

**Laboratory Training Courses for the Staff of Roszdravnadzor's National Network
of Medicines Quality Control Laboratories**

**Saint Petersburg, Russia
July 9-14, 2012**

Trip Report

**Kirill Burimski, Program Manager and Regional Champion, Russia and NIS
Natalia Davydova, Scientific Liaison
Oksana Dmitrenok, Consultant
Natalia Morozova, Consultant
Kornepati Ramakrishna, Scientist IV
Sujatha Ramakrishna, Scientific Liaison**

Promoting the Quality of Medicines Program

Implemented by the U.S. Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852 USA
Tel: (+1) 301-816-8160
Fax: (+1) 301-816-8374
Email: pqm@usp.org

Cooperative Agreement # GHS-A-00-09-00003-00

Sponsoring USAID Mission: USAID/Russia

Grantee: Promoting the Quality of Medicines Program (PQM) Program

Author(s) Name: PQM Staff

Language: English

Date of Publication: August 23, 2012



This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID), under Cooperative Agreement No. GHS-A-00-09-00003-00. The contents are the responsibility of the Promoting the Quality of Medicines Program, implemented by the U. S. Pharmacopeia, and do not necessarily reflect the views of USAID or the United States Government.

Executive Summary

With support from USAID/Russia, the Promoting the Quality of Medicines (PQM) Program, United States Pharmacopeia (USP), and Roszdravnadzor (the Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation) developed laboratory training courses and trained the staff of Roszdravnadzor's national network of medicines quality control laboratories in Saint Petersburg, Russia July 9-14, 2012.

Four training courses on validation of analytical methods, medicine sample preparation, atomic absorption spectroscopy, and identification of residual organic solvents were developed to suit the needs of the Roszdravnadzor staff and translated into Russian by experts in relevant fields. Thirty-four individuals representing ten regional/federal district labs participated in the training courses, which were held at Roszdravnadzor's Saint Petersburg Medicines Quality Control Laboratory.

By the end of the training, participants were competent in validation and verification of analytical methods, sample preparation, atomic absorption spectroscopy and identification of residual organic solvents by gas chromatography.

Table of Contents

| | |
|--|----|
| <u>Acknowledgements</u> | 4 |
| <u>Acronym</u> | 5 |
| <u>Background</u> | 6 |
| <u>Purpose of Trip</u> | 6 |
| <u>Source of Funding</u> | 6 |
| <u>Overview of Activities</u> | 6 |
| <u>Next Steps and Conclusion</u> | 8 |
| Annex 1: List of Participants | 10 |
| Annex 2: Training Program Agenda | 11 |
| Annex 3: Thank you Letter from Roszdravnadzor | 12 |
| Annex 4: Validation of analytical methods evaluation | 14 |
| Annex 5: Basic approaches to sample preparation evaluation | 15 |
| Annex 6: Applications of Atomic Absorption Spectroscopy evaluation | 16 |
| Annex 7: Identification of residual organic solvents by GC evaluation | 17 |

About PQM

The Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID), is the successor of the Drug Quality and Information (DQI) program implemented by the United States Pharmacopeia (USP). PQM is USAID's response to the growing challenge posed by the proliferation of counterfeit and substandard medicines. By providing technical leadership to developing countries, PQM helps build local capacity in medicine quality assurance systems, increase the supply of quality medicines to priority USAID health programs, and ensure the quality and safety of medicines globally. This document does not necessarily represent the views or opinions of USAID or the United States Government. It may be reproduced if credit is given to PQM and USP.

ACKNOWLEDGEMENTS

We would like to thank:

- All of the training participants
- Dr. E.A. Telnova, Dr. V.V. Kosenko, Mr. K.Y. Belanov, and Ms. A. Nikitina of Roszdravnadzor, for their collaboration and support
- The staff of Saint Petersburg Medicines Quality Control Laboratory, for hosting the workshop
- Dr. A.V. Titova, Roszdravnadzor's Federal State Budgetary Institution IMCESACMP (Information and Methodological Center for Expertise, Stocktaking and Analysis of Circulation of Medical Products), for her assistance in preparing the training
- Mr. William Slater, Dr. Nikita Afanasiev, and Dr. Marina Kulikova of USAID/Russia, and Mr. Anthony Boni and Dr. Maria Miralles at USAID headquarters in Washington, D.C. for their support
- Our USP colleagues, especially Ms. Helen Kharab and Drs. Patrick Lukulay and Kennedy Chibwe, for their guidance and helpful insights throughout the preparation of this training, and continuing support

ACRONYMS

| | |
|-----------|--|
| AAS | Atomic Absorption Spectroscopy |
| DQI | Drug Quality and Information Program |
| GC | Gas Chromatography |
| IMCESACMP | Federal State Budgetary Institution "Information and Methodological Center for Expertise, Stocktaking and Analysis of Circulation of Medical Products" |
| MOU | Memorandum of Understanding |
| MQCL | Medicines Quality Control Laboratory |
| PQM | Promoting the Quality of Medicines program |
| RZN | Rosdravnadzor, Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation |
| USAID | United States Agency for International Development |
| USP | United States Pharmacopeia |

Background

The United States Pharmacopeia (USP) has been working in Russia for nearly two decades, through several mechanisms funded by the United States Agency for International Development (USAID).

In 2009, USP and the Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation—known as “Roszdravnadzor” or “RZN”—signed a Memorandum of Understanding (MOU). In one of the provisions, the two organizations agreed to “explore joint and mutually beneficial education and training programs on compendial and allied topics, including proficiency testing, execution of compendial procedures, good laboratory practices, testing to conform to Good Manufacturing Practices, marketplace surveillance, and execution of approaches to combat counterfeit and substandard medicines.”

In 2010-2011, twenty training courses on topics ranging from good laboratory practices to the theory and practical application of advanced analytical test methods were conducted at RZN’s Scientific Centre for Expertise of Medical Products in Moscow and at the Medicines Quality Control Laboratory (MQCL) in Rostov-on-Don. During the courses, laboratory testing of anti-tuberculosis medicines was conducted, whenever possible. Responses from the participants’ evaluations showed their great interest and enthusiasm for attending other courses, including Gas Chromatography (GC), Atomic Absorption Spectroscopy (AAS), and others. In letters to USAID/Russia and USP, Dr. Telnova, Acting Director of RZN, expressed appreciation for the training and conveyed the agency’s wish to collaborate on additional trainings in the future. For 2012, RZN requested an additional four training courses on analytical testing to be conducted at the Saint Petersburg MQCL for the analysts of the recently established regional quality control laboratories.

USP developed the training materials and had them translated into Russian by experts in relevant fields. USP and RZN jointly refined the presentations, tailoring them to suit the needs of the RZN staff.

Purpose of Trip

USP staff traveled to Russia to conduct four trainings for the staff of RZN’s national network of MQCLs.

Source of Funding

This trip was supported by USAID/Russia through the Promoting the Quality of Medicines (PQM) Program. To minimize costs, RZN covered the expenses of its participants, including travel and accommodations, and provided the venue for the training free of charge.

Overview of Activities

Title of Trainings:

- Validation of analytical methods
- Basic approaches to sample preparation
- Atomic Absorption Spectroscopy (AAS)
- Identification of residual organic solvents by Gas Chromatography (GC)

An overview of the trainings is given in the table below:

| Item | Description |
|---|---|
| Specific Objectives/ Expected Outcomes | <ul style="list-style-type: none"> • Presentations and hands-on training on validation and verification of analytical methods, sample preparation, AAS, and GC will be given • By the end of the trainings, participants will be able to understand the importance of appropriate validation and verification, sample preparation, AAS, and GC |
| Venue/Location | Saint Petersburg MQCL |
| Organizers and Sponsors | <ul style="list-style-type: none"> • PQM • USAID/Russia • Roszdravnadzor • IMCESACMP • Saint Petersburg MQCL |
| Trainers and Facilitators | <ul style="list-style-type: none"> • Dr. Kornepati Ramakrishna • Dr. Sujatha Ramakrishna • Dr. Natalia Davydova • Dr. Kirill Burimski • Dr. Oksana Dmitrenok • Ms. Natalia Morozova |
| Trainees | 34 individuals from ten regional/federal district MQCLs participated. See the participant list in Annex 1 for detailed information. |
| Agenda | See Annex 2 for detailed information. |
| Opening Ceremony | <ul style="list-style-type: none"> • Kirill Burimski, PQM • Oksana Dmitrenok, PQM • Anna Titova, IMCESACMP |
| Courses/Modules | <p>Validation of analytical methods (Theory and discussion) – two days</p> <p>Basic approaches to sample preparation – two days</p> <ul style="list-style-type: none"> • Sample preparation (Theory and discussion) • Laboratory skills (Theory and discussion) • Sample preparation (hands-on) <p>AAS – two days</p> <ul style="list-style-type: none"> • AAS Module I (Theory and group discussion) • AAS Module I (hands-on) • AAS Module II (Theory and group discussion) • AAS Module II (hands-on) <p>Identification of residual organic solvents by Gas Chromatography – two days</p> <ul style="list-style-type: none"> • Theory and discussion • Identification of residual organic solvents (hands-on) |

| | |
|---------------------|--|
| Closing Ceremony | <ul style="list-style-type: none"> • Dr. Kornepati Ramakrishna • Dr. Sujatha Ramakrishna • Dr. Natalia Davydova • Dr. Kirill Burimski <p>Certificates of Completion were distributed to the participants.</p> |
| Equipment Provided | Analytical columns for GC, GC Inlet liner, GC ferrules, GC septa, headspace vials, crimp caps/silicone septa, Manual crimper, USP reference standards |
| Training Evaluation | <p>Following the training, Dr. Telnova, Acting Director of RZN, sent a letter to USAID/Russia conveying the agency's thanks and their wish to collaborate with USP in the future (see Annex 3).</p> <p>Participants evaluated the training as very useful, informative, and well-organized. The participants' evaluations of the training courses can be found in Annexes 4-7.</p> |
| Outcomes/Conclusion | The training courses were successful and met the intended objectives. The participants were dedicated and showed great interest in learning all the aspects of the training program. |
| Next Steps | RZN requested that USP continue offering training courses in 2013. USP and RZN will collaborate to develop a list of training courses for the staff of regional MQCLs. |

Training course: Validation of analytical methods

This course provided participants with an overview of validation, and the participants discussed general concepts about analytical method validation as applied to the assay, impurity determination and limit test. Methods of evaluation and requirements for various validation parameters were also presented to enable the participants to design a protocol for executing a method validation. For the majority of the attendees, this was their first introduction to the topic of analytical method validation. The participants acquired sufficient knowledge from the course that, with some guidance, they can plan and perform a method validation. 34 participants attended the course; 33 participants evaluated the course (see **Annex 4**).

Training course: Basic approaches to sample preparation

This course covered topics such as liquid-liquid extraction, solid-liquid extraction, and dispersion and dissolution of oral dosage forms. In addition, basic laboratory techniques were described, along with a laboratory demonstration of a sample preparation from an oral dosage form. 34 participants attended the course; 30 participants evaluated the course (see **Annex 5**).

After completing the first two courses, 19 attendees continued participating in the training. They were divided into two smaller groups. Group #1 attended the training on AAS, while Group #2 attended the training on identification of residual organic solvents by GC.

Training course: AAS

This course introduced AAS concepts, method development and validation, instrument troubleshooting, and pharmaceutical applications to the participants. The morning sessions of the course consisted of lectures focused on theory; the afternoon sessions were devoted to practical experience in the laboratory. Most of the participants had little or no knowledge of AAS. After the course, all the participants left with sufficient knowledge to use AAS for testing the elemental impurities in pharmaceutical samples and also learned how to effectively operate the instrument. Nine participants attended and evaluated the course (see *Annex 6*).

Training course: Identification of residual organic solvents by GC

This course helped participants understand how to apply GC to the identification of organic solvents, to better understand the principles of headspace analysis, and how to optimize the parameters affecting headspace results. Through the lectures and laboratory applications, participants learned how to apply new guidelines to existing and validated methods. Eleven participants attended the training; ten participants evaluated the course (see *Annex 7*).



List of Participants

Employees of MQCLs participating in the PE training courses on July 9-14, 2012

| Last name, First name | Position |
|------------------------------|---|
| Ekaterinburg MQCL | |
| 1. Levchenko, Svetlana | Senior Analyst |
| 2. Durandina, Natalya | Analyst |
| Gudermes MQCL | |
| 3. Hasbekov, Shamil | Analyst |
| Kazan MQCL | |
| 4. Galeev, Ruslan | Head of Analytical lab |
| 5. Aryslanov, Ilshat | Senior Pharmacist-analyst |
| Khabarovsk MQCL | |
| 6. Deryuga, Natalia | Analyst |
| Krasnoyarsk MQCL | |
| 7. Bukov, Yuri | Analyst |
| 8. Galimova, Julia | Analyst |
| Kursk MQCL | |
| 9. Katelnikova, Elena | Pharmacist-analyst |
| 10. Vlasova, Anna | Pharmacist-analyst |
| Rostov-on-Don MQCL | |
| 11. Kononova, Alexandra | Pharmacist |
| 12. Sibileva, Julia | Pharmacist-analyst |
| Saint Petersburg MQCL | |
| 13. Kosenko, Juri | Director |
| 14. Strelkova, Lyubov | Deputy Director |
| 15. Tikhonenko, Anna | Head of Administrative Department |
| 16. Nazarenko, Tatiana | Specialist of Administrative Department |
| 17. Trusov, Sergey | Head of Analytical Lab |
| 18. Pyastkina, Natalia | Analyst |
| 19. Uskov, Kirill | Analyst |
| 20. Medyakova, Julia | Analyst |
| 21. Markova, Eugenia | Analyst |
| 22. Moguchev, Vitaly | Analyst |
| 23. Mametyeva, Anna | Head of Microbiology Lab |
| 24. Rasulova, Larisa | Microbiologist |
| 25. Razukrantova, Nadezhda | Microbiologist |
| 26. Bogdanova, Irina | Head of Pharmacology Lab |
| 27. Shmygova, Valentina | Pharmacologist |
| 28. Batrysheva, Julia | Analyst |
| 29. Tereshkina, Irina | Microbiologist |
| 30. Lobyneva, Tatiana | Microbiologist |
| 31. Lebedeva, Anastasia | Pharmacologist |
| 32. Ilyina, Galina | Analyst |
| Stavropol MQCL | |
| 33. Medvedeva, Olga | Pharmacist-analyst |
| Other participants | |
| 34. Titova, Anna | Senior specialist of IMCESACMP, Moscow |

Training Program Schedule**Laboratory Training Courses
RZN's North West Region MQCL, Saint Petersburg, Russia**

| | Course Title | Date | Group # | Theory and/or Practice |
|----|---|-------------|----------------|-------------------------------|
| 1. | Validation of analytical methods | 7/9-10 | 1-2 | Theory |
| 2. | Basic approaches to sample preparation | 7/11-12 | 1-2 | Theory and Practice |
| 3. | Atomic Absorption Spectroscopy | 7/13-14 | 1 | Theory and Practice |
| 4. | Identification of residual organic solvents by Gas Chromatography | 7/13-14 | 2 | Theory and Practice |



Министерство здравоохранения
Российской Федерации

**ФЕДЕРАЛЬНАЯ СЛУЖБА ПО НАДЗОРУ
В СФЕРЕ ЗДРАВООХРАНЕНИЯ
(РОСЗДРАВНАДЗОР)**

Славянская пл. 4, стр. 1, Москва, 109074
Телефон: (495) 698 45 38; 698 46 11

№ 09-12036/12

На № _____ от _____

Г-ну Уильяму Слейтеру

Директору отдела здравоохранения
Агентства США по международному
развитию (USAID)

Уважаемый г-н Слейтер!

Федеральная служба по надзору в сфере здравоохранения выражает благодарность Агентству США по международному развитию за поддержку проведения тренингов специалистов ФГБУ «Информационно-методический центр по экспертизе, учету и анализу, обращения средств медицинского применения» Росздравнадзора в период с 9 по 14 июля 2012 г. в Санкт-Петербурге.

В процессе тренингов были изучены важные вопросы, представляющие особый интерес и значимость в стандартизации и оценке качества лекарственных средств: пробоподготовка, валидация аналитических методик, определение остаточных растворителей в лекарственных средствах и спирта в спиртосодержащих препаратах методом газовой хроматографии, применение атомно-абсорбционной спектроскопии в анализе лекарственных средств.

Тренинги были проведены на высоком профессиональном уровне, в активном режиме, позволившем не только рассмотреть различные аспекты изучаемых тем, но и найти возможные решения потенциальных проблем.

Рассчитываем, что тренинги, проводимые в рамках сотрудничества между Росздравнадзором и Фармакопсией США вот уже в течение трех лет, будут в дальнейшем пользоваться поддержкой Агентства США по международному развитию.

Врио руководителя

Е.А. Тельнова

English Translation

**Ministry of Health and Social Development
of Russian Federation
Federal Service on Surveillance in Healthcare
of Russian Federation
(Roszdravnadzor)**

4/1 Slavyanskaya Square
Moscow, Russia, 109074
Telephone: (495) 698 45 38; 698 46 11

July 20, 2012

_____ No. _____
To No. _____ dated _____

To: William Slater
Director, Health Department
The United States Agency for International Development (USAID)

Dear Mr. Slater,

The Federal Service on Surveillance in Healthcare (Roszdravnadzor) expresses gratitude to the U.S. Agency for International Development for the support of the training of Roszdravnadzor specialists conducted on July 9-14, 2012 in St. Petersburg. During the training our specialists studied topics of special interest and importance in the area of standardization and QC of medicines: sample preparation, validation of analytical procedures, determination of residual solvents in medicines and alcohol content in alcohol-containing drug products by gas chromatography, application of atomic absorption spectroscopy in analysis of medicines. The training was conducted at a high professional level, with active involvement of the participants, which allowed not only to study different aspects of these topics but also to find possible solutions to potential problems. We hope that such trainings, which have been conducted within the framework of cooperation between Roszdravnadzor and the U.S. Pharmacopeia during three years, will receive support from the US Agency for International Development in the future.

Acting Director

(Signature)

E.A. Telnova

Validation of analytical methods

Evaluations by Participants

Participants are given evaluation forms at the beginning of the course. Participants are asked to rate its educational materials and associated activities. Participants are asked to rate all categories that apply and return the completed form to the instructor.

33 participants returned the forms.

| Indicator | Strongly Agree | Agree | Disagree Somewhat | Strongly Disagree |
|---|----------------|-------|-------------------|-------------------|
| 1. Course objectives were relevant to my needs | 10 | 19 | 4 | |
| 2. I was able to understand the content of the materials presented | 9 | 18 | 6 | |
| 3. In general the course was useful and will help me do my job better | 16 | 16 | 1 | |
| 4. The flow of the course was consistent with my understanding of the materials presented | 10 | 21 | 2 | |
| 5. The instructors were knowledgeable on the subject | 28 | 5 | | |
| 6. The instructors allowed an appropriate level of participation in the class | 25 | 8 | | |

Any other comments/suggestions:

- A very important and useful course (2)
- Thank you (2)
- I like this course (1)
- The course was interesting for me. Trainer answered the questions very clearly and gave information which will help me in my work (1)
- It would be better if there were more examples (1)
- I recommend to include information written on flipchart to training materials for participants (1)

Sample Preparation

Evaluations by Participants

Participants are given evaluation forms at the beginning of the course. Participants are asked to rate its educational materials and associated activities. Participants are asked to rate all categories that apply and return the completed form to the instructor.

34 participants returned the forms.

| Indicator | Strongly Agree | Agree | Disagree Somewhat | Strongly Disagree |
|---|----------------|-----------|-------------------|-------------------|
| 1. Course objectives were relevant to my needs | 19 | 12 | 3 | |
| 2. I was able to understand the content of the materials presented | 25 | 9 | | |
| 3. In general the course was useful and will help me do my job better | 24 | 10 | | |
| 4. The flow of the course was consistent with my understanding of the materials presented | 23 | 11 | | |
| 5. The instructors were knowledgeable on the subject | 28 | 6 | | |
| 6. The instructors allowed an appropriate level of participation in the class | 26 | 8 | | |

Any other comments/suggestions:

- Thank you (2)
- There should be more practice (1)

AAS

Evaluations by Participants

Participants are given evaluation forms at the beginning of the course. Participants are asked to rate its educational materials and associated activities. Participants are asked to rate all categories that apply and return the completed form to the instructor.

8 participants returned the forms.

| Indicator | Strongly Agree | Agree | Disagree Somewhat | Strongly Disagree |
|---|----------------|----------|-------------------|-------------------|
| 1. Course objectives were relevant to my needs | 8 | | | |
| 2. I was able to understand the content of the materials presented | 7 | 1 | | |
| 3. In general the course was useful and will help me do my job better | 7 | 1 | | |
| 4. The flow of the course was consistent with my understanding of the materials presented | 7 | 1 | | |
| 5. The instructors were knowledgeable on the subject | 7 | 1 | | |
| 6. The instructors allowed an appropriate level of participation in the class | 8 | | | |

GC

Evaluations by Participants

Participants are given evaluation forms at the beginning of the course. Participants are asked to rate its educational materials and associated activities. Participants are asked to rate all categories that apply and return the completed form to the instructor.

10 participants returned the forms.

| Indicator | Strongly Agree | Agree | Disagree Somewhat | Strongly Disagree |
|---|----------------|-------|-------------------|-------------------|
| 1. Course objectives were relevant to my needs | 6 | 4 | | |
| 2. I was able to understand the content of the materials presented | 6 | 4 | | |
| 3. In general the course was useful and will help me do my job better | 6 | 4 | | |
| 4. The flow of the course was consistent with my understanding of the materials presented | 4 | 5 | 1 | |
| 5. The instructors were knowledgeable on the subject | 6 | 4 | | |
| 6. The instructors allowed an appropriate level of participation in the class | 6 | 4 | | |

- The course was useful. Please pay more attention to development of experiment in case of absence of the column specified in the compendium.
- Include a “model experiment” to optimize the analysis conditions into the course. Show on practice how changing parameters affect the result (on example of a mixture of residual organic solvents) of GC headspace.