of contracts:** Two years after the last day of the contracting deadline

**1.11 Final date for disbursements:** One year after the end date for the execution of contracts

## **2. Overall Objective and Project Purpose**

### **2.1 Overall Objective:**

The overall objective of the project is implementation of the *acquis communautaire* in the field of Free Movement of Goods and protection of community health in accordance with the EU norms through capacity building of vaccine and sera quality control laboratories

### **2.2 Project purpose:**

Biological Control and Research Laboratory of RSNPHA is ready to apply for accreditation in preparation for designation as an EU Official Medicinal Control Laboratory (OMCL).

### **2.3 Link with AP/NPAA / EP/ SAA:**

#### **AP Priority**

The Accession Partnership with Turkey (AP) 2008 sets out the principles, priorities and conditions as decided by the Council. Under Chapter 1: Free Movement of Goods, there is the statement “address the remaining issue on regulatory data protection for pharmaceutical products” as a short-term priority expected to be completed or taken forward over the next few years. However data protection is not the only remaining issue in this area as other priorities of the AP 2006 as follows still need to be addressed. The Free Movement of Goods heading in AP 2006 covered completing the removal of technical and administrative barriers to trade, ensuring effective in-market control and free movement of goods, reinforcing existing market surveillance and conformity assessment structures with equipment and training and creating compatible administrative infrastructure. Supporting the RSNPHA laboratories will contribute to the settlement of the concerns of 2006 AP which are still in place.

#### **NPAA Priority**

The National Programme for the adoption of the *Acquis* (NPAA) 2008 under Chapter 1: Free Movement of Goods gives priority to addressing the issue on regulatory data protection for pharmaceutical products as Priority 1.4. referring to the remaining issues in the chapter. Although the alignment and the implementation of the legislation in the field of medicinal products has been improving, the priorities of the NPAA 2003 have not been sufficiently met yet with respect to implementation, inclusive of the improvement of the infrastructure of RSNPHA national reference laboratories within the framework of the analysis for authorization of medicinal products and market control.

NPAA 2008 within the scope of institutional capacity building requirements for legislative approximation and implementation as relates to Priority 1.4, refers to MoH for institutional capacity building by establishment of the Turkish National

Pharmaceuticals and Medical Device Institution scheduled for the period 2009 – 2013. Financial requirements and resources for MoH (Table 1.4.3) specify investment and training areas including quality control of pharmaceuticals.

NPAA 2008 also refers to “Restructuring of Refik Saydam Hygiene Center as National Institute of Public Health in order to meet today’s requirements and in accordance with national and international needs as Priority 28.1: Further aligning with the consumer acquis and ensuring administrative structures and enforcement capacity within Chapter 28: Consumer and Health Protection. This being scheduled for 2008-2009, also encompasses the financial requirements for investment and legislative approximation and implementation including training, consultancy and other related areas. The Biological Control and Research Laboratory of RSNPHA will serve both of the above-mentioned institutions being the only laboratory in Turkey capable of vaccine testing and authorized by the Minister of Health as “the National Control Laboratory for Vaccines and Sera” therefore strengthening of this laboratory through the twinning and supply components of this project is closely linked to NPAA 2008.

#### **2.4 Link with MIPD:**

MIPD 2008-2010 under Component I Transition Assistance and Institution Building - 1. Objectives and choices, states transposition and implementation of the acquis notably in priority areas with voluminous legislative alignment and high investments needs as agriculture, environment, justice, freedom and security, obligations stemming from the Customs Union agreement and other areas of the acquis among which Free Movement of Goods (support for quality assurance at testing and calibration laboratories) is also included. Institution building support will be provided through a twinning agreement supplemented with supply of equipment to strengthen the Biological Control and Research Laboratory of RSNPHA to prepare it for EDQM audit followed by ISO 17025 accreditation to be recognized by the European Directorate for Quality of Medicines (EDQM) as an Official Medicinal Control Laboratory (OMCL)

#### **2.5 Link with National Development Plan:**

In the 9<sup>th</sup> Development Plan (2007-2013) article 4.2. Activation of the Health Care System, it is stated that during the 244<sup>th</sup> plan period, major progress was made in health indicators such as health personnel supply, bed supply and utilization ratios, infant mortality rate and vaccination. However, the final target has not been reached yet. Article 7.3.2 Activation of Health Care System 611 points out that relying on the principle that “prevention precedes treatment”, preventive care services such as communicable diseases, mother and child health, food, consumer and environmental health will be prioritized in allocating resources.

#### **2.6 Link with national/ sectoral investment plans(where applicable):**

N/A

### **3. Description of the project**

#### **3.1 Background and justification:**

##### **Approximation and Implementation of the Acquis**

The conclusions of the Helsinki European Council in December 1999 having recognised Turkey as a candidate for membership to the European Union, the European Council agreed in December 2004 to start the accession negotiations after October 2005; Turkey as a candidate country has to approximate and implement the EU *acquis communautaire*. For the approximation of legislation in the area of Free Movement of Goods, Turkey has a head start due to the existence of the Customs Union between Turkey and the EU since 1996. According to Decision 1/95 of the EC-Turkey Association Council, completing the Customs Union, Turkey had to finalise, the harmonisation of its technical legislation, in areas of direct relevance to the Customs Union before the end of 2000.

According to the Association Council Decisions n° 1/95 and 2/97, a Framework Law relating to the preparation and implementation of the technical legislation regarding products was adopted by the Parliament on 29.06.2001, published in the Official Gazette on 11 July 2001 and entered into force on 11 January 2002. This Framework Law establishes the legal basis for full harmonisation with the EC legislation, and lays down the basic principles for product safety and the implementation of Old and New Approach Directives. It sets out the conditions of the placing on the market of the products, the liabilities of the producers and distributors, the conformity assessment bodies, notified bodies, post marketing control and inspection, the prohibition of the placing on the market of certain products, the withdrawal and destruction of the marketed products as well as the notifications relating to these arrangements.

The Framework Law is complemented by five pieces of secondary legislation covering post marketing control and control of the products, use and affixing of the CE conformity mark, working principles and procedures for conformity assessment bodies and notified bodies, their assignments, exchange of information on national measures derogating from the principle of the free movement of goods, notification procedures between Turkey and the EC regarding technical legislation. From 2002 onwards, Ministries accelerated their work regarding harmonization of the technical legislation that started with the Customs Union Decision of 1995 and also have taken significant steps in order to establish the necessary mechanisms for their implementation.

The main responsibility of the adoption and implementation of the *acquis* in the field of medicinal products lies on the Ministry of Health with Refik Saydam National Public Health Agency authorized as the national control laboratories to conduct the safety and efficacy tests required by the relevant EU legislation. Biological Control and Research Laboratory (BCRL) of the agency carrying out these tests requires training, assistance and some equipment to further develop its vaccine testing capacity, to standardize its test methods and to be accredited to raise its status to the level of an EU Official Medicinal Control Laboratory (OMCL) to ensure being designated as an OMCL in the future .

## **Refik Saydam National Public Health Agency (RSNPHA)**

The Founding Law of RSNPHA issued in 1940 (Law no: 3959) gives the agency the responsibility “to produce vaccines, sera and other biological and chemical preparations identified by the Ministry of Health” and “to control domestic and foreign preparations, vaccines, sera, other vital preparations, chemical substances and medical products in accordance with their specific legislation”. The agency is also responsible for carrying out scientific research and investigations to protect and promote public health and to combat diseases, and also for training and publications.

Biological Control and Research Laboratory of RSNPHA was established in 1982 to conduct internal quality control of the vaccines and sera produced by the agency. However vaccine production at RSNPHA was stopped in 1996 due to the heavy cost of upgrading the production techniques and implementing the GMP procedures and was replaced by imports as decided by the MoH.

At this stage, the Biological Control and Research Laboratory was designated as “the National Control Laboratory for Vaccines and Sera” by an Official Decision of the Minister of Health to carry out the required safety and efficacy tests of the imported vaccines and sera for licensing purposes (batch release) to ensure their immunization potential and to eliminate possible adverse effects on consumer health. With respect to sera production, currently RSNPHA is only producing tetanus and scorpion sera for domestic use in a total amount of approximately 100.000 vials/year.

A Draft Law restructuring RSNPHA has been prepared recently in parallel to the Draft Law establishing the Medicinal Products and Medical Devices Agency of Turkey. However these laws will not alter responsibilities of RSNPHA except for widening the scope of its fields of study and changes in its organizational chart. With respect to biological products, namely vaccines and sera, the Biological Control and Research Laboratory, being the only laboratory in Turkey capable of testing vaccines and sera, with its capacity and expertise to be further strengthened with this project, will continue its task as the National Control Laboratory for Vaccines and Sera within the new structure providing laboratory services to both agencies.

The Biological Control and Research Laboratory is equipped with sufficient number of staff who have received training on quality control of vaccines and sera within the scope of a project supported by the Japanese International Cooperation Agency (JICA) carried out during the period 1993-1998. The project has also supported the infrastructure of the laboratories with the equipment required and raised the quality of the tests carried out by the laboratory to the WHO standards. Since then, the laboratory has received some support within other programs for improvement.

The Animal Testing Research Center Project (MAT07/TR/8/15) carried out within the scope of the MATRA Programme in 2008 in cooperation with the National Institute for Public Health and the Environment of the Netherlands (RIVM) has provided further opportunities for training of the laboratory staff in animal testing and vaccine quality control procedures. The Laboratory Safety Project (MAT07/TR/8/4) also conducted in collaboration with RIVM has provided support to the laboratory staff providing training on biosafety.

The laboratory has also participated in the activities of the Good Laboratory Practice (GLP) Twinning Project (TR 0402.03) during the period 2006-2008, receiving training and assistance for implementing GLP principles in the laboratory to acquire GLP compliance. However GLP certification of the laboratory is dependent on TURKAK to be fully operational as the National GLP Monitoring Authority.

Furthermore, the staff have participated in training activities related to quality systems including ISO 17025 organised within the scope of the Health Transition Project supported by the World Bank, the in-house trainings organized by the Quality Management Unit of the agency and prepared the quality documents required. Additional training on quality systems and requirements will be provided within the scope of the Establishment of an Accredited Calibration Laboratory Project of RSNPHA under the IPA 2007 Program.

With respect to ISO 17025 accreditation, the necessary infrastructure, training and the documents are in place on a large scale, the only missing element being participation of the laboratory in the inter-laboratory proficiency testing of the European Directorate for Quality of Medicines (EDQM), a prerequisite for accreditation of the laboratory which is planned to be carried out within the twinning component of this project..

The laboratory carries out the tests required by the “Regulation on Licensing of Medicinal Products for Human Use”, published in the Official Gazette No. 25705 date: 19 January 2005. The Regulation transposing the Directive 2001/83/EC lays down the procedures and the requirements for market authorization of medicinal products, including vaccines and sera, carried out by the Ministry of Health.

BCRL is divided into nine sub-divisions conducting in vivo, in vitro, chemical, immune-chemical and physico-chemical test methods; WHO test methods are applied for in vivo tests and some alternative test methods that are being used in EU Member States are adopted. Duration of the test methods ranges from one day to 8 weeks depending on the methodology used. Information on the current situation of BCRL including the organizational chart of the laboratory with a staff list, a list of the equipment available and data related to analysed samples and applied tests are given in Annex 6: Needs Assessment and Feasibility Study. A high majority of the equipment used by BCRL in vaccine testing date back to the JICA project with some additions over the last years. The Annex also provides an outline of the problems encountered and the tests that cannot be implemented by the laboratory pointing out the possible health risks for the consumers, ie. the general public with respect to possible adverse effects and insufficient protection against diseases and also the impact on free movement of goods.

Since 1996 when RSNPHA stopped producing vaccines, the MoH has been importing the vaccines required according to the National Immunization Program from a variety of producers in Europe (France and Croatia), Asia (India, Korea, Indonesia), Africa (Egypt) and the USA, the total amount being approximately 70-80 million doses per year. The quantity and the types of the vaccines imported has been increasing continuously since the very beginning and the budget allocated by the MoH for immunization has also been increasing during the last couple of years. This of course leads to an increasing workload of the BCRL in terms of both the number and the

variety of the tests conducted and the related testing costs. Annex 6 also provides data related to the vaccine import of the MoH and the tests carried out by the laboratory over the years from which can be derived some specific conclusions; to give an example, while in 2005 only 5 to 6 series of combined vaccines were analysed by BCRL, in 2008 the types of vaccines imported added up to 6.000.000 doses and the number of vaccine products was 85 series

The Immunization Policy of the Ministry for the period 2009 to 2013, as also demonstrated by the MoH Strategic Plan, foresees a further increase of the scope of the National Immunization Program, thus leading to an increase in the quantity and the types of the vaccines to be imported and consequently analysed in this period. As an example, the Ministry will be including Hepatitis A and Rotavirus vaccines in the National Immunization Program which will bring an 80 to 90 fold increase in the product series to be tested. Thus to be able to respond to the needs of the Ministry within the coming years, RSNPHA aiming to strengthen its BCRL has planned to receive EU support through this project proposal.

Currently in Turkey there is no production of vaccines and thus no export to be considered. RSNPHA has explored possible interest of the pharmaceuticals industry in vaccine production in the late 1990's, however due to the costly process and possibly the low profit level expected, the private sector has not shown much interest. Meanwhile although there is no more vaccine production within RSNPHA, its Founding Law still in force foresees vaccine production to protect public health and the organization chart still encompasses the Vaccine Production Department. The MoH on the other hand is planning to resume vaccine production in Turkey; initially about 5 or 6 vaccine types are planned to be imported in bulk to be bottled and packaged in Turkey. However the fact that the BCRL has not yet acquired ISO 17025 accreditation which is necessary to be an EDQM recognized OMCL and to provide batch release testing of produced vaccines, is an important obstacle standing in the way of these plans.

Taking into consideration the continuous expansion of the types and the increasing amount of the vaccines imported in line with the policy and strategic plans of the Ministry and the requirement for ISO 17025 accreditation of the laboratory to respond to the needs of future domestic production, it is obvious that the BCRL needs to standardize its methodologies, implement additional test methods, set up new laboratories with new equipment, switch to alternative test methods where possible (to comply with the EU legislation related to the protection of animals), apply less time consuming European Pharmacopoeia test methods instead of some time consuming WHO methods currently used, participate in inter-laboratory proficiency testing of the EDQM and have the capacity to carry out more tests in parallel to reduce the testing time for products. This requires further training, assistance and equipment also to replace some of the equipment dating back to over a decade. Data related to the equipment required identifying the reasons, objectives and expected results including their contribution to the health and well being of the community and the free movement of goods are given in Annex 6. It is considered that, to raise the status of the BCRL to that of an EU Official Medicinal Control Laboratory (OMCL) in terms of laboratory functions, the most appropriate route would be through a twinning project with an EU OMCL as the twinning partner. The laboratory already has the will, the necessary infrastructure and the staff to carry out this project with a strong



support provided by the International Relations, EU and Project Department of RSNPHA for implementation and monitoring of the Project.

As there is no domestic vaccine production, no importers other than the MoH and no laboratories alternative to the BCRL available in Turkey for outsourcing, the only stakeholder is the MoH. The general public targeted in the Immunization Program have to consult the MoH for any complaints or concerns, thus no stakeholders other than the MoH have been consulted at the stage of preparation of the project proposal.

The safety and efficacy testing of vaccines is crucial for public health; any incompliance affecting directly the health and well being of the people involved or reducing their immunity for the target diseases. The consumers with this respect are in most cases babies and children. BCRL is the only laboratory that applies these tests for batch release of the vaccines imported by the MoH which is the only importing authority. Non-ability to perform certain tests by the laboratory poses a serious health risk for the community. Strengthening the laboratory will certainly benefit the whole population with regard to protection and promotion of public health. On the other hand, capacity building and accreditation of the laboratory to become an internationally recognized OMCL will also benefit the Free Movement of Goods.

To quote some major points demonstrating the importance of the project for consumer protection and the free movement of goods; the MoH is planning to include in the immunization program the Rotavirus, Hepatitis A HPV, typhoid polysaccharide vaccines. The results of the project will enable testing of these vaccines for batch release enabling a controlled immunization to protect public health and a reduction of the incidence of these diseases in the community. It will also contribute to the free movement of these vaccines of European origin. On the other hand, application of the European Pharmacopoeia test methods and conducting parallel testing for vaccines will result in a reduction of the time required for the tests that will end up in a faster release of the samples and their availability on the market benefiting the producer as well.

Reaching status of an OMCL through standardization and accreditation of the test methods will increase the demand for batch release from both EU and non-EU countries and most vaccine producing countries being outside the EU will have an economic contribution. This will help to meet the conditionality for future domestic vaccine production in Turkey as well. The project will provide an increase in the alternative test methods replacing animal testing helping to reduce the laboratory animals used in line with the EU legislation on the protection of animals and contributing to the protection of the environment.

The project is designed as a twinning with a supply component. The MS Twinning Partner should be an experienced OMCL to ensure realization of the aimed project results laying down a detailed work plan in cooperation with the beneficiary institution within the twinning contract. The supply and the twinning components are designed to run in parallel; the equipment will be installed by the end of the 4th quarter of the Project duration and the trainings will be completed by the end of the 6th quarter. A delay in the supply component is not expected and considered a risk as the necessary laboratory infrastructure is already in place, the human resources with sufficient commitment and a strong support from the upper management is available and technical specifications of the equipment are already prepared as given in Annex 7 of the Project Fiche ready to be incorporated into the tender dossier.

### **3.2 Assessment of project impact, catalytic effect, sustainability and cross border impact:**

#### **Project Impact**

The project will have a significant impact on the social society with respect to protection and promotion of consumer health and reduction of the disease incidence rates, to the free movement of goods through reducing the time required for testing for batch release and introducing new techniques and establishing new laboratories to analyse a wider range of vaccine types. The availability of an accredited and EDQM approved OMCL with the authority of testing for licensing (batch release) of domestically produced vaccines will open the way to vaccine production in Turkey as planned by the MoH and export opportunities for the sector. It will also have an impact on the protection of the environment through reducing the animals used for testing.

#### **Catalytic Impact**

The financial assistance to be provided by the EU will have a catalytic effect in the implementation of the related acquis. The presence of a trustworthy accredited OMCL will help to motivate the pharmaceutical companies in producing vaccines taking into consideration the large quantities of vaccines imported and also the future export capacity. The BCRL will also provide leadership in assisting and supporting the internal quality control laboratories of the producers.

#### **Sustainability**

Being the only laboratory in Turkey conducting batch release analysis of vaccines and sera, BCRL will also provide laboratory services to the “National Drugs and Medical Devices Agency” to be established in accordance with the NPAA. As the national immunization programs have been showing a trend of continuous increase both in quantity and type of the vaccines used and the tendency is demonstrated to continue in the 2009-2013 program, a well equipped, upgraded, standardized, accredited laboratory for vaccine and sera testing and batch release approved as a member of the international OMCL network will ensure sustainability of the project results.

RSNPHA will ensure sustainability of the laboratory and its accreditation by financing the maintenance and running costs of the equipment, additional supplies, consumables, training, audits and payments for ISO 17025 certification. The agency in addition to the national budget has a revolving fund the income being generated by the fees for testing and other services provided by the agency. In 2008, the income generated by testing of vaccines by BCRL was approximately 3.350.000 TL whereas the amount spent from the budget for the maintenance, repair costs and consumables of the laboratory amounted to 200.000 TL.

#### **Cross-border impact**

The project resulting in an accredited OMCL will have a positive cross-border impact as the Member States and the neighboring non-EU countries are expected to benefit from the laboratory for batch release of the vaccines and sera they produce facilitating international trade. Future producers in Turkey will also benefit from the laboratory as it will open the way for exporting their products.

### 3.3 Results and measurable indicators:

<b>Project purpose</b>	<b>Objectively verifiable indicators</b>
Biological Control and Research Laboratory of RSNPHA is ready to apply for accreditation in preparation for designation as an EU Official Medicinal Control Laboratory (OMCL)	<p>Variety of the test types increased 20 % by the end of the project</p> <p>80 % of demands for tests met by the end of the project</p> <p>80 % of repetitious tests declined by the end of the project</p> <p>BCRL equipped with the knowledge and infrastructure to give internationally recognized Batch Release Certificates</p>
<b>Results</b>	<b>Objectively verifiable indicators</b>
<p>1. Test results obtained accepted by the European Directorate of Quality of Medicine (EDQM).</p> <p>2. BCRL audited by EDQM, application for ISO 17025 certification submitted to TURKAK</p>	<p>Inter-laboratory proficiency tests completed successfully in the 8th quarter verified by the official statement of EDQM and the list of OMCL's of the EDQM</p> <p>Audit report by EDQM received, application for ISO 17025 inspection submitted in the 8th quarter</p>

### 3.4 Activities:

#### 3.4.1. Installation of the equipment supply will be completed by the 4th quarter

#### 3.4.2. International trainings for the lab personnel will be completed by the end of 3rd quarter of the Project

3.4.2.1. Study visits to a different OMCL;

3.4.2.2. BCG vaccine (Virulent mycobacteria' count of viable units after freeze-drying, temperature stability ve PPD test tuberculin identity and potency test)

3.4.2.3. Diphtheria, Tetanus (challenge, Pertussis (acellular component) Identity and Potency

3.4.2.4. In vivo and invitro potency test for Poliomyelitis (Inactivated) single and combined vaccine forms

- 3.4.2.5.Total and Free PRP tests for Hemophilus type B conjugate vaccine (adsorbed) single and combined vaccine forms;
- 3.4.2.6.In-vivo and in-vitro potency test for Hepatitis B (rDNA) vaccine (adsorbed) and Hepatitis A (Inactivated) single and combined vaccine forms;
- 3.4.2.7.Measles, mumps, rubella, varicella combined vaccine Identity ,virus amount, thermo stability for each component;
- 3.4.2.8.Meningococcal polysaccharide vaccine Assay content for each polysaccharide, identity for each type;
- 3.4.2.9.Rabies vaccine and immune sera potency test and inactivation test;
- 3.4.2.10.Non-destruction test for all biological products (post operative procedures
- 3.4.2.11.Detection of aluminum content by physico-chemical tests, detection of free formaldehyde content, residual humidity, LAL test, 2-fenoksi ethanol content (GC), phenol /m-cresol content, tiomersal content;
- 3.4.2.12.Sterility test for all biological products;
- 3.4.2.13.Diphtheria, tetanus, scorpion, snake anti-serums identity and potency tests,
- 3.4.2.14.Human Papilloma virus (rDNA) vaccine: Identity,in-vivo and in-vitro potency test;
- 3.4.2.15.Rotavirus vaccine virus content, total virus content;
- 3.4.2.16.Typhoid Polysaccharide vaccine: O-acetyl groups content, Vi polysaccharide content (assay), molecular size;
- 3.4.2.17.Osmalality, residual BSA, Degree of adsorption, ovalbumin ,particular size, sodium chloride(NaCl), residual human albumin content;
- 3.4.2.18.ELISA and ToBI implementation in tetanus vaccine potency test;
- 3.4.2.19. Additional study tours will be organized and training areas covered if necessary

**3.4.3. By the end of the 6th quarter of the Project, practical trainings to be supported by experts will be completed in the Biological Control and Research Laboratories**

- 3.4.3.1.BCG vaccine (Virulent mycobacteria' count of viable units after freeze-drying, temperature stability ve PPD test tuberculin identity ve potency test)
- 3.4.3.2.Diphtheria, Tetanus (Challenge), pertussis (acellular component) Identity and Potency, invivo and invitro potency test for Poliomyelitis (Inactivated) single and combined vaccine forms;
- 3.4.3.3.Total and Free PRP tests for Hemophilus type B conjugate vaccine (adsorbed) single and combined vaccine forms;
- 3.4.3.4.In-vivo and in-vitro potency test for Hepatitis B (rDNA) and Hepatitis A (Inactivated) vaccine (adsorbed) single and combined vaccine forms
- 3.4.3.5.Measles, mumps, rubella, varicella combined vaccine Identity ,virus content, termostabilite for each component;
- 3.4.3.6.Meningococcal polysaccharide vaccine Assay content for each polysaccharide, identity for each type;
- 3.4.3.7.Rabies vaccine (in vivo) and immune sera potency test (in vivo and in vitro) and inactivation;
- 3.4.3.8.Non-destruction tests for all biological products (post operative procedures) ;
- 3.4.3.9.Detection of aluminum content by physico-chemical tests, detection of free formaldehyde content, residual humidity, LAL test, 2-fenoksi ethanol content (GC), phenol /m-cresol content, tiomersal content ;
- 3.4.3.10.Sterility test for all biological products;

- 3.4.3.11. Diphtheria, tetanus, scorpion, snake anti-serums identity and potency tests,
- 3.4.3.12. Human Papilloma virus (rDNA) vaccine: Identity, in-vivo ve in-vitro potency test;
- 3.4.3.13. Rotavirus vaccine virus content, total virus content;
- 3.4.3.14. Typhoid Polysaccharide vaccine: O-acetyl groups content, Vi polysaccharide content (assay), molecular size;
- 3.4.3.15. Osmolality, residual BSA, Degree of adsorption, ovalbumin ,particular size, sodium chloride (NaCl), residual human albumin content;
- 3.4.3.16. ELISA and ToBI implementation in tetanus vaccine potency test;
- 3.4.3.17. Additional training areas will be covered if necessary

**3.4.4 Assistance will be provided by the Twinning Partner in preparation for and implementation of the EDQM Inter-laboratory proficiency tests**

**3.4.5. Assistance will be provided by the Twinning Partner in preparation for the EDQM audit**

**3.4.6. Assistance will be provided by the Twinning Partner in preparation for ISO 17025 accreditation to be certified by the Turkish Accreditation Agency (TURKAK)**

**3.4.7. By the end of 8th quarter BCRL will be audited by EDQM and will apply for ISO 17025 accreditation**

- 3.4.7.1. RSNPHA will apply for an EDQM audit.
- 3.4.7.2. Corrective measures will be taken for the incompliances detected by EDQM
- 3.4.7.3. Application for ISO 17025 accreditation certification will be submitted to the Turkish Accreditation Agency (TURKAK)

**3.4.8. Kick-off and Final Meetings will be held for the Project, Steering Committee meetings will be held in each quarter and Interim Quarterly Reports will be prepared.**

**3.5 Conditionality and sequencing:**

N/A

**3.6 Linked activities**

**JICA Project**

Japanese International Cooperation Agency (JICA) project, which was launched between RSNPHA and the Japanese International Cooperation Agency (JICA) in 1993, was completed in 1998 and personnel working in the Biological Control and Research Laboratory were trained in both Ankara/Turkey and in Japan regarding the quality control of vaccines used in common immunization. Under the JICA Project, laboratories were provided with materials, supply, equipment and infrastructure and technical assistance.

**Animal testing Center Project (MAT07/TR/8/15)**

The project carried out within the MATRA Program of the Netherlands in collaboration with the National Vaccine Institute (NVI) and the National Institute for

Public Health and the Environment of the Netherlands (RIVM) provided training on quality control of vaccines, laboratory animal science and alternative test methods

#### **Laboratory Safety Project (MAT07/TR/8/4)**

The project carried out within the MATRA Program of the Netherlands in collaboration with the National Institute for Public Health and the Environment of the Netherlands (RIVM) provided training on biosafety in laboratories

#### **GLP Twinning Project (TR0402.03)**

The project coordinated by RSNPHA and carried out in collaboration with the Slovak Republic as the MS Twinning Partner, provided training and assistance for GLP compliance to 5 state-owned laboratories including the BCRL. The laboratory has gained the knowledge and the infrastructure to achieve GLP compliance and is waiting for the Turkish Accreditation Agency (TURKAK) to become fully operational as the National GLP Monitoring Authority to conduct GLP inspections and to issue GLP compliance certificates..

#### **Health Transition Project of the World Bank**

The project is supporting restructuring of RSNPHA and establishment of its quality infrastructure providing training for the staff on quality systems and quality management.

#### **Accredited Calibration Laboratory Project (TR0702.10)**

The project carried out within the IPA 2007 program aims establishment of an accredited calibration laboratory within RSNPHA. Laboratory staff will be participating in the trainings of the project on a variety of quality systems and calibration. The established calibration laboratory will support ISO 17025 accreditation of the BCRL as well.

### **3.7 Lessons learned**

The GLP Twinning project experience has shown us the importance of the experience of the Twinning Partner in conducting a twinning project in addition to being experienced in the technical aspects of the project. With this Project, we will apply the lessons learned from the GLP project also with respect to coordination of the activities, organization of meetings and training programs, preparation of reports, selection of trainees and administration of the project. Other projects have also provided us experiences in supply and TA which we will be using in implementation of the project. Personnel to be trained shall be selected among those, who work in the laboratory and the trained personnel will be reserved in the place of assignment. Devices and equipment will be installed and validated right before the start of practical trainings and a committed project team shall be in place for a successful project.

#### 4. Indicative Budget (amounts in EUR)

			SOURCES OF FUNDING										
			TOTAL EXP.RE	TOTAL PUBLIC EXP.RE	IPA COMMUNITY CONTRIBUTION		NATIONAL PUBLIC CONTRIBUTION						PRIVATE CONTRIBUTION
ACTIVITIES	IB (1)	INV (1)	EUR (a)=(b)+(e)	EUR (b)=(c)+(d)	EUR (c)	% (2)	Total EUR (d)=(x)+(y)+(z)	% (2)	Central EUR (x)	Regional/Local EUR (y)	IFIs EUR (z)	EUR (e)	% (3)
Activity 1													
Twining contract	X	-	2.085.000	2.085.000	1.980.750	95%	104.250	5%	104.250				-
Activity 2													
Supply contract	-	X	1.502.200	1.502.200	1.276.870	85%	225.330	15%	225.330				-
.....													
<b>TOTAL IB</b>			<b>2.085.000</b>	<b>2.085.000</b>	<b>1.980.750</b>		<b>104.250</b>		<b>104.250</b>				
<b>TOTAL INV</b>			<b>1.502.200</b>	<b>1.502.200</b>	<b>1.276.870</b>		<b>225.330</b>		<b>225.330</b>				
<b>TOTAL PROJECT</b>			<b>3.587.200</b>	<b>3.587.200</b>	<b>3.257.620</b>		<b>329.580</b>		<b>329.580</b>				

NOTE: DO NOT MIX IB AND INV IN THE SAME ACTIVITY ROW. USE SEPARATE ROW

Amounts net of VAT

(1) In the Activity row use "X" to identify whether IB or INV

(2) Expressed in % of the **Public** Expenditure (column (b))

(3) Expressed in % of the **Total** Expenditure (column (a))



## 5. Indicative Implementation Schedule (periods broken down per quarter)

Contracts	Start of Tendering	Signature of contract	Project Completion
Twining Contract 1.1	2010 II Q	2011 I Q	2013 I Q
Supply Contract 1.2	2010 II Q	2011 I Q	2012 I Q

All projects should in principle be ready for tendering in the 1<sup>ST</sup> Quarter following the signature of the FA

## 6. Cross cutting issues (where applicable)

### 6.1 Equal Opportunity:

Equal participation of women and men will be secured through appropriate information and publicity material, in the design of the project and access to the opportunities it offers. An appropriate men/women balance will be sought on all the managing bodies and activities of the programme and its projects. RSHC (as other public institutions which have academic functions in Turkey) is in a good position with respect to equal opportunity. The ratio of women to men in RSHC (49:51) is traditionally high and especially in the field of pharmaceuticals the majority of the laboratory personnel is women. Equal opportunity will be ensured by this situation. Trainees will be selected in accordance with their professional background and laboratory assignments. Records of professionals' participation in all project related activities will reflect this and will be kept with the project documentation.

### 6.2 Environment :

The project consists of a twinning and supply of equipment for BCRL and will not have a detrimental impact on the environment. Furthermore by replacing some animal tests by alternative tests will also contribute to the protection of the environment by reducing the number of laboratory animals used for testing. ISO 17025 accreditation is one of the project targets which will ensure disposal of the chemical wastes to be in conformity with the standard while for disposal of biological waste, legislative requirements of the Ministry of Environment and Forestry are followed.

### 6.3 Minorities :

According to the Turkish Constitutional System, the word minorities encompasses only groups of persons defined and recognized as such on the basis of multilateral or bilateral instruments to which Turkey is a part. This project has no negative impact on minority and vulnerable groups.

### 6.4 Civil Society

BCRL is not directly related to the civil society; in relation to producers there is no vaccine production in Turkey and the Ministry is the only authority who imports the vaccines. As regards the consumers, any complaints, problems or adverse effects are reported to the Ministry and the Ministry consults RSNPHA for comments which are discussed by commissions composed of scientists and if necessary the samples are re-tested by the BCRL. The Project is too technical to involve civil society however during its implementation, if deemed necessary, representatives of non-governmental organizations such as the Infectious Diseases Association and the civil society will be consulted and involved in the project activities.

## ANNEXES

- 1- Log frame in Standard Format
- 2- Amounts contracted and Disbursed per Quarter over the full duration of Programme
- 3- Description of Institutional Framework
- 4 - Reference to laws, regulations and strategic documents:
  - Reference list of relevant laws and regulations
  - Reference to AP /NPAA / EP / SAA
  - Reference to MIPD
  - Reference to National Development Plan
  - Reference to national / sector investment plans
- 5- Details per EU funded contract (\*) where applicable:
  - For *TA contracts*: account of tasks expected from the contractor
  - For *twinning covenants*: account of tasks expected from the team leader, resident twinning advisor and short term experts
  - For *grants schemes*: account of components of the schemes
  - For *investment contracts*: reference list of feasibility study as well as technical specifications and cost price schedule + section to be filled in on investment criteria (\*\*)
  - For *works contracts*: reference list of feasibility study for the *constructing works* part of the contract as well as a section on investment criteria (\*\*); account of services to be carried out for the *service part* of the contract

(\*) non standard aspects (in case of derogation to PRAG) also to be specified

(\*\*) section on investment criteria (applicable to all infrastructure contracts and constructing works):

  - Rate of return
  - Co financing
  - compliance with state aids provisions
  - Ownership of assets (current and after project completion)
- 6- Needs Assessment, Feasibility Study data and Market Survey
- 7- Technical Specifications

**ANNEX 1: Logical framework matrix in standard format**

LOGFRAME PLANNING MATRIX FOR Project Fiche	Program name and number	
	Quality Control Tests for Human Vaccines and Sera	
	Contracting period expires	Disbur
	Two years after the signature of the Financing Agreement	1 year of cont
	Total budget : 3.587.200€	IPA bu

Overall Objective	Objectively verifiable indicators	Sources of Verification	
Implementation of the acquis communautaire in the field of Free Movement of Goods and protection of community health in accordance with the EU norms through capacity building of vaccine and sera quality control laboratories	To become an OMCL which is recognized by the EDQM (European Directorate of Quality of Medicine) by the end of 2013	EDQM (European Directorate Quality Of Medicine) OMCL (Official Medicinal Control Laboratory) list	
Project purpose	Objectively verifiable indicators	Sources of Verification	Assum
Biological Control and Research Laboratory of RSNPHA is ready to apply for accreditation in preparation for designation as an EU Official Medicinal Control Laboratory (OMCL)	Variety of the test types increased 20 % by the end of the project  80 % of demands for tests met by the end of the project  80 % of repetitious tests declined by the end of the project  BCRL equipped with the knowledge and infrastructure to give internationally recognized Batch Release	RSNPHA statistics  Interim Quarterly Reports  Minutes of Steering Committee Meetings  Final Report	

	Certificates		
<b>Results</b>	<b>Objectively verifiable indicators</b>	<b>Sources of Verification</b>	<b>Assum</b>
<p>1. Test results accepted by the European Directorate of Quality of Medicine (EDQM).</p> <p>2. BCRL audited by EDQM, application for ISO 17025 certification submitted to TURKAK</p>	<p>Acceptance of inter-laboratory proficiency tests by EDQM in the 8th quarter</p> <p>BCRL audited and approved by EDQM, application for ISO 17025 inspection submitted in the 8th quarter</p>	<p>Official statement of EDQM</p> <p>Project interim quarterly reports</p> <p>Audit report of EDQM</p> <p>Application for ISO 17025 certification</p>	<p>Equipm calibrat</p> <p>Trainin 6th qua</p>
<b>Activities</b>	<b>Means</b>	<b>Costs</b>	<b>Assum</b>
<p>3.4.1 Installation of the equipment supply will be completed by the 4th quarter</p> <p>3.4.2. International trainings for the lab personnel will be</p>	<p>Supply contract</p>	<p>Supply contract 1.502.200 € (IPA 1.276.870 €)</p> <p>Twinning contract 2.085.000 € (IPA 1.980.750 €)</p>	<p>Adequ supply</p> <p>Comm coordin</p>

<p>completed by the end of 3rd quarter of the Project</p>	<p>Twinning contract</p>	<p>Total 3.587.200 €</p>	<p>Adequ receiv</p>
<p>3.4.3 By the end of the 6th quarter of the Project, practical trainings to be supported by experts will be completed in the Biological Control and Research Laboratories</p>	<p>Twinning contract</p>		
<p>3.4.4 Assistance will be provided by the Twinning Partner in preparation for and implementation of the EDQM Inter-laboratory proficiency tests</p>	<p>Twinning contract</p>		
<p>3.4.5. Assistance will be provided by the Twinning Partner in preparation for the EDQM audit</p>			
<p>3.4.6. Assistance will be provided by the Twinning Partner in preparation for ISO 17025 accreditation to be certified by the Turkish Accreditation Agency (TURKAK)</p>			
<p>3.4.7. By the end of 8th quarter BCRL will be audited by EDQM and will apply for ISO 17025 accreditation</p>			
<p>3.4.8. Kick-off and Final Meetings will be held, Steering Committee meetings will be held in each quarter and Interim Quarterly Reports will</p>			

be prepared.

--	--