

**RPM RUSSIA IMPACT EVALUATION REPORT**

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## I. EXECUTIVE SUMMARY

The Management Sciences for Health (MSH) Rational Pharmaceutical Management (RPM) Russia Project was a unique activity that addressed critical problems in the Russian pharmaceutical sector through a highly participatory process at the local decision-making level. The project was designed to enhance sustainability of pharmaceutical sector reforms, improve the availability of drugs, reduce waste, and promote managerial efficiency, principally by capacitating decision-makers.

The objective of the present RPM Impact Evaluation, as recommended by the RPM Evaluation Team in July 1997, is to document and assess the impact of RPM in Russia to-date. The impact evaluation data was collected at 32 health facilities in Ryazan, Novgorod, and Pskov oblasts, analyzed by RPM staff, and incorporated in the present report.

### Key Findings

The survey results showed that, in general, all recommended formulary system elements were established in all three RPM oblasts. There are positive indicators that this system is sustainable, including the following:

1. The formulary system was institutionalized in the oblasts, and became a part of the oblast health development plans, formally approved by local governments. Formulary committees were established in 61 hospitals and in all three oblast health administrations. A model of legislative reform related to rational drug management was developed in Novgorod.
2. Drug selection/formulary development was performed according to standard procedures outlined in the RPM-developed *Manual for the Development and Maintenance of Hospital Drug Formularies*. As a result, the number of drugs used in oblasts was reduced by an average of 34%. Financial data obtained from several hospitals show that significant sums were reallocated for the procurement of selected essential drugs. In 1995, Ryazan Oblast Hospital deleted unsafe and non-efficacious drugs worth 229,266,158 rubles, approximately \$51,000. In 1996, Novgorod Veterans Hospital deleted 202,556,000 rubles' worth, approximately \$35,000. In April 1997, Ryazan Oblast Clinical Hospital published the first Russian hospital formulary manual, which is currently used by 59% of the surveyed hospitals. The Novgorod formulary manual was printed in May 1998, and the Pskov Oblast formulary manual is due in the fall of 1998.
3. Formulary system maintenance programs, such as drug information systems, mechanisms for updating formulary lists, drug use review (DUR) programs, and training programs in formulary system implementation, were established in the oblasts
4. Formulary-based drug procurements were successful in limited trials:
  - In 1995, the Ryazan Health Administration conducted a limited tender for insulin that resulted in savings of \$585,000, compared to what would have been paid if the insulin had been bought through direct purchases.
  - In 1996, the Pskov Health Administration conducted a restricted tender and achieved savings of approximately 10% when compared to wholesaler price lists.
  - In Novgorod, Oblast Health Administration estimated that the 1997 limited tender led to a total savings of 970.2 million rubles (approximately \$165,000), and 22–68% better prices for the first-line TB drugs.
  - The Novgorod 1998 procurement list was created on the basis of the *Novgorod Oblast Formulary*. The oblast estimated that this process would reduce expenditures for 1998 by 60 to 80 percent compared to

1997 levels.

The impact evaluation survey also provided an opportunity for participating hospitals to describe practical obstacles that remained to be overcome, and to offer recommendations for improvement in the administrative, technical and maintenance phases of the formulary process.

Overall, the RPM program met or exceeded its goals. In addition to the pilot and roll-out oblasts, RPM methodology was adapted in at least six other sites in Moscow, Saint Petersburg, Ekaterinburg, Perm, and Vladivostok. RPM Russian language materials have also been requested in other NIS countries, including Ukraine, Moldova and Kazakstan.

## **II. BACKGROUND**

The MSH RPM Russia Project, which began in November 1993, was a unique activity that addressed critical problems in the Russian pharmaceutical sector through a highly participatory process at the local decision-making level. The project was designed to enhance the sustainability, reduce waste, and promote managerial efficiency of the public sector drug supply, principally by capacitating decision-makers.

Given the large size of the country, and on the request of the Russian Federation Ministry of Health, it was initially decided that the project would begin in one Russian oblast as a pilot site to focus on the development of effective strategies for pharmaceutical sector reform. After the selection of the demonstration site of Ryazan oblast, an in-depth pharmaceutical sector assessment was conducted. This required orientation of local specialists to Western pharmaceutical concepts. The assessment process, as well as the Policy Options Workshop that followed, resulted in the creation of a large number of stakeholders.

After two reconnaissance visits, in November 1993 and February 1994, Ryazan Oblast was chosen as the demonstration site. The roll-out oblasts of Novgorod and Pskov were chosen in April 1995. The field work for the Ryazan pharmaceutical sector assessment was conducted in May 1994 and the Novgorod/Pskov assessments were conducted in November–December 1995.

Key assessment findings were grouped into five distinct areas:

### **1. Drug selection**

Systems did not exist at the health administration or facility levels for rationally selecting drugs for procurement and use in any of the three oblasts. The funds for drug procurement were extremely limited and cost-effectiveness was not considered when selecting drugs. Some drugs used were of unproven quality or efficacy. There had been a significant increase in the number of drug suppliers operating in oblasts and an increase in the number of therapeutic alternatives and drug products available on the market. While many previously unknown drug products had been introduced, decision-makers did not have access to unbiased sources of drug information for making rational drug selection decisions. Physician and pharmacist training in clinical pharmacology were inadequate.

### **2. Drug utilization review**

The oblasts had no system in place for the regular and continuous review of drug prescribing and use. Public health officials and decision-makers did not have the tools to evaluate if drugs were being used rationally. If problems were detected in drug use, interventions were punitive, resulting in a disincentive to collect information about drug prescribing and use.

### **3. Drug procurement**

Determining drug needs and quantities was done manually and based on historical ordering information without the use of standard formulas. The drug supplier market, on the whole, was very fragmented. Competitive tender practices were not employed and drug purchases were most often made through negotiations with a large number of drug distributors and manufacturers, which lead to financial waste. Decision-makers often used information provided by pharmaceutical sales representatives to make procurement decisions, rather than current objective information. Health facilities and pharmacies reported long delivery times in getting drugs from wholesalers.

#### **4. Rational drug use**

Standard treatment guidelines were present and used in public health facilities, but were in need of revision. Prescribing was excessive for patients eligible to receive drugs free of charge or at reduced prices, and not limited by restrictive drug lists.

#### **5. Community pharmacy management**

Delays in reimbursement for exempt prescriptions, as well as punitive tax structures, contributed heavily to financial difficulties of community pharmacies. Although pharmacy managers may have functioned well under a centralized system, there were significant gaps in knowledge and experience necessary to operate efficiently in a market economy.

The principal challenge for RPM on the regional level was to establish a properly managed rational pharmaceutical system. Policy options workshops were conducted in all three oblasts.

These resulted in plans to improve pharmaceutical services in the following areas:

- Cost-effective drug selection/formulary development
- Drug utilization review (DUR)
- Drug procurement
- Community pharmacy management
- Rational drug use
- Drug information development

During 1994–1997, RPM assistance to three oblasts in the above technical areas was carried out through workshops on-site, short-term technical assistance, study tours, and the development and use of a variety of tools.

In July 1997, the project was evaluated by the RPM Evaluation Team, which recommended documenting and assessing the impact of RPM in Russia to-date.

### III. RPM IMPACT EVALUATION DESIGN

The evaluation tools consisted of a four-part survey, interviews, and reports from academic institutions and drug information centers. The evaluation sought to examine the impact related to the formulary development process, including changes in how decisions were made regarding inclusion or deletion of drug products in the formulary. Results also included process information on an RPM-introduced methodology (DUR) for regular monitoring and evaluating of prescribing and use of key drugs.

The survey instruments were built around two RPM manuals, the *Manual for the Development and Maintenance of Hospital Drug Formularies*, and *Guidelines for Implementing Drug Utilization Review Programs in Russian Hospitals*. Both manuals offered Russian specialists a step-by-step approach to the implementation of formulary systems in oblasts and health facilities. The evaluation tools were designed with the assumption that compliance of Russian counterparts with the recommended approach would result in more rational drug management, selection and use, and that these would contribute to the establishment of rational market and clinically oriented pharmaceutical systems.

The evaluation consisted of a four-part survey instrument:

1. The Formulary System Implementation Questionnaire: This was designed to capture information about how the system was implemented in health facilities, and whether all its elements were in place and properly managed.
2. The Drug Selection Questionnaire: This was designed to document the changes in drug selection patterns in hospitals, specifically what drugs were deleted from use, reasons for deletion, and costs of deleted drugs.
3. The Drug Utilization Review (DUR) Questionnaire: This instrument was to give process information on the implementation of RPM-introduced methodology for regular monitoring and evaluating of the prescription and use of key drugs.
4. The DUR Results Questionnaire: The questionnaire provided information on monitoring and evaluation efforts actually undertaken as part of DUR programs. The DUR implementation process had begun only recently, and the data would enable RPM and local experts to finalize and improve the methodology of the step-by-step implementation approach to the complex DUR process.

Other methods utilized during the impact evaluation process included:

- Interviews with health administrations and health facilities;
- Reports from Russian medical schools on their RPM-related activities and changes in curricula; and
- Reports from Drug Information Centers.

The data were collected from 32 major hospitals in Ryazan, Novgorod, and Pskov Oblasts, selected for the survey by oblasts health administrations.

While empirical data are not available for a full comparative “before” and “after” analysis, the RPM Russia Project has a wealth of directly observable results and accomplishments. In collaboration with local experts, RPM established a sustainable system for rational selection, procurement, distribution, and use of pharmaceuticals in the oblasts.

Key RPM impact evaluation findings are presented in chapter IV.

#### **IV. KEY FINDINGS**

The survey results showed that, in general, all recommended formulary system elements were established in all three RPM oblasts. There are positive indicators that this system is sustainable, including the following:

##### **1. The formulary system was institutionalized in the oblasts**

The formulary system became a part of the oblast health development plans, formally approved by local governments. Formulary committees were established in 61 hospitals and in all three oblast health administrations. Written policies and procedures regulating drug selection and use were developed and approved by hospital and oblast health administrations.

A model of legislative reform related to rational drug management was developed in Novgorod. Drug management and rational use activities are outlined in the oblast law "On the Legal and Organizational Basis of the Oblast Health System," and competitive procurement is codified in the oblast decree "On State Guarantees on Drug and Medical Supplies Procurement."

##### **2. Drug selection/formulary development was performed according to standard procedures**

All surveyed hospitals followed the step-by-step methodology for selecting drugs recommended by RPM in the *Manual for the Development and Maintenance of Hospital Drug Formularies*. Printed versions of the Russian manual were widely disseminated, and an electronic version is available on the Internet.

By the fall of 1997, 61 formulary drug lists were developed in the three oblasts. The survey of 32 selected hospitals showed that, through the process of formulary system development, the number of drugs used in all the hospitals was reduced by an average of 34%. The majority of drugs were deleted from formulary lists because of low efficacy. The second most frequent reason was unproven safety, followed by high cost and lack of availability from suppliers. In 24 (75%) of the hospitals, not only the cost of a drug, but also the cost of course of treatment was calculated and taken into consideration.

It is important to note that, given the still diminishing budget for health care in the majority of Russian oblasts, it is not reasonable to think in terms of overall expenditure reductions for drug products. However, it is possible to evaluate impact in terms of maintaining a consistent supply of cost-effective products, and reallocating scarce resources toward essential drug purchases. Financial data obtained from several hospitals show that significant sums were reallocated for the procurement of selected essential drugs.

Another effective mechanism for enhancing the rational use of drugs that was implemented in these three oblasts was setting prescribing restrictions for certain products to specific departments or selected specialists. In 38% of the hospitals, prescribing restrictions were introduced for products with high drug cost, narrow therapeutic index, potential for significant adverse reactions, complex administration regimens, and need for special monitoring.

### 3. Formulary system maintenance programs were established in oblast health facilities

Drug information systems were developed and implemented in all three oblasts to provide reliable, current, unbiased information to prescribers. Mechanisms were established to make this information available at any time. Between 1995 and 1997, six drug information centers (DIC) were established, two in each of the RPM oblasts. These centers were equipped with computers, Internet access, and printers. They were also provided with comprehensive drug information sources in both paper and electronic format, and RPM assisted oblasts in developing their own reliable local drug information sources. In April 1997, Ryazan Oblast Clinical Hospital published the first Russian hospital formulary manual, which is currently being used by 59% of the surveyed hospitals. The Novgorod formulary manual was printed in May 1998, and the Pskov Oblast formulary manual is due in the fall of 1998.

Oblast DICs are active in providing drug information to prescribers, reviewing hospital formulary lists, and participating in formulary system development at the oblast level. The Ryazan Educational Information Center, located at Ryazan Medical University, is active in promoting RPM methodology through its medical school curricula for students and post graduate continuing education programs.

Mechanisms for updating formulary lists have been developed in all the hospitals that were surveyed. The principal changes to-date have been the deletion of unsafe drugs and less efficacious, and the addition of drugs with proven efficacy and safety. In some cases, inclusion or deletion from the formulary was based on drug cost. Nearly 20% of the drugs were deleted because they were not readily available from suppliers, or because they were no longer manufactured.

Although RPM activities in the oblasts did not specifically target development or revision of standard treatment guidelines (STGs), site participation in the process resulted in the development of new standards, or review of existing standards of treatment, in a number of hospitals. Data on STGs were received from 20 hospitals. The introduction of new STGs led to the deletion of drugs, as mentioned above, by formulary committees. However, formulary lists in 75% of the hospitals were drafted in compliance with existing STGs, while STGs were modified in 15% of hospitals in the course of formulary implementation.

Drug utilization review programs have been implemented in seven hospitals. It is anticipated that as hospitals continue development of their formulary systems, a greater number will implement DUR programs. The collegial process that is essential to helping physicians become better prescribers is a new approach for physicians and administrators alike. Working together on formulary committees has contributed to forming a solid basis for proceeding to DUR.

The formulary development process also calls for establishing adverse drug reaction (ADR) monitoring systems by a health facility. RPM activities in oblasts were not targeted on development of such systems, although their importance was continuously emphasized in the *Manual for the Development and Maintenance of Hospital Drug Formularies*, and at RPM workshops. An ADR Monitoring Program is fully functional in only one hospital, although ADR reporting forms were developed in three hospitals. A number of hospitals are attempting to establish an ADR reporting system; six of them have completed tables on adverse drug reactions reported in the past six months. Other hospitals indicate a lack of data on ADRs, or that no ADRs had taken place in the previous six months.

To enhance sustainability of the RPM project, DIC and collaborating medical universities have been involved in educational activities. They are active in providing on-site and academic training in formulary system implementation issues. The most comprehensive changes were made at Ryazan Medical University to the standard curricula for medical students and postgraduate education. The university adapted RPM materials for use in courses. During 1996–1997, it provided training for about 2,150 third and fourth year medical students, and more than 220 health specialists from other cities, including Perm, Ekaterinburg, Tula, Kurgan, Chelyabinsk, and Magnitogorsk.

#### **4. Formulary-based drug procurements were successful in limited trials**

The formulary-based drug procurement trials were successful. Several competitive procurement trial activities took place during 1995–1997. In 1995, the Ryazan Health Administration conducted a limited tender for insulin that resulted in a savings of \$585,000, compared to what would have been paid for the same product through direct purchases.

In 1996, the Pskov Health Administration conducted a restricted tender for cardiovascular drugs, antibiotics, and antispasmodics for oblast health facilities, and achieved savings of approximately 10%, when compared to wholesaler price lists. Based on this experience, the governor of the oblast issued a decree mandating competitive procurement for drugs and medical supplies. In Novgorod, the Oblast Health Administration estimated that the 1997 limited tender led to a total savings of 970.2 million rubles (approximately \$165,000 dollars).

Novgorod oblast had implemented the widest application of competitive procurement. The 1998 procurement list was created on the basis of the *Novgorod Oblast Formulary*. It contained approximately 400 drugs for competitive procurement. The oblast estimated that this would reduce expenditures for 1998 by 60 to 80 percent compared to the 1997 levels.

The detailed description of impact evaluation findings follows below.

## V. FORMULARY SYSTEM IMPLEMENTATION

A formulary system includes a process where the medical staff of an institution, working through a Formulary and Therapeutics Committee, evaluates and selects from the numerous available drug products those that are considered most efficacious, safe, and cost effective. As such, a formulary system is a mechanism to streamline procurement activities, minimize costs, and optimize patient care.

The result of the drug selection process is a drug formulary list. The list contains all drugs approved for procurement and use in a given health facility. A drug formulary list is not synonymous with an essential drugs list in that formularies are restrictive, while essential drug lists do not confine the drug use and procurement to only the drugs contained on that list.

According to the *RPM Manual for the Development and Maintenance of Hospital Drug Formularies*, the formulary system may be considered in place if:

- A. The formulary system is institutionalized, the Formulary and DUR Committees are established, policies and procedures for drug selection, use, and procurement are adopted, and the enforcement mechanisms operational.
- B. A formulary drug list exists, and is revised regularly.
- C. There is a mechanism for ongoing monitoring and evaluation programs that ensure proper use of drugs in the facility and interventions implementation.
- D. Drug information on formulary drugs is readily available for the medical staff at any time.
- E. Drugs are procured according to the formulary list.

### A. Institutionalization of Formulary System in Oblasts

#### 1. Gaining administrative support for implementing a system to ensure the rational selection and use of drugs

The desire to implement a formulary system may arise from either operation- or administration-level personnel. Regardless of where this desire arises, successful implementation requires support from both the medical staff and administrators.

The need for establishing oblast hospital committees responsible for creating and maintaining lists of drugs approved for procurement and use was not immediately recognized by the Russian counterparts. Possible reasons for this include:

- Historically, physicians in Russia seldom faced the problem of product selection. The number of registered drugs was approximately 3,000 drug names, most of those produced either in Russia, or in the Eastern Bloc. Those drugs were well known to prescribers, taught in medical schools, and centrally procured.
- With the collapse of the Soviet Union, the Russian economy evolved from command-driven to market-oriented. The brief period of drug shortages on the market was followed by an influx of foreign drugs, with more than 10,000 drugs registered and available in Russia, physicians were able to prescribe almost any drug they desired.
- Intense marketing efforts by drug companies created an atmosphere in which it was felt that more, not fewer, drugs were needed.

- Industry-sponsored drug information sources like *PDR* and *Vidal* were the only widely available sources of drug information. These, however, did not supply physicians with adequate information for making unbiased drug selection decisions.
- In the highly centralized Soviet economy, physicians were not accustomed to thinking about the financial implications of drug selection decisions.

At the initial stages of RPM activities in 1994, the following methods were used to obtain the support of public health workers:

- Meetings and discussions were held with Ryazan oblast decision-makers and politicians.
- A comprehensive oblast pharmaceutical sector assessment was conducted, part of which was the selection of an oblast demonstration site at the oblast clinical hospital, and a case study of the drug use and procurement patterns at that hospital.
- Oblast key decision-makers took an active role in assessment report writing at the MSH head office in Washington, DC, and had a chance to familiarize themselves with how the system worked in the U.S. through field visits to the U.S. health institutions.
- A policy options workshop was conducted at the end of 1994, for approximately 80 officials and specialists from Ryazan, Moscow and Saint Petersburg. Assessment findings were presented and participants drafted work plans for each RPM/Russia technical area. The workshop resulted in the further creation of stakeholders.

After the formulary system was implemented at the Ryazan oblast clinical hospital during 1995, and the first tangible results were made known oblast wide, 18 more hospitals in the oblast joined the RPM implementation process. RPM was then made a part of the overall oblast health development plan and reform strategies. In just one year, the Ryazan oblast hospital reduced the number of drugs in use from approximately 1,500 to 480, deleting unsafe, duplicated, non-efficacious, or non-essential drugs worth 136 million rubles, or \$30,000.

In April of 1995, RPM rolled-out to two additional oblasts, Novgorod and Pskov. Prior to that, RPM adapted and translated the *Rapid Pharmaceutical Management Assessment: An Indicator-Based Approach* manual, and conducted a Self Assessment Workshop for Novgorod and Pskov oblasts in September 1995. As a result of the workshop and manual, the indicator portions of the assessments in those oblasts were conducted entirely by local specialists. This activity served to convince local officials of the value of routine collection of information for use in decision making.

At the request of oblast officials, who were already aware of RPM implementation impacts in Ryazan, the Self-Assessment Workshop was immediately followed by a Formulary System Implementation workshop for 25 chief physicians of major Novgorod and Pskov hospitals. The enthusiasm was so great that formulary system implementation in Novgorod and Pskov began before the assessment was completed.

The activities undertaken by RPM to gain administrative support, and subsequent efforts of health administrators on the oblast and facility level proved to be successful.

- Oblast health administration level: Health administrations in Ryazan, Novgorod and Pskov fully supported the proposed RPM technical activities in oblasts, and redesigned the oblasts health development plans to include formulary system implementation as part of them.

- At the facility level: Thirty of the 32 facilities reported no opposition to the formulary system implementation. The information most commonly utilized by chief physicians to obtain medical staff support for formulary efforts in facilities are shown in Table 1.

#### Information used to obtain staff support for formulary system

Type of Information Used	Number of Committees (%)
Figures of diminishing drug budgets	29 (87%)
Number of drugs utilized by the hospital	29 (87%)
Number of duplicative products	13 (44%)
Results of ABC/VEN analysis	17 (53%)

It should be noted that information on drug-related mortality and incidence of adverse drug reactions (ADRs) was used in only 3 percent and 25 percent of hospitals, respectively, to justify formulary system implementation. ADRs are an area of great concern. For example, in the United States, reports state that annually ADRs are responsible for 8.7 million hospital admissions, which cause about 200,000 drug-related deaths, and cost \$47.4 billion.

Although 30 (91%) of the facilities reported no opposition to formulary system implementation, only 16 (50%) of surveyed facilities adopted the regulation that only the drugs on the formulary list would be routinely procured and used in the facility. Fourteen (44%) facilities stated that the formulary was a recommended list only.

The reasons for this discrepancy are unclear, but it is possible that this was a compromise between oblast and hospital administrations' understanding and desire to reduce waste, and the physicians' reluctance to limit the drug choices to a formulary list. The latter may be due to a reluctance or inability of physicians to invest the time needed for the research leading up to the drug selection process.

## 2. Establishment of the Formulary and Therapeutics Committees

After the hospital administration decides to implement a formulary system, the decision should be properly documented and incorporated as hospital policy. This may require changes in the health facility charter, or amendments to labor agreements with health providers.

Formulary Committees were established in the 61 RPM hospitals: 18 in Ryazan; 36 in Novgorod and seven in Pskov. Committees were also established in all three oblast health administrations. In the majority of hospitals, the number of committee members was about 10 persons, as recommended by MSH. Sometimes it was as high as 21, which can make reaching a consensus difficult, or as low as four, which could narrow the focus of the committee.

Typically, a formulary committee is represented by one or two hospital administrators (all physicians), four to five chiefs of hospital wards, two therapists (general practitioners), one to two surgeons, and specialists, depending on hospital specialty (infectious disease specialists, pulmonologists, neurologists). Of concern is the fact that only a few hospitals have representatives of finance (7, or 22%), purchasing (1 hospital), and pharmacy (18, or 56%) on formulary committees. This lack of expertise impedes correct purchasing decisions.

RPM conducted two training sessions in clinical pharmacology in 1995 in Ryazan and in Novgorod. This resulted in 49 physicians trained in clinical pharmacology in 25 of the 32 surveyed hospitals. However, seven of the 32 hospitals surveyed still reported a lack of expertise in clinical pharmacology in their formulary committees. The role of clinical pharmacology cannot be underestimated, as it is extremely important in drug selection. At the same time, the absence of a clinical pharmacologist should not discourage formulary committees from making drug selection decisions based on the practical experience of the medical and pharmacy staff. Situations where academics assist hospitals in the drug selection process are rare, and within the RPM framework, were limited to the Ryazan Oblast Clinical Hospital. There are four professors from the Ryazan Medical University on the Formulary Committee staff. There are also clinical pharmacologists in the non-RPM oblasts such as the Tomsk Institute of Cardiology, and St. Petersburg Medical University clinic.

The main objectives of the Formulary and Therapeutics Committees are the development and implementation of professional policies on drug selection, evaluation, procurement, safe use, and drug information in a given health facility or oblast-wide. Committees also assist in the formulation of education programs designed to meet the needs of the professional staff for current and complete knowledge of matters related to drugs and drug practices.

The table below illustrates the stated functions of the committees and their actual functions in the surveyed hospitals, as specified in either written policies or administrative orders.

**Functions of Formulary Committees**

Functions of Formulary Committees	Stated function		Actual function	
	# of hospitals	%	# of hospitals	%
Develop the criteria for evaluating drugs for inclusion on the hospital formulary	23	72%	23	72%
Serve in an advisory capacity to the medical staff and administration in all matters pertaining to drug use	23	72%	15	47%
Aid in providing optimal drug therapy to all patients through the development of standard treatment guidelines	15	47%	16	50%
Objectively evaluate clinical data regarding new drugs proposed for use in the health facility	18	56%	14	44%
Prevent unnecessary duplication of drugs	19	59%	21	66%
Develop the list of drugs accepted for procurement and use in the hospital	24	75%	26	81%
Recommend and approve additions and deletions from the formulary	21	66%	20	63%
Establish and plan suitable educational programs for professional staff on pertinent matters relating to drugs and their use	12	38%	5	16%
Review reported adverse reactions to drugs administered	16	50%	10	31%
Conduct ongoing drug use evaluation programs	12	38%	7	22%

The table shows the following tendencies in formulary committee activities:

- Committees were not very active in advising the medical staff on drug use. This may be due to an inability to disseminate information.
- Committees do not have adequate expertise in the evaluation of new drugs proposed for use in the facilities.
- Adverse drug reactions are not properly reported and reviewed.
- As was anecdotally reported, some hospitals do not believe that the implementation of DUR programs are worth the effort. However, seven hospitals have been implementing DUR and report that it is very useful exercise.
- Committees do not have the capacity to design and conduct on-site staff training.

**3. Establishing Policies and Procedures**

Developing policies and procedures is imperative for successful formulary system implementation. These should be approved by the chief physician or chief administrator in the organization. The Formulary and Therapeutics Committee is then empowered to make and implement decisions, and request compliance from the medical staff. Additionally, the policies and procedures serve as a tool to create organization, structure and planning of the workload.

Seventy-five percent of hospitals have developed policies and procedures for criteria for drug selection. The reasons given for this included a justified need for the drug (78%), justified cost (75%), availability from suppliers (75%), and additions/deletions to the formulary (63%).

In addition, in the 32 hospitals surveyed, policies exist for writing orders and prescriptions in 29 hospitals (91%) and use of floor stock items in 28 (88%).

At the same time, several very important issues were not adequately covered in the formulary committee written policies and procedures. Thus, only 20 (63%) of the hospitals surveyed had a policy to list drugs in the formulary only under generic name, may be considered very low, as it is crucial for an effective formulary to list generic drug names. The same can be said for policies for generic and therapeutic substitution, used in 17 hospitals (53%), and 15 (46%) respectively. Procurement practices by hospital pharmacies are greatly enhanced when an effective policy is in place for generic or therapeutic substitution.

Some important issues were only cursorily addressed in the surveyed hospitals, such as the rules for drug manufacturer and wholesale representatives to follow when dealing with hospital staff. Only six hospitals (19%) formulated this regulation, and five (16%) formulated a policy on medication error reporting. The activities of drug manufacturer representatives very often create a false impression with physicians that all drugs are necessary for use, and may downplay adverse reactions. These activities may adversely affect the decisions regarding cost-effective drug selection and use.

A vendor policy was developed in only five hospitals (16%) to monitor the activities of sales and manufacturer representatives.

In five hospitals (16%), a policy exists that permits the Formulary Committee to specify a particular brand name, e.g., by a specific manufacturer, in cases where there are issues of product quality and bioavailability. Insistence on the use of a particular brand name drug product by the committee is justified if bioavailability and bioequivalence of drug products from different manufacturers vary so significantly that they can alter the desired therapeutic effect. This mainly applies to cardiac glycosides, anticonvulsants, hormones, antiarrhythmics, anticoagulants and other drugs with a narrow therapeutic index.

### **Comments and recommendations**

All surveyed hospitals institutionalized implementation of the formulary system and developed written policies and procedures. It is advisable, though, that hospitals reconsider the importance of enforcement of certain issues, and pay more attention to the following:

- Where possible, the drug selection process should be in accord with STG development, and Diagnostic-Related Groups (DRGs) developed by medical insurance funds. At the facility level, the administration should enforce physician compliance with written formulary policies. Physicians must accept the need for restricting drug use, and be willing to change prescribing habits. Those responsible for drug procurement must agree to buy only drugs on the formulary list, with only rare exceptions.
- Appropriate incentives should be put in place to encourage listing drugs in formularies only under generic names. This should also be done for formulary-based procurement lists. In the reality of diminishing drug budgets, and patients having to buy their own drugs, policies should be established to enforce use of formulary drugs by the patients.

- Issues of generic and therapeutic substitutions should be clearly addressed in written policies and procedures.
- Control over drug-related morbidity and adverse drug reaction reporting should be increased. An ADR monitoring system will allow hospitals to more critically approach the drug selection process, and reduce expenditures on treating ADR.
- Formulary committees should establish closer cooperation with hospital pharmacies, and include their representatives on committees. Formulary committees should give more attention to educating medical staff on formulary system issues. Formulary committees should develop and enforce a policy on activities involving sales representatives.

## **B. Development of Formulary Drug List**

A critical first step in maximizing the therapeutic benefit of public sector expenditures on drugs is rational selection of drug products. Ideally, a formulary list is formed through a careful examination of morbidity patterns, previous consumption patterns and treatment costs. Once in place, the formulary list should be revised on a regular basis. An active revision process is another indicator of a functional formulary system.

The list may be further developed into a formulary manual containing basic drug information for use by prescribers, pharmacists and nurses, as was done at the Ryazan Oblast Clinical Hospital, and by the Novgorod Health Administration in 1997.

There are certain steps that a formulary committee should follow in order to rationally select drugs. Those steps include:

### **1. Information is collected and made available to drug selection decision-makers prior to therapeutic drug class review process**

All hospitals surveyed began the selection process with the presumption that all drugs currently in use in the hospital constitute the initial hospital formulary list. During the course of the review process, drugs were deleted, and in some cases, new drugs were added. This approach gave physicians the chance to gradually adjust themselves to formulary selection process, as opposed to the approach where there is no formulary list at all, and the formulary is developed one drug class at a time during the review process. Of 32 surveyed hospitals, 30 (94%) used the M. D. Mashkovski Therapeutic Classification Scheme, which is well known to Russian physicians.

The decision was made by hospitals that the formulary should be tailored to their own patient population. Prior to the selection of drugs, data and statistics on prevalent diseases and patient characteristics were obtained by 31 (97%) hospitals. However, only 13 (40%) rank ordered diseases and conditions, developing a list of the top 50 diagnoses and the top 50 reasons for admission. Twelve (37%) hospitals calculated the percentage of total morbidity that was caused by the list of diseases. Twenty-seven hospitals (87%) collected data on drug purchases for the known period of time.

The *Manual for the Development and Maintenance of Hospital Drug Formularies* recommended that hospitals conduct ABC and VEN analyses. Using both systems provides the Formulary and Therapeutics Committee with important information that facilitates decision making on which drugs can be eliminated from use, which drugs need to be incorporated into the formulary, and which drugs are being over- or under-utilized. ABC/VEN analysis was conducted by 17 hospitals (53%), but only 25% of hospitals utilized the data to develop the drug class review schedule. Thirty-eight percent of the committees relied upon their knowledge of problematic drugs. ABC and VEN analyses showed that, in many cases, drugs that were classified by hospitals as non-essential (N) were responsible for significant drug expenditures. Examples of these include: vitamin C injectable, 5.6% of drug budget in Novgorod oblast hospital; Analgin, 16% of drug budget in Ryazan oblast Kasimov rayon hospital; Ampiox, 7.8% of drug budget in Pskov oblast Palkino rayon hospital.

Some hospitals included disposable medical supplies such as bandages, cotton wool and gloves, in the analyses. Those accounted for a large proportion of drug budgets. At Ryazan oblast hospital, bandages accounted for 10%, gauze 5.7% and blood transfusion systems 3.9% of the budget.

There was no consistency among hospitals in classifying drugs. Although certain drugs, particularly antibiotics, such as Ampiox, oxacillin, bicillins 3 and 5, and gentamycin, in some hospitals were classified as vital (V) drugs, in some hospitals these same drugs were considered as N drugs (non-essential). Cephalosporins, fluoroquinolones and ethanol were considered as both V and E drugs. Essential (E) drugs also included metamizole sodium, papaverine, bendazol drotaverine, cotton wool, gauze, bandages and imipenem. This may be a reflection of the specialist nature of different hospitals.

## 2. Information used during drug class reviews and drug selection process

Drug class reviews were performed by the Formulary Committees (100%), and in some cases non-committee experts from hospital staff (16%), or outside experts, such as medical university faculty (9%).

To select drugs within classes, hospitals used information that clearly falls into the following categories:

### a. Drug information available at all times from any source, including package inserts, as required by federal registration regulations:

Indications	100%
Contraindications	94%
Efficacy	100%
Side effects profile	94%

### b. Specific drug information available from selected sources:

Safety in use in pregnancy	50%
Safety in use in lactation	44%
Safety in use in children	59%
Drug-drug interactions	53%
Drug-food interactions	34%
Required monitoring	28%
Treatment of overdose	25%

Survey data on drug information sources explains the situation. The surveyed hospitals listed 19 sources of utilized drug information, of which nine were used only in one of the hospitals, including *Meyler's Side Effects of Drugs* edited by M. N. G. Dukes, 1983. The top drug information sources in hospitals were:

Vidal	91%
M. D. Mashkovski	88%
Ryazan Oblast Hospital Formulary Manual (developed within RPM framework)	59%
Russian Drug Register	34%
USP DI	22%
PDR	16%
other sources	less than 10%

Although popular, the *Vidal* cannot be considered a source of unbiased information, since it does not contain complete information on all drug products, the information is provided by drug manufacturers, and the publication is industry-sponsored. *Drug Products* by M. D. Mashkovski can be considered an unbiased source, but it is not comprehensive, particularly in the field of safety. Usually it gives information only on common side effects. Neither of those sources gives comparative drug information. Thus, the information on drug efficacy obtained by 100% of hospitals is misleading and may not be reliable.

Certainly, the best reference book on safety is *Meyler's Side Effects of Drugs* edited by M.N.G. Dukes. However, it was used in only one facility, and that was the 1983 edition. The most comprehensive and objective source of information is *Drug Information for the Health Care Professional* (USP DI), which is updated annually. The USP provided this edition to hospital Drug Information Centers in Ryazan, Novgorod and Pskov. However, it was used in only 22% of hospitals, probably because the book is in English. As of July 1997, Pharmedinfo had translated only the sections on cardiovascular and central nervous system (CNS) drugs into Russian.

It should be noted that the *Ryazan Oblast Hospital Formulary Manual* was named as a reliable source of drug information by 19 hospitals. The manual was developed jointly by the Ryazan Oblast Hospital Formulary Committee, Ryazan Medical University, Pharmedinfo, and RPM consultants, and was printed and disseminated using RPM funds.

### 3. Information on cost of treating a course of a disease or condition

In the past, economic considerations in making formulary decisions dealt mainly with the acquisition cost of a drug. Increasingly, economic analysis has expanded to include other costs and/or expenses associated with drugs. These costs are part of the institution's overall cost related to drug therapy and need to be taken into consideration as well. Because drug product acquisition costs are only one cost aspect to consider, medication formulary decisions must consider the full impact of medication use (see Annex 1).

Of the 32 surveyed hospitals, 24 (75%) claimed to have used information on the cost of the course of treatment for a disease or condition. However, statistics show that there is room for improvement and reconsideration of methods used. The cost of the course of treatment is not merely the cost of drugs used. Of 24 hospitals that made efforts to calculate treatment expenses, only 14 included disposable equipment. As ABC analysis performed in hospitals that included medical supplies showed, these are responsible for almost 30% of total expenditures. Twelve hospitals calculated costs associated with co-administered drugs, for example those used to treat common side effects, such as antihistamines. Unfortunately, very little attention was paid to important line items, such as drug preparation costs, which were considered in only one hospital. A number of the surveyed hospitals have pharmacies that do considerable extemporaneous compounding, that is, preparation of a finished product from ingredients, according to a written prescription. Some oblast hospitals may produce as much as 400–500 liters of intravenous solutions (IVS), a labor and energy intensive production. Other costs include drug monitoring costs (laboratory), and drug administration time by hospital staff.

#### 4. Drugs deleted from use

As a result of formulary system development, the number of drugs used in all the hospitals was reduced on average by 34%, ranging from 3.9% (Pskov oblast Nevel Rayon Hospital) to 73.2% (Ryazan Oblast Clinical Hospital). The majority of drugs were deleted from formulary lists because of low scores on the efficacy criteria. The second most frequently mentioned reason was safety, followed by cost and availability from suppliers. In 75% of the hospitals, not only the cost of a drug, but the course of treatment cost was calculated and taken into consideration.

Depending on the morbidity pattern, facility specialization, number of beds, and other factors, drugs were deleted from the formulary varied among hospitals. In many facilities, the primary drugs deleted from the formulary list were drugs of low efficacy or safety. Examples include: low efficacy, long-acting nitroglycerin; obsolete and unsafe sympatholytics and ganglionic blockers; antihypertensive drugs that are not drugs of first, second, or even, third choice for the treatment of hypertension; herbal diuretics and cholergics; unsafe antibiotics of low efficacy; and tissue metabolism stimulators of unproved clinical efficacy.

Another major reason for deleting drugs was duplication. In many cases, the same drug was supplied under several different brand names. For example, nitroglycerin was listed as Nitrogranulong, Sustak, Sustanik, Nitrolong and Triniyrolon.

About 17% of drugs were deleted because they were not readily available from suppliers, and two drugs were excluded because they were no longer manufactured. In one hospital, captopril was deleted because of low patient compliance, and changed to Enalapril, with a similar therapeutic effect, but with a more favorable profile for patient compliance.

Annex 4 provides more detailed information on drugs recently deleted/added to formulary lists.

#### Drugs Deleted in 26 Hospitals Implementing Formulary System

Number of drugs deleted	6,903
Range	13–1,275
Average/hospital	265.5
Main category of drugs deleted	Cardiovascular

These reductions are expected to improve clinical efficacy. The more detailed description of deleted drugs by drug classes can be found in Annex 2, "Drugs Deleted from Use."

Below are summary data from the RPM pilot site, Ryazan Oblast Clinical Hospital. The hospital provided data on 647 drugs deleted from use during the formulary system implementation process. The main categories are outlined in the table below:

#### Drugs Deleted from Pharmacy at Ryazan Oblast Clinical Hospital

Category of Drug	Number of Drugs	Percentage of Drugs	Main Reason(s) Deleted
Antimicrobial agents	89	13.75%	Unsafe Polypharmacy Not in STGs
Central nervous system	84	12.98%	Duplication Not in STGs
Hormones/Drugs affecting metabolism	72	11.1%	Duplication Not in STGs
Affecting GI function	70	10.81%	Duplication Not in STGs
Analgesics/antipyretics	39	6.02%	Polypharmacy Not in STGs
Vitamins	27	4.17%	Duplication Not in STGs
Drugs affecting hemostasis	19	2.93%	Duplication Not in STGs
Affecting renal function	7	1.08%	Duplication Not in STGs
Miscellaneous	168	25.6%	Unsafe Polypharmacy Not in STGs
<b>Total</b>	<b>647</b>	<b>100%</b>	

The top 40 domestic drugs purchased by Ryazan Oblast Clinical Hospital during June–August 1997 included drugs such as inosine tablets. These were deleted from the formulary as having no therapeutic value. Also deleted were other drugs such as nicethamide injections, which is of questionable therapeutic value. Therefore, although a great deal of progress has been made in implementing the formulary system in Ryazan Oblast and at Ryazan Oblast Clinical Hospital, this process needs ongoing review and further streamlining.

In the reality of still diminishing health and drug budgets (see table in chapter V, section D), it is almost impossible to calculate the economic effect of drug selection process. Even with funds saved by not procuring the deleted drugs, hospitals experience drug budget shortages. It may be safe to assume, though, more efficacious drugs are purchased by RPM hospitals with what funds they do have. Financial data obtained from several hospitals show that significant sums were freed for procurement of the selected drugs.

For example, Ryazan oblast hospital in 1995 deleted unsafe and non-efficacious drugs worth 229,266,158 rubles (1995 prices, approximately \$51,000); Novgorod Veterans Hospital deleted 202,566,000 rubles' worth (1996 prices, approximately \$35,000). Data on financial impact were obtained from only a few hospitals, and even those were incomplete. For example, hospitals had information on the volume of deleted drugs (number of packs or vials), but they do not maintain a database on prices, as there is no computerized system in place.

## 5. Drugs added

Among the 98 drugs added to the formulary lists, the main reason for addition was high efficacy. Ten percent of drugs were included because they were safer to use than drugs previously used. Ten percent of drugs were added when new treatment guidelines specifying these drugs were adopted in the hospitals, and ten percent of drugs were added because of popular demand. Four percent of drugs were added because of the STG changes, two drugs were added because of favorable patient compliance considerations, one drug due to its high quality, and one drug was included because it was readily available from suppliers.

### Drugs Added to Initial Formulary List

Number of drugs added	98
Main categories of drugs	Cardiovascular Antibiotics
Main reasons for adding drugs	High efficacy Safety New treatment guidelines

The detailed description of drugs added may be found in Annex 3, "Drugs Added to Initial Formulary Lists."

The survey results indicate that additions may not have been rational in all cases. For example, cost was not always considered before drugs were added to the formulary lists. In addition, the following four drugs have not been used for treatment even though they have been added to the list: ceftriaxone, simvastatin, ambroxol and ipratropium (Ryazan oblast hospital data). Possibly there is a need for these drugs, but budgetary restraints prevent the hospital from purchasing them. Of the seven drugs added to the initial formulary lists, ethacizine, dobutamine, Gnetum, sulphiride, ondansetron, norfloxacin and nedocromyl sodium have not been utilized as expected. Furthermore, some hospitals added to the formulary lists obsolete, less efficacious and drugs with a narrow therapeutic index drugs, for example: Triresid K, Orazo (enzymes of *Aspergilla Oryzae*), and ketorolac.

## 6. Drug use restrictions

In 12 hospitals (38%), diagnosis, prescriber, and pharmacological restrictions were set for drug use. Diagnosis restrictions identify indications that constitute acceptable uses for a formulary drug within the health-care setting. The use of toxic, potentially dangerous, or expensive drugs may be justified when the risk of developing side effects or the cost is outweighed by the efficacy in specific diagnoses or medical conditions.

**a. Diagnostic restrictions****Examples of Diagnostic Restriction from 12 Out of 32 Hospitals Surveyed**

<b>DRUG</b>	<b>DIAGNOSIS</b>	<b>REASON</b>
Imipenem	Sepsis, pneumonia that doesn't respond to other antibiotics	High cost, wide spectrum, risk of developing antimicrobial resistance
Claforan (Cefotaxime sodium)	Sepsis, pneumonia	High cost, risk of developing antimicrobial resistance
Unasine (ampicillin+sulbactam)	Generalized peritonitis, pelvioperitonitis	High cost, risk of developing antimicrobial resistance
Doxycycline (tab.)	Feminine genital diseases	Developed resistance to doxycycline, side effects
Tetracycline (tab.)	Cholera	Developed resistance to doxycycline, side effects
Alkeran (Melfalan)	Acute leucosis	High cost
Hydrea (Hydroxycarbamide)	Acute leucosis	High cost
Idarubicin	Acute leucosis	High cost
5-Ftoruracil (Fluorouracil)	Acute pancreatitis	High cost

Use of the drug for indications other than these would fall outside the approved diagnosis criteria.

**b. Prescriber restrictions**

Prescriber restrictions identify prescribers approved to use specific formulary drugs or drug classes. Examples of restrictions include:

<b>DRUG</b>	<b>PRESCRIBER</b>	<b>REASON</b>
Insulins	Endocrinologist	Requires specific experience and monitoring
Cephalosporins	Deputy chief physicians	High cost; prevent development of antimicrobial resistance
Streptokinase	Reanimatologist	High cost, requires experience of use
Indomethacin	Reanimatologist	High toxicity, requires experience of use
Perlinganit (sol. Nitroglycerin)	Reanimatologist	Intravenous, requires experience of use, and special monitoring

**c. Pharmacological restrictions**

Pharmacological restrictions identify approved doses, frequency of administration, duration of therapy, or other aspects that are specific to the use of a formulary drug. Examples of pharmacological restrictions are shown in the table below.

DRUG	PHARMACOLOGICAL RESTRICTION	REASON
Reserve antibiotics	Duration of treatment course, schemes, doses	High cost
Streptomycin IM 1.0	Duration of treatment course not more than 3 months	Nephrotoxicity, ototoxicity
Kanamycin IM 1.0	Duration of treatment course not more than 3 months	Nephrotoxicity, ototoxicity
Rifampicin 0.45 or 0.6	Duration of treatment course not more than 6 months	To prevent antimicrobial resistance
Gentamicin	Duration of treatment, doses	To prevent antimicrobial resistance, required monitoring

Other restrictions: Novgorod City Hospital #1 set restrictions on all expensive drugs. The policy states that use of expensive drugs, especially antibiotics and cancer drugs, should be approved, in each case, by the chief physician of the hospital.

Establishment of drug use restrictions is one component of a sound formulary system. It should be noted that restrictions were set by the hospitals that participated in the RPM Formulary Development Workshops in 1995–1996, or participated in the High Level Technical Meeting in October 1996. Conversely, restrictions were not established by hospitals that initiated formulary system development later, were not formally trained by RPM, or did not have the chance to discuss implementation problems with their colleagues from other hospitals.

### **7. Hospitals formulary lists approved for use in the health facilities**

After the Formulary and Therapeutics Committee creates the list of drugs for inclusion in the formulary, the list is usually approved by the chief physician, who then should issue an order of compliance with the formulary drug list. This rule was followed by 27 (84%) hospitals.

### **8. Distribution of formulary lists and education of hospital staff on policies and procedures pertaining to formulary drug use**

The survey revealed certain deficiencies in the dissemination of formulary lists and hospital staff education efforts. While most of the hospital chiefs of ward (100%) and physicians (82%) have access to formulary lists, only 51% of pharmacists, and 14% of nursing staff received a copy. This may be due to a simple lack of a photocopying machine, but may also demonstrate neglect of the pharmacy and nursing staff.

Problems were identified with staff education on policies and procedures on non-formulary drug use, additions and deletions to the formulary, and generic and therapeutic substitution. In most cases, staff was educated at hospital staff meetings (in 50–63% of hospitals). Only three hospitals (9%) managed to find resources to produce and distribute written policies and procedures. In three (9%) of the hospitals surveyed, policies and procedures were not developed at all.

## 9. Non-formulary drug use in hospitals

Deficiencies in policies and procedures, and possibly lack of education of hospital staff, lead to poor compliance with some of the main principles of a formulary system, for example, in limiting the use of drugs to only those that were rationally selected by Formulary and Therapeutics Committees. Non-formulary drug use is controlled in 79% of hospitals; in the remaining 21% it is not controlled. A non-formulary drug request form was developed in only five hospitals. In the sample, 56% of the committees regularly review non-formulary drug use.

Approved formulary drugs are routinely purchased in only 56% of hospitals. Data on non-formulary drug purchases were provided by 14 hospitals, and show that effective and safe drugs, such as the H<sub>2</sub>-blocker ranitidine, second- and third-generation cephalosporins, and fluoroquinolones were procured by hospitals. However, hospitals also procured sympatholytics (raunatin, reserpine), nitrates (Suctac, Sustonit), inosine (Riboxin), kanamycin, Reopyrin (aminophenazone+phenylbutazone) and other drugs of low efficacy and safety. In many cases, hospitals justified purchases and use of non-formulary drugs by claiming patient demand, stating that patients wanted drugs with which they were familiar. This raises the issue of patient education and training of physicians in how to address such patient demands. These areas were outside planned RPM activities, but apparently, require more serious attention.

## 10. Recent additions/deletions to formulary lists

Changes to initial official formulary lists were made in 12 hospitals. The principal reason for changes was to delete less efficacious and unsafe drugs, and add those of proven efficacy and safety. The table below illustrates the latest deletions from formulary lists, and reasons for those deletions:

### Drugs Deleted from Formulary Lists in 12 Hospitals during the Last Quarter of 1997

Drug Classes (main)	Reasons
Cardiovascular drugs	Low compliance, not readily available from suppliers
Drugs acting on CNS	Low efficacy, unsafe, not included into STGs, rarely used, high cost
NSAIDs	Unsafe, not readily available from suppliers
Hormones	Low efficacy, unsafe, not used
Drugs stimulating tissue metabolism	Low efficacy, unsafe, not readily available from suppliers
Drugs affecting GI functions	Low efficacy, unsafe, not readily available from suppliers, high cost

After the initial formulary lists were officially adopted, hospitals tended to add more drugs than they deleted. For example, data from 10 hospitals showed that 56 drugs were added to the existing lists while only 37 drugs were deleted.

- In most cases, safer and more efficacious drugs were added instead of those of unproven efficacy. Thus, in many hospitals, cimetidine was replaced with ranitidine (safer drug), pirenzepine replaced with H<sub>2</sub>-blockers (efficacy and safety), captopril was substituted for enalapril (efficacy, pharmacokinetic advantages, increased patient compliance), Gnetum (levodopa+carbidopa) was changed for Madopar (levodopa+benseracid, efficacy, better cost/effect ratio).
- In some cases, potentially unsafe drugs were included because of their efficacy, such as anti-

inflammatory agents as ketorolac and indomethacin. A probable reason for such inclusion could be lack of information on drug adverse reactions. Sometimes the inclusion or deletion from the formulary was determined by the drug cost. For example, Gnetum was substituted for Madopar because of lower cost, and bismuth subcitrate was excluded from the formulary in one hospital because of its high cost.

Hospital staff are usually informed about additions/deletions to the formulary at staff meetings. Written policies on generic substitutions exist in three hospitals and policies on therapeutic substitutions in five hospitals. Decisions on therapeutic drug substitutions are usually made by the prescribing physician or the Formulary Committee. Examples of therapeutic equivalents were given by 10 hospitals. Three hospitals gave examples of generic equivalents instead of therapeutic equivalents. This could imply that physicians in these hospitals do not understand the difference between generic and therapeutic equivalents, or that their knowledge of clinical pharmacology is inadequate for making those decisions.

### Comments and recommendations

The RPM impact evaluation assessment showed that all 32 surveyed hospitals have conducted the drug selection process according to the methodology recommended by RPM, and described in the *Manual for the Development and Maintenance of Hospital Drug Formularies*. Formulary drug lists exist in every hospital and are revised on a regular basis. Recent additions to and deletions from formulary lists suggest that the drug selection process in hospitals is ongoing, an essential characteristic of functioning formulary systems.

The survey revealed the following drug selection and use issues in the hospitals:

- In collecting data on drug selection decisions, only 53% of the hospitals used ABC/VEN analysis as a tool to define priority drug classes. It is recommended that hospital Formulary Committees should establish VEN criteria and classify drugs prior to performing the ABC analysis. Unfortunately, some hospitals included into their ABC/VEN analysis such items as disposable medical supplies, which in Russian hospitals normally account for up to 30% of drug budget. It may be useful to perform separate ABC analyses for pharmaceuticals and medical supplies, in order to give a better picture of what specific drugs and medical supplies account for the largest portion of drug budgets.
- Most of the surveyed hospitals experienced a marked lack of reliable and unbiased information, needed for rational drug selection decisions. However it is expected that situation will improve in the near future, when oblast formulary manuals are published and disseminated. Oblast Health Administrations should make sure that the manuals are well distributed to all health facilities.
- A very positive outcome of changing administrator and prescriber mindsets was evident in that 75% of hospitals attempted to consider total treatment costs, as opposed to only drug cost, in making drug selection decisions. This move should be supported and enhanced either by formal training within the RPM project framework, or through educational programs in pharmacoeconomic issues by health administrations. A closer link with Regional Mandatory Medical Insurance Funds may have a positive influence in this regard.
- All surveyed hospitals were tremendously successful in removing unsafe and non-efficacious drugs from use in their facilities. Further efforts should be made to refine the lists. It is strongly recommended that all drugs be listed in formularies only under generic names, unless there is firm scientific and clinical evidence that a specific brand name drug has unique properties, for example, phenytoin. At present, some formularies list up to 60% of drugs under brand names; this complicates competitive procurement.

- Some hospitals, and even whole regions such as Ryazan in 1997, experienced difficulties in obtaining some drugs they selected for use. It may be some time before budget allocations for health and drugs approach a desirable level. Until such time, oblast health administrations may be able to enhance the level of pharmaceutical care by urging facilities to strictly adhere to a formulary list. In addition, it may be advantageous to coordinate bartering procurement with the oblast formulary list. A good example of this is taking place in Novgorod oblast, where steps are being taken to establish pooled procurement on the basis of the oblast formulary list, which was created in accordance with facilities' lists. It is anticipated that the Novgorod Health Administration will share its experience with other RPM and non-RPM oblasts during 1998.
- Within a facility, the use of the formulary list should be strictly enforced. To-date, 84% of the hospitals have issued an order of compliance with the formulary drug list. It is recommended that the remaining 16% of health facilities strengthen their policy on formulary drug use, and specifically, enforcement.
- A very positive indication of formulary system development in hospitals is the introduction of drug use restrictions. This will have a positive impact on clinical outcomes, and prevent development of antimicrobial resistance.
- Certain deficiencies were noted in hospital staff education on formulary issues. It is recommended that hospital administrators rely more on written forms of information dissemination such as newsletters and written policies and procedures, as well as verbal communication at staff meetings.

### **C. Formulary System Maintenance Programs**

The formulary process does not end with the production and distribution of the formulary list, and the Formulary and Therapeutics Committee should be considered a permanent decision-making body. During the development phase, frequent committee meetings, as often as weekly, may be necessary. After that, the chairperson or group may decide that monthly meetings are sufficient to perform maintenance activities. The number of maintenance activities may vary from oblast to oblast, and hospital to hospital. Usually, these activities would include:

1. Development and implementation of drug information systems
2. Development and implementation of standard treatment guidelines
3. Implementation of a DUR program
4. ADR monitoring
5. Mechanisms for updating the formulary list and manual
6. Ongoing education of health providers on formulary system issues

The RPM project has been actively implementing formulary systems in oblasts for only two and a half years, and most hospitals have not yet progressed through all the necessary stages. RPM activities to help oblasts fine tune the formulary systems were planned for 1998–1999. The survey of 32 hospitals showed, though, that attempts to build formulary system maintenance mechanisms are already under way.

#### **1. Development and implementation of drug information systems**

As was mentioned earlier, one of the most serious constraints for a rational drug selection process is the lack of reliable unbiased information, and mechanisms to make this information available to prescribers at any time. The drug information component of RPM tackles this problem.

Between 1995 and 1997, six DICs were established in RPM oblasts (two in each), equipped with computers, printers, Internet access, and provided with unbiased drug information sources in both paper and electronic format. The RPM collaborator, Russian Center for Pharmaceutical and Medical Information (Pharmedinfo) began adapting and translating the USP drug information database into Russian, and monitoring the activities of oblasts' drug information centers. Due to serious financial difficulties in the oblasts, DICs became active participants of formulary system implementation when the drug selection process in health facilities was under way—Ryazan DIC in 1996, Novgorod in early 1997, and Pskov in late 1997—and are still experiencing severe financial shortages.

Oblast DICs are active in providing drug information to prescribers, and reviewing hospital formulary lists. Thus, in Ryazan, the oblast hospital DIC revised and made comments to all 19 formulary lists developed so far, and provides information to the health administration to facilitate drug-related managerial decisions. In Novgorod oblast, the director of the DIC is an active member of the Oblast Formulary Committee, and editor-in-chief of the Novgorod Oblast Formulary Manual. The Ryazan DIC, located at Ryazan Medical University, is very active in promoting RPM methodology through medical school curricula for students and postgraduate continuous education programs.

A big step toward the development of oblast-specific unbiased drug information was made in April 1997 in Ryazan through the creation of the *Ryazan Oblast Hospital Formulary Manual*. It is already being used in 59% of the surveyed facilities. In Novgorod Oblast, in December 1997, the first oblast formulary manual in Russia was published. This manual was revised and printed in May 1998. The *Pskov Oblast Formulary Manual* is also due in 1998. Thus, it is anticipated that the drug information situation will improve dramatically during 1998.

It was the decision of both Novgorod and Pskov Health Administrations to concentrate financial and human resources on production of oblasts formulary manuals. This does not rule out specific hospital activities aimed at producing their own manuals. Thus, 41% (13) of hospitals expressed interest in developing hospital-specific formulary manuals, but all claimed lack of funds for developing and printing the manual. Others lack sources of drug information (3), qualified staff members (4), and time to do the required work (6). At the time of the survey, only Novgorod Oblast Hospital so far was committed to work on a hospital-specific formulary manual.

As shown in the survey, prescribers do have access at all times to basic drug information on: generic names (84%), common brand names (72%), pharmacology (72%), indications (91%), contraindications (88%), side effects (72%), dosage forms and strengths (81%), usual dose (75%), and adverse reactions (78%). Although those figures may seem high, the very nature of prescriber activities presupposes a 100% access to this information.

Other figures indicate that formulary-specific information is poorly disseminated in hospitals. For example, information on criteria for drug selection was readily available in only 53% of hospitals, on additions/deletions 41%, and generic and therapeutic substitutions 31 and 34% respectively.

## **2. Development and implementation of standard treatment guidelines**

Unlike in the West, standard treatment guidelines (STGs) are not as strictly enforced or complied with in the Russian hospitals surveyed. In many cases, the STGs may not include specific pharmacotherapeutic recommendations. RPM consultants, in several cases, observed instances at formulary committee meetings, when prescribers referred to various non-hospital-specific treatment guidelines in an attempt to promote specific products to a formulary list. In order to promote and strengthen STGs and improve patient care, there is a wide range of activities that may be undertaken within the RPM framework, or independently by hospital formulary

committees or health administrations. These include:

- Review existing guidelines, their drug therapy portions in particular, especially those STGs that require antimicrobial treatment
- Issue a policy that would require prescriber compliance with the existing STGs
- Review the compliance of STGs with hospital developed formulary lists
- Promote peer review practices
- Develop drug use review criteria for drugs in STGs
- Establish collaboration with medical insurance companies, and set regulations on STG-related drug use
- Develop a STG manual that would cover major oblast-specific morbidity patterns

### 3. Implementation of a drug utilization review program

In order to introduce the concept of DUR in Russia, RPM conducted a workshop in Ryazan oblast in September 1996 for participants from all three oblasts. Of the 51 participants, the majority were physicians of health facilities throughout the three oblasts, although pharmacists and health administrators were also present. The workshop was of a practical nature and participants were able to begin the step-by-step process as described in the *Guidelines for Implementing Drug Utilization Review Programs in Russian Hospitals*, developed by RPM. DUR committee members were identified, drugs to review selected, and study criteria for the first drug evaluations developed. Subsequent to the workshop, RPM visited various formulary and therapeutic committees, and provided technical assistance as DUR activities began in the hospitals.

To measure the impact of the DUR technical work, RPM surveyed 32 hospital programs. Seventeen responded as follows.

#### a. Results from the questionnaire:

	Number of Hospitals (%) (n=17)
How is the DUR committee formed?	
Formulary committee has responsibility for DUR	15 (88%)
Special DUR committee has responsibility for DUR	2 (12%)
The committee responsible for DUR meets:	
Weekly	1 (6%)
Monthly	3 (17%)
As required	11 (65%)

The majority of DUR activities in the reporting hospitals are being coordinated through existing formulary committees.

This is quite acceptable since the concept is still new to physicians in Russian health care settings. However, as the economic situation improves and responsibilities increase for members of the formulary committees, the hospitals may want to consider establishing a subcommittee to conduct DUR programs. As DUR programs mature, the frequency of meetings often decreases, so it is not surprising that the programs in the reporting hospitals are meeting only as required. These programs may find that quarterly or biannual meetings are sufficient to monitor drug use in their hospitals as they mature.

	Number of Hospitals (%)
Do DUR written policies and procedures exist? Yes	12 (38%)
No	20 (62%)
Do the written policies and procedures include?	
An order of the chief physician supporting DUR program	12 (100%)
Description of goals and major activities of DUR program	11 (92%)
Committee membership	12 (100%)
Frequency of committee meetings	9 (75%)
Aspects of drug use to be evaluated	10 (31%)
Requirements for development of study criteria	9 (75%)
Dissemination of findings to hospital staff	10 (83%)
Types of interventions to employ for drug use problems	8 (66%)
An evaluation of DUR program on a regular basis	5 (41%)

Responses to the above questions indicate that the guidelines provided by RPM are not followed. Whether for beginning or mature programs it is imperative to establish guidelines for providing continuity as committee members rotate in and out of the DUR program. Only the 38% of programs with written procedures have followed recommendations in the RPM guidelines.

	Number of Hospitals (%) (n=32)
Number of committees performing regular program evaluations:	10 (31%)
Regular evaluation of the DUR program includes:	(n=10)
Appropriateness of drugs chosen for inclusion	10 (100%)
Criteria development	9 (90%)
Number and types of problems identified	7 (70%)
Effectiveness of interventions	6 (60%)
Results of evaluations were disseminated	5 (50%)

At the end of each DUR program cycle (an annual cycle is recommended by RPM), the responsible committee should evaluate if procedures have been followed, and if any aspect of the program needs modification, based on the experience gained during the cycle. Although RPM has recommended regular evaluation by committees to strengthen their DUR programs, only a third of the hospital programs have done so at this time. For those committees performing regular evaluations, the components they have selected for program evaluation follow

the recommendations in the RPM guidelines.

While DUR programs provide adequate means for monitoring and improving the rational use of drugs in hospitals, they do require additional time and effort by physicians, pharmacists and nurses who practice there. RPM guidelines recommend that a cost-benefit analysis of DUR activities be incorporated into the normal DUR program, to help justify the additional effort required during planning and implementation of activities.

There are costing activities that will demonstrate cost avoidance for a hospital when rational use techniques are implemented. For example, using ABC/VEN analysis, procurement costs of drugs before and after the implementation of formulary and DUR systems can be compared, and quantify the degree of cost avoidance. This can be refined by quantifying costs of unnecessary laboratory tests, and drugs prescribed for specific illnesses, during subsequent DUR evaluations.

Although committees performed ABC analysis before drug selection in nine out of the eleven evaluations (see below), none of the hospitals surveyed have actually reported any resulting financial impact. RPM highly recommends including cost benefit analysis to further promote the sustainability of the DUR programs.

#### **b. Results from specific drug use reviews**

Seven of the 32 hospitals surveyed have completed at least one drug use review.

#### **Selection of Drugs for DUR**

Number of drugs evaluated by therapeutic category:	(n=11)
Antibiotics	8
H <sub>2</sub> antagonist	1
Bronchodilator	1
Antidepressant	1
Number of drugs where analyses were done before selection:	
ABC analysis	9
VEN analysis	7
Number of drugs selected for evaluation because of:	
High unit cost	2
Frequently prescribed (high volume)	9
Used in treatment of high risk patients	4
Reported or suspected adverse reactions	2
Narrow therapeutic index	2
Possible severe side effects	1
Possible drug interactions	1

The RPM model recommends that drugs be included in the DUR programs after analyzing those drugs most frequently used in the hospital, and the financial impact of the current therapy. This could be done using ABC/VEN analysis. The reporting hospitals have followed these recommendations in selecting the initial drugs for study. As the programs mature, DUR committees may also want to focus on patient care aspects, by comparing actual treatment with standard treatment guidelines adopted by the hospital.

**Establishing Criteria and Thresholds for Selected Drugs**

Number of drugs where criteria were established:	5
Total number of criteria established for all drugs	41 (average 8 criteria/drug)
Number of drugs where information source was used for establishing criteria:	(n=4)
J. Sanford Antimicrobial Therapy	2
Navashin Rational Antibioticotherapy	2
Manual of Medical Therapeutics, Washington University	1
M. D. Mashkovski Drugs	2
Number of criteria where thresholds were established:	41
Must meet threshold 95–100% of time	37
Must meet threshold 90–95% of time	1
Must meet threshold 60% of time	3
Number of times where specific criteria were used during evaluations:	(n=41)
Appropriate indication for use of drug	4
Correct dosing	4
Appropriate monitoring, e.g., blood and urine tests, ECG	4
Dose adjustment for patients with renal insufficiency	3
Undesired concomitant use with certain drugs	3
Correct duration of treatment	2
Various others (each with a frequency of one)	21

Establishing criteria for drugs selected for inclusion in a given DUR program cycle is imperative in order to carry out the DUR. Unfortunately, this survey reports criteria for only five of the eleven drugs evaluated, upon which the following comments are based. The criteria established by the committees were selected from unbiased sources of information. However, as prescribed by the RPM guidelines, it is best for a DUR committee to have available STGs approved by the hospital. This provides a basis for comparing actual with recommended treatment practices, and decreases the need to utilize outside resources. This becomes more important as a committee increases the number of drug evaluations performed annually.

From the survey results, it appears that the reason for establishing thresholds for a given criterion is not clear to all the DUR committees. Thresholds are utilized during criteria development as a means of indicating importance of a specific criterion. For the most critical criteria, actual treatment practices must indicate the criteria are being met 100% of the time. For less critical criteria, however, the committee may establish that actual treatment practices are successful if they meet the criteria 90–95% of the time. Establishing a threshold that can be met less than 90% of the time, indicates that the criterion is not very important, and that no data probably needs to be collected for it.

**c. Dissemination and intervention techniques used after DUR evaluations**

Comparing actual study results with established thresholds:	(n=41)
Number of criteria where established thresholds were met	15
% of times thresholds were met	37 %
Number of drug evaluations where results were disseminated:	3
Number of times dissemination type was used:	
Weekly prescribers' meetings	1
Monthly prescribers' meetings	1
Ad hoc meetings	1
Posting of results	1
Number of drug evaluations where interventions were employed:	3
Types of interventions employed:	(n=3)
Informal and formal counseling	3
In service educational program	1
Reduction in procurement	1

An important finding from the survey results above is that thresholds were met only 37% of the time, indicating that established STGs are not being followed. The RPM guidelines instruct that the DUR committee, based on findings of this type, will then identify specific problematic treatment practices, and develop appropriate interventions, such as reeducation.

Of the eleven drug evaluations done by hospitals in the survey, dissemination of findings and development of intervention mechanisms were done for only three of the evaluations. In all three, however, recommendations from the RPM guidelines were followed almost explicitly. Those committees that did evaluations, but have not disseminated findings to the hospital staff, should do so in order to ensure transparency of the DUR program, and hopefully remove any doubt about the usefulness of the program.

**Comments and recommendations**

DUR is a continuous review process used primarily as a means to detect irrational, inappropriate, and unnecessarily costly drug therapy. It is performed by the medical staff as a criteria-based, ongoing, planned, and systematic process designed to continuously improve the appropriate and effective use of drugs. The process is well described in *Guidelines for Implementing Drug Utilization Review Programs in Russian Hospitals*. The basis for criteria selection should be STGs.

If the data evaluation shows that a drug use problem exists, corrective action must be taken. Possible actions include:

- removing a drug from the formulary
- restricting a drug to specialized services with specifically trained personnel
- developing special order forms for specific drugs
- counseling prescribing physicians
- developing staff education programs

- disseminating information on rational drug use through newsletters, or discussion at meetings

Once corrective action has been taken, and system changes have been put in place, a mechanism should be implemented that can evaluate the impact of the actions. This is most easily accomplished by repeating the same DUR as previously performed after six or twelve months.

At the end of a DUR cycle, usually one year, the committee should evaluate the program to determine:

- the appropriateness of drugs chosen for evaluation and thresholds;
- the effectiveness of data collection approaches;
- the appropriateness of actions taken;
- economic impact; and
- the adequacy of personnel utilized.

The program for the next year should be designed based on this evaluation, and a new ABC analysis report should be produced to facilitate drug selection. Drugs for which no problems are detected can be eliminated from the program.

It is important that hospital formulary or DUR committees systematically evaluate the economic effect of drug use review programs. The impact of expenditure control through wise selection and procurement will allow the best allocation of scarce resources.

#### **4. Adverse drug reaction monitoring**

An adverse drug reaction is defined as any undesired or unintended response to medication that requires treatment or alteration of therapy. Established ADR reporting is an important part of a formulary system. RPM technical assistance to oblasts in establishing ADR reporting systems was part of the work plan for 1998–1999.

There are certain obstacles to the implementation of ADR reporting systems in Russian hospitals, some of which are typical of health care systems worldwide. Very often physicians are reluctant to report adverse reactions for fear of punishment. In Russia, there is no tradition of peer review activities, and in the situation where reliable unbiased information is scarce, some adverse reactions may be misinterpreted as symptoms of other diseases or conditions. Another problem is the lack of a computerized patient record system. In many cases, a prescriber would not know the patient's history of reactions to drugs, or would not know what drugs were prescribed by other specialists, in order to avoid drug interactions.

In the former Soviet Union, a formal ADR reporting system existed, and physicians were supposed to report every serious case to the central level (MOH institution). At present, prominent Russian scholars and physicians are attempting to restore the system, and build up a database of reported ADR cases. A MedWatch type reporting system (U.S. Food and Drug Administration) was established at the Friendship University Medical School in Moscow by academician V. K. Lepakhin, and the State Institute of Preclinical and Clinical Expertise of Drugs of the Russian Medical Association in Moscow, but it was only in 1997 that the institutions received financial support from the Russian Government.

In the three surveyed oblasts, the evaluation showed that an ADR reporting system does not yet exist. An Adverse Drug Reaction Monitoring Program is fully functional in only one hospital of the 32 surveyed, although ADR reporting forms were developed in three hospitals.

At the same time, though non-systematically, RPM hospitals are making attempts to establish the reporting system. Six hospitals completed tables on adverse drug reactions reported in the past six months (20 reactions in total). Other hospitals indicated that the information on ADRs was not available, or that no ADR had taken place in the past six months.

ADRs were reported for 13 antimicrobial drugs, two local anesthetics, one vitamin and four non-steroidal anti-inflammatory drugs and analgesics. Three quarters (75%) of reported ADRs were allergic or pseudo-allergic, 20% toxic, and one ADR was pharmacodynamic. The reported severity was: two fatal cases, 35% had reactions of moderate severity, and 55% had mild reactions. The probability of ADR was most often defined as probable (without using the Naranjo scale). The table below illustrates the situation with ADRs.

#### ADRs Reported by Six Hospitals (six-month period, 1997)

	Drug (name, strength, dosage form)	Type of Reaction 1. pharmacodynamic 2. toxic 3. allergic 4. pseudo-allergic 5. idiosyncratic 6. drug-induced disease 7. withdrawal 8. drug interaction induced	Severity 1. Fatal 2. Severe 3. Moderate 4. Mild	Probability of ADR, (if known) 1. Definite 2. Probable 3. Possible 4. Doubtful
1.	1. Isoniazid 10% sol.	3	3	1
	2. Isoniazid 0.6 tab.	3	4	2
	3. Rifampicin 0.45 caps.	2	3	2
	4. Pirazinamide 1.5 tab.	3	3	1
	5. Pirazinamide 1.5 tab.	2	3	2
	6. Streptomycin 1.0 IM	3	3	2
	7. Kanamycin 1.0 IM	3	3	2
2.	1. Benzylpenicillin	3	4	1
	2. Gentamycin	4	4	1
	3. Ac. Acetylsalicylicum	4	4	2
	4. Vit. B12	3	4	1
	5. Furadonin	2	1	2
3.	1. Kanamycin	2	4	3
4.	1. Ampicillin-Na 500mg vials	3	4	3
	2. Metamizol (Analgin) sol. 50%- 2 ml	3	4	1
5.	1. Ampicillin	3	4	2
	2. Paracetamol	3	4	2
	3. Procaine (Novocaine)	3	4	1
6.	1. Ketorolac (Ketorol) tab.	1	3	3
	2. Lidocaine 2% inj	3	1	3

The Formulary Committees of the six hospitals took certain measures to prevent future adverse reactions. One drug, Furadonin, a domestically produced antimicrobial, was deleted from a formulary list as unsafe. Other measures included modifications of patient monitoring procedures, education of physicians on proper drug use, and patient education. Two drugs were proposed for inclusion into the DUR program: rifampicin and pyrazinamide.

### Comments and recommendations

Although there was little data on ADR, what was collected showed that even non-systematic ADR reporting reveals many drug use problems that require immediate interventions. At the same time, it is common knowledge, drawn from international experience, that the ADR reporting system is one that requires strict regulations and enforcement.

There is every opportunity within RPM health facilities to establish a sound ADR reporting mechanism. The main reason is that drug use control and management bodies already exist in hospitals, and oblast health administrations. The Formulary and Therapeutics Committee should be solely responsible for maintaining an adverse drug reaction reporting program. The goal of this program should be to provide ongoing surveillance of adverse drug reactions at the health facility.

The Formulary and Therapeutics Committee should be responsible for ensuring that adverse drug reactions are reported, collected data are analyzed, and appropriate action taken to improve drug therapy if needed. Surveillance should result in actions designed to eliminate or improve management of adverse reactions, including the following:

- changes in the formulary;
- implementation of new prescribing procedures;
- modification of patient monitoring procedures;
- inclusion of drugs in DUR programs; and
- development of education programs for prescribers and patients.

The reporting mechanism for adverse drug reactions should include the following elements:

- Any health professional (physician, pharmacist, nurse) who detects an ADR should notify the attending physician and document the reaction in the patient's case history.
- The reporting professional should then promptly complete an Adverse Drug Reaction Reporting Form, and send it immediately to the inpatient pharmacy or the responsible member of the Formulary and Therapeutics Committee. Reporting forms should be available in all areas of the hospital where drugs are utilized. It is advisable that the medical staff use the reporting forms developed by the Russian Medical Association—Annex 9 of RPM's *Manual for the Development and Maintenance of Drug Formularies*.
- The Formulary and Therapeutics Committee should then analyze all cases, summarize, and report the results to health professionals in the hospital.
- The Formulary and Therapeutics Committee should then initiate changes in drug use and procedures, or design educational programs if necessary. Adverse drug reaction data should be considered when making formulary decisions.

- The information on adverse drug reactions should be collected and processed by oblast DICs, since they were specially equipped by RPM to serve as links among oblast health facilities. DICs, unlike most hospitals, also have access to the most recent drug information, including those on ADRs. The USP regularly supplies the Centers with the latest data on drug recalls and detected ADRs via the Internet.
- Given the lack of a history of an ADR system, it may be necessary to further educate oblast and hospital administrations and to explore potential positive incentives for physicians to report ADRs.

## **5. Mechanisms for updating the formulary list**

As was reported by hospital formulary committees prior to the survey, they normally meet monthly (31%) or quarterly (66%). Formulary committees were asked to fill out the table for drugs deleted or added to the lists during the last quarter of 1997, or since the official formulary list was adopted.

It is obvious that a formulary list is not static. If regular committee meetings are held, the list of drugs on the formulary will probably change at every meeting, due to requests for additions and deletions.

### **Comments and recommendations**

Changes to formulary lists made by hospitals after the initial formulary list had been approved demonstrates the existence of established formulary systems.

Changes to a formulary may be communicated orally at hospital staff meetings and physicians' conferences (as was done in 100% of hospitals), but written communication will be more reliable (in 53% of hospitals updated lists were disseminated among personnel).

It is advisable that the hospitals coordinate additions with Drug Information Centers, that can provide information on pharmacokinetic profile of a drug, and its side effects, that may not be included in the package inserts.

## **6. Ongoing education of health providers on formulary system issues**

The initial training of health providers in formulary system implementation was provided by RPM consultants and permanent staff between 1994 and 1996. More than 400 physicians, pharmacists, and administrators were oriented and trained in indicator-based pharmaceutical assessments, policy options decision making, rational drug selection and prescribing, and DUR.

To ensure the sustainability of the RPM project, educational functions were delegated to the DICs. They are operational in providing both on-site and academic training in formulary system implementation issues.

### ***Ryazan Medical University Educational Information Center***

The Ryazan Medical University proved to be a good match for the educational objectives of the RPM project, because the university employs highly qualified faculty members, and has access to a broad audience of health providers. There are 11 teaching departments for students, and the Department of Post-graduate education, where physicians and pharmacists improve their knowledge and skills in continuing education programs.

The priority issues for education include technical areas addressed through the RPM project in Ryazan and other RPM oblasts. They include the following:

- principles of rational drug use;
- formulary systems and drug use evaluation; and
- unbiased therapeutic and drug information.

The faculty of the Center provide training for:

- medical students—both within the curriculum, and during extra-curriculum classes;
- interns, physicians, and pharmacists—within training curricula at the Department of Post-graduate education;
- teachers of nursing colleges; and
- post-graduate students and faculty members of the University.

The most substantive changes were made to the standard curriculum for medical students. The university developed RPM-based materials and, between 1996 and 1998, provided training for about 2,150 third and fourth year students in:

- Principles of rational drug use
- Unbiased drug information
- Importance of drug information for patients
- Concepts of cost-effective drug selection
- Generic drug names
- Principles of drug formulary development and maintenance
- Concepts of drug use evaluation
- ABC and VEN-analysis
- New drugs, evaluation of justification for prescribing
- The WHO Personal-drug concept

Ryazan State Medical University actively disseminates RPM concepts Russia-wide. Training in RPM methodology was provided to more than 220 health specialists from Perm, Ekaterinburg, Tula, Kurgan, Chelyabinsk, Magnitogorsk and many other cities.

Educational activities of Ryazan Medical University based on RPM concepts are described in detail in Annex 5, “Report of Ryazan State Medical University on Rational Pharmaceutical Management Project (1995–1998).”

### ***Oblast Drug Information Centers***

Oblast DICs provided training and consultancy to oblast prescribers on-site. The Ryazan DIC focused its activities not only on providing assistance to oblast hospitals in formulary development, but also worked with individual health providers from Ryazan Oblast Hospital, the Ryazan Oblast Children’s Hospital, and physicians and pharmacists from rayons. In 1997, the Ryazan DIC conducted two seminars on drug selection and clinical pharmacology, and trained specialists from Lkhovicki Rayon Hospital of Moscow Region in drug information and principles of formulary system implementation.

In Novgorod, the DIC conducted two seminars on drug procurement issues, and several seminars on rational drug use of antimicrobials. The DIC is also responsible for monitoring drug use review programs in the Novgorod Oblast Hospital. Special attention was given to the DUR of gentamycin, cefazolin, aminophylline, and ranitidine. DUR results were presented at a physician's conference and an Oblast Formulary Committee meeting. Educational interventions were undertaken to ensure that the antibiotics are used properly. The Novgorod DIC is also active in the development of educational information newsletters, for example on drug-food and drug-drug interactions and on antimicrobial resistance.

### **Comments and recommendations**

In the course of RPM project implementation in Russia, medical schools and universities expressed great interest in the development of RPM-based educational materials for students and post-graduates. No doubt, the leading role here belongs to RPM collaborator Ryazan State Medical University. Specifically, this issue was discussed in May 1997, at the RPM/WHO workshop Integration of Rational Prescribing in Medical Undergraduate Curricula in the NIS. As was anecdotally reported, changes in medical student and postgraduates' curricula to include RPM methodology were made at St. Petersburg Medical University, Perm Pharmaceutical Academy, Stavropol Medical University, Volgograd Medical Academy, Chita Medical Academy, and many others. All those institutions are using RPM teaching materials disseminated through congresses, workshops, and the Internet.

It would very advantageous to develop a mechanism for the medical schools to share their experiences.

Oblast DICs have the capacity to serve as on-site trainers in rational drug use and formulary system development. Within a very short period of time they have managed to build up a database on rational drug use, and to develop the expertise necessary for training health providers.

It should be noted that oblast DICs depend largely on oblast health administrations for financing. They were designed as not-for-profit state enterprises, and provide information and training free of charge. While in Novgorod, the DIC became a part of the Oblast Formulary Committee and, as such, enjoys support and respect from health decision makers and health providers. In Ryazan and Pskov, DICs are financed and supported by oblast hospitals, which in turn, are facing severe financial shortages. Economically, the DICs' activities do not have an obvious quick return on investment. However, if health administration financial departments were to calculate the financial impact of DICs' activities, such as funds saved by rationalizing treatment, drug selection, use and procurement, improved patient outcomes, or other pharmacoeconomic analyses, the value of DICs should become apparent.

### **D. Drug Procurement and Tender Management**

In the former Soviet Union, drug procurement was done at the central level according to aggregate needs for the entire country. Oblast Pharmacias were primarily responsible for the storage and distribution of drugs and information received from the federal warehouses or manufacturers. The transition period to a market economy caused chaos in drug procurement and distribution, because the right and responsibility to procure drugs was delegated to the oblast level that had neither the experience, nor systems in place, to effectively purchase drugs. Another impediment was diminishing drug budgets, a trend still observable at the present time. These conditions created a challenge for RPM technical assistance in implementing competitive procurement techniques.

The table below shows the continuing tendency toward health and drug budget reductions.

### **Health and Drug Budgets in Ryazan, Novgorod and Pskov Oblasts in Billions of Rubles and Millions of**

## Dollars

Years	Ryazan		Novgorod		Pskov	
	Health budget	Drug budget	Health budget	Drug budget	Health budget	Drug budget
1994	n/a	n/a	n/a	n/a	81.7 (\$27.3 mil)	8.8 (\$2.9 mil)
1995	n/a	n/a	n/a	n/a	145.7 (\$32.4 mil)	12.8 (\$2.8 mil)
1996	450 (\$77.6 mil)	n/a	242 (\$41.7 mil)	41 (\$7.1 mil)	266 (\$45.8 mil)	25 (\$4.3 mil)
1997 planned	454 (\$76.9 mil)	89 (\$15.1 mil)	258 (\$43.7 mil)	44 (\$7.5 mil)	248 (\$42 mil)	22 (\$3.7 mil)
actual for 11 months 1997, Ryazan	327 (\$55.4 mil)	44 (\$7.5 mil)				
1998 (planned)	435 (\$70.1 mil)	n/a	233 (\$37.5 mil)	43 (\$6.8 mil)	n/a	n/a

The project proposed to improve the efficiency of procurement through introducing competitive tendering techniques. Training was provided to oblast decision makers through the Policy Options Workshop in Ryazan in 1994, the study tour to the U.S. in 1995, and the Policy Options Workshop for Novgorod and Pskov in 1996. All three oblasts established Tendering Committees within their Oblast Health Administrations, but have not yet fully realized the potential of tendering to reduce costs.

Several trial competitive procurement activities took place during 1995 and 1997. In 1995, Ryazan Health Administration conducted a limited tender for insulin that resulted in savings of US\$585,000 when compared to what would have been paid for the same product through direct purchases.

In 1996, the Pskov Health Administration conducted a restricted tender for cardiovascular drugs, antibiotics, and antispasmodics for oblast health facilities, and achieved savings of approximately 10%, compared to the wholesaler price lists. Based on this experience, the Governor of the Oblast issued a decree mandating competitive procurement for drugs and medical supplies, however, severe financial shortages have prevented conducting any subsequent tenders. Pskov is still very interested in increasing its use of tendering.

The most impressive competitive purchases were done in Novgorod oblast in May 1997. Eleven vital drugs were selected, including insulins, and drugs for oncology, surgery, and tuberculosis. In Novgorod, accepted procedures for restricted tender were followed. This was the first real competitive tender conducted in RPM oblasts. The table below shows prices before and after the tender.

## Comparative prices on drugs before and after May 1997 tender, Novgorod

##	Brand Name	Generic Name	Unit	Unit Purchase Price for Health Facilities (\$ and Rubles)		% Difference
				Previous Purchase Price	Tender Price	
1	Humulin (Lilly) 40 MU/1 ml 10 ml	Human insulin	vial	\$11.50	\$7.00	- 40%
2	Humulin (Lilly) 100 MU/1.5 ml	Human insulin	5 vial pack	\$28.00	\$17.00	- 40%
3	Methotrexate 50 mg	Methotrexate	vial	\$3.20	\$1.30	- 60%
4	Platinol 25 mg	Cisplatin	vial	\$10.90	\$7.60	- 30%
5	Arduan 4 mg	Pipecuronium bromide	25 pack	\$47.20	\$26.80	- 43%
6	Lidocaine 2% 2.0	Lidocaine	10 pack	5,550 rbl	4,350 rbl	- 22%
7	Prozerine 0.05% 1.0	Neostigmine	10 pack	6,325 rbl	4,900 rbl	- 23%
8	Pirazinamide 250 mg	Pirazinamide	100 pack	\$10.00	\$6.00	- 40%
9	Isoniazid 300 mg	Isoniazid	10 pack	1,644 rbl	1,179 rbl	- 28%
10	Streptomycin 1.0 g	Streptomycin	vial	1,601 rbl	1,250 rbl	- 22%
11	Rifampicin 150 mg	Rifampicin	20 pack	19,998 rbl	6,322 rbl	- 68%

As was estimated by the Oblast Health Administration, the tender led to a total savings of 970.2 million rubles (approximately US\$165,000), including 578.2 million rubles (\$98,000) saved in prices on insulins, and 392 million rubles (\$66,440) on other vital drugs, and ensured the availability of those vital drugs.

Compared to the 1996 procurement, prices for the first-line TB drugs decreased on average by 50%, for oncological by 30%, and for vital drugs used in surgery by 20%.

In November 1997, Novgorod Oblast Health Administration approved the final Oblast Formulary List of about 600 drugs for 1998 procurement and use by oblast health facilities. A smaller list of about 400 vital drugs was created for pooled-procurement through competitive techniques. The list contains drug names, and dosage forms, and quantities. It is notable that 69% of drugs are still listed by brand names and not generic names as was recommended by RPM. Novgorod oblast estimates that drug expenditures for 1998 will decrease from 1997 levels by 60–80%.

### Comments and recommendations

The information obtained from oblasts on drug procurement shows that further attempts should be made to enhance the system. There is a clear tendency in oblasts towards competitive procurement, whereas in 1994 and 1995, oblasts made purchases directly from suppliers, wholesalers and manufacturers, at quoted prices. With RPM technical assistance, elements of competitive negotiations were introduced at Novgorod SE Pharmacia. Subsequently, the mechanism has progressed through competitive negotiations in Ryazan and Pskov in 1996, to restricted tenders in Novgorod in 1997.

With the establishment of formulary systems in Ryazan, Novgorod, and Pskov, the next step in enhancing procurement capacity of health administrations should be the development of mechanisms for pooled competitive procurement of drugs for public health needs. This is in accord with the latest requirements of the Russian Government and the President, outlined in the Russian Government Enactment #197/2731 of December 31, 1997, "On Training Specialists in Organization and Conducting Competitive Procurement of Goods for the Government Needs," and the Presidential Decree of April 8, 1997, "On the Immediate Measures of Corruption Prevention and Reduction of Budgetary Expenditures for Public Procurement."

In this situation, options may include:

- Restricted versus open tender: So far, tenders conducted in oblasts were restricted to known reliable suppliers within the oblast. An open tender may bring in more reputable suppliers, especially now that oblasts aim at pooled procurement, and large quantities of drugs may allow more cost-efficiencies. Although open tender results in a heavier workload for procurement offices, it also brings the lowest possible prices.
- Oblast or Russia-wide scope: At least for some items, a Russia-wide competitive tender, whether open or restricted, will almost always result in lower prices than a tender limited to the oblast market.

However, much work remains in the area of procurement. Respondents also reported that hospitals experienced problems due to local policies and administrative decisions taken at municipal and oblast levels. In Ryazan oblast, for example, due to financial shortages, the 1997 drug procurement was largely based on mutual accounts, where drugs were bartered by Oblast Health Administration for another commodity (alcohol). Drug nomenclature was limited to what the manufacturer offered, and, in many cases, these were not formulary drugs. In Pskov oblast, the mayor of Pskov City assigned all city hospitals to one procurement agency, Municipal Pharmacy #3, which had not participated in the formulary development process. As a result, City Hospital #1, which had invested much effort in developing one of the best formulary lists among RPM hospitals, cannot get its formulary drugs, and experiences severe drug shortages, because it has to buy drugs from the pharmacy at non-competitive prices.

At the present point though, while the tendering system in the oblasts is only under consideration or in the first stages of implementation, there is at least one immediate and simple step that oblasts can make in order to maximize the benefit of pharmaceutical purchases, and minimize possible favoritism in procurement. That is to use only generic names on procurement and tender lists. At present, approximately 60% of the Novgorod 1998 procurement list appears as brand names.

Further training in tender management and pooled procurement for Russian oblasts is needed. This may be achieved through workshops structured to give technical assistance in quantifying drug needs, designing a tender list of essential drugs, and conducting a competitive tender.

These activities could use teaching materials based on the MSH publication *Managing Drug Supply*, widely used in other RPM countries. Also available for teaching and practical purposes are Russian language tender documents, developed by RPM consultants in 1995 for RPM tender trials in Ryazan oblast, and those developed during tendering process in Novgorod.

## VI. CONCLUSION AND RECOMMENDATIONS

Overall, the RPM program met or exceeded its goals. In addition to the pilot and roll-out oblasts, the RPM methodology was adapted in at least six other sites in Moscow, Saint Petersburg, Ekaterinburg, Perm, and Vladivostok. RPM Russian language materials have also been requested in other NIS countries, including Ukraine, Moldova and Kazakstan.

The RPM Impact Evaluation Study focused on the process of formulary system development. Survey responses support the conclusion that Russian administrators and health professionals have adapted the process to the Russian health care system and are using it as a method to improve patient care.

The impact evaluation survey also provided an opportunity for participating hospitals to describe practical obstacles that remained to be overcome, and to offer recommendations for improvement in the administrative, technical and maintenance phases of the formulary process. Recommended refinements include the following:

1. Additional and refresher information should be provided for physicians, if needed, to emphasize the importance of adhering to the formulary list for all but exceptional circumstances.
2. Written hospital-specific policies related to enforcement of the use of formulary drugs, the use of non-formulary products in the hospital, use of generic drug names, generic and therapeutic substitution, and activities involving sales representatives should be developed.
3. As high quality products become available from multiple sources, all drugs in formularies should be listed by generic name in order to facilitate competitive procurement.
4. Broader use of drug product restrictions in the formulary should be instituted, if appropriate, in order to improve clinical outcomes.
5. Written information on drug formulary policies and changes should be more broadly used.
6. Links among the current drug information centers should be established to encourage sharing of information and experience.
7. Peer review practices related to standard treatment guidelines and drug use review should be developed and/or encouraged.
8. Standard treatment guidelines, particularly of local major causes of morbidity should continue to be improved.
9. The DUR process should continue to be developed and the findings disseminated to the hospital staff to ensure that the process is understood and to promote support for usefulness of the program.
10. The adverse drug reporting systems, including systems for improving management of adverse drug events and the incentives for doing so should continue to be developed.
11. A mechanism that would allow medical universities to share their experiences and disseminate materials on rational pharmaceutical management should be established.
12. Drug procurement processes should continue to be enhanced to emphasize the transparency of the process and optimize the quality and cost-effectiveness of procurement.

Evaluation of the long-term financial and health outcomes of implementation of RPM-introduced interventions will be possible as more data become available. RPM recommends tracking the following four indicators to provide information on how well the concepts of rational pharmaceutical management are understood, and to measure the impact of the formulary process and drug use review:

1. The percentage of drugs on the formulary of unproven efficacy (or alternately, the percentage of the drug budget spent on drugs of unproven efficacy)
2. The percentage of drugs products on the formulary, that are fixed dose combination products
3. The percentage of drugs listed in the formulary under the generic names (or alternately, the percentage of the drugs procured under the generic names)
4. Evaluation of the appropriateness of prescribing by examining the use of a tracer group of drugs, for example, cardiovascular drugs and antibiotics

RPM project assistance and how it was provided had a profound impact on the management culture and broader decision-making process within health facilities and oblast health administrations. These changes are critical to the sustainability of RPM activities in the target oblasts and to the replication of those activities in other parts of Russia.

## **ANNEXES**

### ANNEX 1: COST OF DISEASE TREATMENT CALCULATION

The goal of a drug formulary should not be to decrease the drug budget alone, but to decrease the overall costs needed to manage specific diseases. An example of a very basic analysis follows.

#### Community-acquired pneumonia

Treatment options: Cefotaxime 1 gm IV q8h x 7-10 days versus  
Ceftriaxone 1 gm IM q24h x 7-10 days<sup>1</sup>

	Unit Cost (\$)	Daily Cost (\$)	Cost for Course (\$)
<b>Cefotaxime 1 gm IV q8h x 7-10 days</b>			
Drug Cost	<b>12.66</b>	37.98	265.86 - 379.80
Medical Supply Costs			
syringe/needle	0.65	1.95	13.65 - 19.50
IV set	0.35	1.05	7.35 - 10.50
<b>Total Cost<sup>2</sup></b>			<b>286.86 - 409.80</b>
<b>Ceftriaxone 1 gm IM q24h x 7-10 days</b>			
Drug Cost	<b>33.64</b>	33.64	235.48 - 336.40
Medical Supply Costs			
syringe/needle	0.65	0.65	4.55 - 6.50
<b>Total Cost<sup>2</sup></b>			<b>240.03 - 342.90</b>

If a Formulary Committee were to consider only acquisition cost, ceftriaxone appears to be considerably more expensive than cefotaxime (\$33.64 - \$12.66 = \$20.98 more per dose). However, when dosing frequency and the cost of supplies needed to administer the drugs are also considered, ceftriaxone is actually more cost effective to use than cefotaxime (\$409.80 - \$342.90 = \$66.90 less for a ten-day treatment course).

<sup>1</sup> Please note that neither treatment would be considered a treatment of first choice since both cephalosporins provide a broader spectrum coverage than necessary. It is simply the author's intent to demonstrate that a lower acquisition cost sometimes decreases the drug budget but not the overall cost to the institution.

<sup>2</sup> The estimated total costs are not necessarily complete figures, as they include only the acquisition costs for drugs, syringes, needles and IV sets. Costs for nursing time, and other potential supplies, such as alcohol swabs, were not included. Drug costs were quoted from the Red Book, 1995 edition. The acquisition costs for syringes, needles and IV sets were quoted from *The Drug Estimation and Monitoring System*, prepared by MSH.

If the cost of the labor required to prepare doses were also considered, greater savings could be shown. However, adding labor costs to the analysis is only valid if the savings can actually be applied, such as through reduction in staff, or reassignment of a staff member from drug preparation to another task.

## ANNEX 2: DRUGS DELETED FROM FORMULARY LISTS

### By Health Facility

Data were received from 28 hospitals. As a result of the formulary system development, all hospitals reduced the number of drugs in use.

#*	Health Facility	Type	# Beds	# of Drugs in Use Before and after Formularies Implemented	
				Before	After
1	Novgorod Oblast Hospital	Multi-ward	910	423	368
2	Novgorod City Hospital # 1	Multi-ward	510	446	272
3	Novgorod Central City Hospital	Multi-ward	600	251	228
4	Novgorod. Oblast TB Hospital	Hospital	175	350	280
5	Novgorod Zarubino Central Rayon Hospital	Central Rayon Hospital	125	320	241
6	Novgorod Okulovo Central Rayon Hospital	Multi-ward	300	253	208
7	Novgorod Borovichi Oblast Sexually Transmitted Diseases Hospital	Dermatological	85	200	150
8	Novgorod City Hospital #2	Therapeutic	255	no data	
9	Novgorod Borovichi Onkological Hospital	Oncological	100	no data	
10	Novgorod Chudovo Central Rayon Hospital	General surgery, pediatrics, gynecology, infectious, neurology	165	414	392
11	Novgorod Neurological Hospital	Psychoneurology	125	92	69
12	Novgorod Veterans Hospital	Therapeutic	100	400	300
13	Novgorod Borovichi Central Rayon Hospital	Multi-ward	No data	710	520
14	Novgorod Staraya Russia Central Rayon Hospital	Multi-ward	710	820	468
15	Ryazan Oblast Hospital	Multi-ward	1,100	1,366	434
16	Ryazan Mihailovo Central Rayon Hospital	Multi-ward	240	551	436

17	Ryazan Scopin Central Rayon Hospital	Multi-ward	600	~1,500	284
18	Ryazan Korablino Central Rayon Hospital	Multi-ward	320	600	374
19	Ryazan Semashko Hospital	Multi-ward	440	1,075	319
20	Ryazan Kasimov Central Rayon Hospital	Multi-ward	635	620	317
21	Ryazan Sasovo Central Rayon Hospital	Multi-ward	560	400	235
22	Ryazan Oncological Hospital	Oncological	265	~1,000	225
23	Ryazan City Hospital #11	Multi-ward	800	no data	
24	Pskov Oblast Hospital	Multi-ward	810	have only 52 drugs in stock, out of 250 needed	
25	Pskov Veterans Hospital	Therapeutic	80	360	186
26	Pskov Pechory Central Rayon Hospital	Multi-ward	171	360	305
27	Pskov Nevel Central Rayon Hospital	Multi-ward	230	330	317
28	Pskov Ostrov Central Rayon Hospital	Multi-ward	265	480	281
29	Pskov Palkino Central Rayon Hospital	Rayon Hospital	100	500	304
30	Pskov Velikie Luki City Hospital	Multi-ward	840	no data	
31	Novgorod Khvoynaya Central Rayon Hospital	Multi-ward	185	340	300
32	Novgorod Children Hospital	Multi-ward	540	no data	

## By Drug Classes From All Facilities

### Cardiovascular drugs

#### Nitrates:

Nitroglycerin (Nitrogranulong, Sustak, Sustanit, Nitrolong, Trinitrolon, Pentaeritritil Tetranitrate (Erynite))  
Those nitrates were deleted mainly for the reason of their low efficacy. Formulary Committees kept Isosorbide Dinitrate in the formulary lists as a more efficacious drug.

#### Calcium-channel blockers:

Fenidilin (Senzyt, Difril Falicor)—low efficacy and rare use  
Verapamil (Isoptin, Finoptin)—mainly as a duplicate drug

#### Beta-adrenergic blockers:

Pindolol (Visken), Nadolol (Corgard), Oxprenolol (Trazicor), Talinolol (Cordanum)—high cost, or as duplicate drugs.

#### ACE inhibitors:

Captopril—efficacy, unsafe, and disadvantageous pharmacokinetics

#### Sympatholytic Agents:

Reserpin, Raunatin (Rauwolfia alkaloids), Adelphan (Reserpin 0.1 mg, Dihydralasin 0.1 g), Adelphan Esiddrex (Reserpin 0.1 mg, Dihydralasin Sulfate 0.01 g, Hydrochlorthiazide 0.01 g), Brinerdin (Reserpin 0.1 mg, Clopamid 5 mg, Dehydroergocristin Mesilat 0.5 mg), Cristepin (Dehydroergocristin Mesilat 0.5 mg, Reserpin 0.1 mg, Clopamid 5 mg), Triresid (Reserpin 0.1 mg, Dihydrolasin Sulfate 0.1 g, Hydrochlorthiazide 0.01 g), Triresid K (Reserpin 0.1 mg, Dihydrolasin Sulfate 0.1 g, Hydrochlorthiazide 0.01 g, Potassium Chloride 0.35 g), Sinepress (Dehydroergotamin Methansulfonat 0.6 mg, Reserpin 0.1 mg, Hydrochlorthiazide 10 mg)  
Simpatholitics are obsolete drug group of low efficacy and safety. Currently they are not included in the therapeutic schemes of hypertension.

#### Vasodilating drugs:

Hydralasin (Apressin), Sodium Nitroprussid

#### Ganglionic blocking agents:

Ganglifen Hydrochlorid (Gangleron)—unsafe  
Azamethonium Bromide (Pentamin)—not readily available from suppliers

#### Alfa-adrenergic blockers:

Pyrroxan, Phentolamin

#### Antihypertensive drugs stimulating central adrenergic receptors:

Clonidin (Clofelin, Hemiton, Katapressan), Methyldopha (Dopegit)

Arterial and arterio-venal dilatators, alfa-adrenergic blockers and central acting antihypertensive drugs are not the drugs of first, second, or even third choice for hypertensive disease treatment. They were deleted due to their low safety and rare use.

Diuretics:

Chlortalidon (Oxodolin)—not readily available from suppliers

Amonium Chloridum, Folium Uvae Ursi, Lespenephri (Lespedeza Capitata) Spironolacton—unsafe Etacrinic acid—low efficacy

Cardiac Glycosides:

Digitoxin, Lanatosid C (Isolanid, Celanid), Corglycon (Convallaria Glycosides), Cordigit (Digitalis Glycosides)

All these drugs were deleted due to their low safety and rare use. Cordigit and Corglycon contain several poorly standardized glycosides that can give unpredictable side effects.

Antiarrhythmic drugs:

Disopyramide (Rythmilen), Moracezin (Aethmozin)—high cost

Tinctura and Extractum Fructus Cretegi—low efficacy

Miscellaneous cardiovascular agents:

Carbochromen (Intensain, Intencordin), Molsidomin (Corvaton, Sidnopharm), Inosin (Riboxin, Inosie-F), Xantinol Nicotinat (Complamin)

Clinical efficacy of the majority of these drugs have not been proved. They were deleted mainly for the reason of rare use, low efficacy and sometimes for high cost, especially Inosie-F.

**Drugs acting on central nervous system**

Hypnotics:

Bromisoval, Barbitol Sodium, Medinal, Reladom (Cyclobarbital 0.1 g, Diazepam 0.01 g, Flunitrazepam (Rogipnol), Phenobarbital, Benzobarbital

Barbiturates were deleted unsafe.

Bromisoval—non-efficacious

Flunitrazepam—costly and duplicating

Opioid Antagonists:

Buprenorphin—not available from suppliers

Omnopon—low efficacy

Tramadol (Tramal)—is expensive; Trimepiridin (Promedol)—rarely used

Anticonvulsants:

Phenobarbital, Benzobarbital (Benzonal), Valproate Sodium, Carbamazepin, Clonazepam, Phenytoin (Diphenin), Beclamid (Chloracon), Ethosuxemid, Gluferal (Phenobarbital 0.025 g, Bromisoval 0.07 g, Coffeinum Natrii Benzoate 0.005 g, Calcium Gluconate 0.2 g)

Phenobarbital, Benzobarbital, Ethosuxemid, Gluferal—unsafe drugs

Beclamid, Gluferal—low efficacy

Valproate Sodium, Carbamazepin, Clonazepam, Phenytoin (Diphenin)—rarely used

**Anti-Parkinson's drugs:**

Sinemet (Levodopa 0.25, Carbidopa 0.025), Nacom (Levodopa 0.25, Carbidopa 0.025), Diphenil Tropin (Tropacin), Levadopa, Biperidin (Akineton):

Levadopa—low efficacy

Sinemed and Nacom—expensive

Diphenil Tropin and Biperidin (Akineton)—rarely used

**Analeptics:**

Camphora, Nicetamid (Cordiamin), Lobelin, Cythizine (Cytiton)

All the analeptics were deleted as unsafe drugs.

Cythizine and Lobelin are no longer manufactured

**Neuroleptics:**

Practically all hospitals deleted a significant number of various neuroleptics, mainly because general type hospitals rarely use those drugs.

Specialized neuro-psychiatric hospital deleted the following:

Dicarbine dihydrochloride (Carbidin), Chlorprothixene, Pimoside, Reserpin, Dicarbine and Pimoside—low efficacy

Chlorprothixene—not readily available from suppliers

Reserpin—low efficacy, unsafe

**Antidepressants:**

In all hospitals the number of antidepressants was significantly reduced. In multi-ward hospitals, the most often deleted drugs were:

Pipofizin (Azafen)—low efficacy

Amitriptyline, Pirlindol, Imipramine and Clomipramine—not included in treatment protocols, rare use

In the specialized hospital, Pipofizine was deleted as a low efficacy drug, Fluoxetine and Doxipine as highly expensive drugs, and Clomipramine (Anafranyl) as not readily available from suppliers.

**Litium Salts:**

In many hospitals Litium Carbonate and Litium Oxybuterate were deleted as unsafe and rarely used.

**Anxiolitics:**

Significant numbers of those drugs was deleted. Prior to formulary system implementation, an average of 10 anxiolitics was used in each hospital. The most frequently deleted were:

Trimetozin (Trioxazin)—low efficacy

Chlordiazepoxide (Elenium), Nitrazepam, Alprozolam, Temazepam and Oxazepam—duplicating drugs.

Medazepam—not available from suppliers

**Sedative Drugs:**

All hospitals significantly reduced the number of sedatives, mainly Valeriana and Lianurus in different oral forms, Sodium Bromide, and a large number of different combination drugs (Valocordin, Corvalol, Belaspon, Beloid, Valosedan, etc.) due to their low efficacy and rare use.

**Nootrops:**

The most often deleted drugs were Aminobutiric Acid (Aminolon) because of its low efficacy, and Cerebrolizine because of its high cost.

**Non-Opioid Analgetics and NSAID:**

Prior to formulary system implementation, the average number of those drugs in hospitals was 15–25. In the course of the selection process, many hospitals deleted:

Aninophenazon (Amidopirin)–not safe

Metamizol Sodium (Analgin), Paracetamol–duplicative

Baralgin Metamizol and spasmolitics), Ascofen, Cofalgin, Pentalgin, Tepmalgin–combination.

Among NSAIDs, almost all hospitals deleted Phenylbutazon (Butadion) and Reopyrin (Phenilbutazon and Aminophenazon) as unsafe drugs. Other frequently deleted drugs were Indomethacine, Piroxicam and Naproxen because of low safety. Mephenam Acid was deleted as unsafe and low efficacious, and Cetorolac mainly as a highly expensive drug.

**Antimicrobial drugs**

**Penicillins:**

In the penicillin group the most commonly deleted drugs were:

Methycillin–unsafe

Oxacillin–low efficacy

And combination drugs: Unazin (Ampicillin plus Sulbactam)–rarely used; Ampiox (Ampicillin plus Oxacillin)–highly expensive, Bicillin 3" (Benzylpenicillin Sodium plus Benzathine Benzylpenicillin) and Bicillin 5" (Penicillin-Procaïne plus Benzathine Benzylpenicillin)–not readily available from suppliers

**Cephalosporins:**

The most commonly deleted cephalosporins were Cefazolin and Cefaclor, as they are no longer included into treatment protocols.

Ceftriaxone and Cefotaxime Sodium were deleted in some hospitals as unavailable from suppliers.

Cefuroxime Axetil (Zinnat) was deleted as highly expensive.

**Other beta-lactam antibiotics**

Some hospitals deleted Imipenem because of its high cost.

**Aminoglycosides:**

Practically all hospitals deleted from use first generation aminoglycosides: Neomycin, Kanamycin and Monomycin as not safe and obsolete. For the same reason some hospitals deleted Streptomycin and Gentamycin. In some hospitals Amycacin was deleted because of high cost, and non inclusion in STGs, and Tobramycin as unavailable from suppliers and obsolete.

**Tetracyclines:**

Practically all hospitals deleted tetracyclin and tetracyclin hydrochloride as unsafe and non-efficacious. Some hospitals deleted Methylmorpholintetracyclin (Morphocyclin) for the same reasons. Metacyclin was deleted as a duplicative drug.

Combination drugs: tetracycline with nystatin, and combination of tetracyclin with Macrolide Aleandomycin (Oletetrin, Tetraolean–as no longer included in STGs.

**Macrolides/Azalides:**

The most commonly deleted was Oleandomycine because of its low efficacy. Some hospitals had to delete the new generation macrolides Azitromycin and Claritromycin because they were not readily available from suppliers.

**Polymixins:**

Polymixin M—was deleted by several hospitals as unavailable from suppliers.

**Rifamycins:**

Rifampicin was deleted from formulary lists by many hospitals as rarely used (only for specific diseases, like TB).

**Fluoroquinolons:**

Pefloxacin and Norfloxacin were deleted because of changes in STGs.

**Sulfamides:**

Prior to formulary selection activities, hospitals would procure an average of 10 sulfamides. The following sulfamides were deleted by various hospitals as unsafe and non-efficacious: Sulfanilamide, Sulfadimidine, Sulfamethoxine, Sulfadimethoxine, Sulfathiazol, Sulfalen, Sulfaguanidine, Sulfacarbamide, Salazosulpiridine, Sulfaaethydiol, phthalylsulphathiazole.

**Nitrofurans:**

In the majority of cases Nitrofurantoin (Furadonin, Furazolidon, Furazidin (Furagin)) was deleted as no longer included in treatment guidelines.

**Other antimicrobial drugs:**

Almost all hospitals deleted Chloramphenicol (Levomycitin) as unsafe drug.

**Anti-TB drugs**

In the majority of cases Phtivazid, Ethionamid and Saluzid were deleted because of their rare use.

**Drugs used in the treatment of trichomoniasis and amebiasis:**

Almost all hospitals deleted Tinidazol as a duplicate drug.

**Antimalarial drugs**

Chloroquine was deleted as non-efficacious and unsafe.

**Anthelmintics:**

In the majority of cases Extractum Filicis Mari was deleted as unsafe. Piperazine Adipinat was deleted as low efficacious, and some hospitals deleted it as highly expensive. Pyrantel Embonat was deleted as it is no longer included in the treatment guidelines, and Mebendazole was deleted as rarely used.

**Antifungal drugs**

Very often such drugs as nystatine and grizeofulvin were deleted as drugs of low efficacy. Levorine, clotrimasol and Fluconazol were deleted by some hospitals as duplicate drugs. Ketoconazol was deleted as an expensive drug. Amphotericin was deleted as a rarely used drug.

**Uroseptics**

The most commonly deleted were Hexamethylen, Tetramin, Acedum Pipemedicum, Acedum Oxolinicum and

Nitroxolin as no longer included in treatment guidelines, or rarely used. Some hospitals deleted Acedum Nalidixicum as a non-efficacious drug.

### **Antiviral drugs**

Remantadin Hydrochloride and Oxolin ointment were deleted from formularies as obsolete. In several hospitals Bromnaphthachinon, Interferon, and Acyclovir were deleted as rarely used.

### **Drugs affecting gastrointestinal functions**

Appetite stimulating drugs:

Apelac (bee milk) as rarely used, and of unproven efficacy.

Spasmolytics:

Atropine Sulfate, Platiphyllin Hydrotartrat and Metacine were deleted mostly as unavailable from suppliers. Drotaverine (No-spa in tablets) was deleted as non-efficacious.

Antacids:

All hospitals dramatically reduced the number of antacids. Different antacids were deleted in different hospitals. The most commonly deleted drugs were: Vicalin (Bismuthi Subnitras 0.35, Magnesi Carbonate 0.4, Sodium Hydrocarbonate 0.2, Rhizoma Calami 0.025, Cortex Frangulae 0.025, Rutine 0.005, Kellin 0.005) and Vicair (Bismuthi Subnitras 0.35, Magnesi Carbonate 0.4, Sodium Hydrocarbonate 0.2, Rhizoma Calami 0.025, Cortex Frangulae 0.025). Most were deleted because of unproven efficacy. Maalox (Aluminium Hydroxide 0.4, Magnesium Hydroxide 0.4) was deleted because of its high cost. Aluminium Phosphate (Phosfalugel)—as unsafe and expensive.

H<sub>2</sub> blockers:

Many hospitals deleted cimetidine as an unsafe, non-efficacious and costly drug. Nizatidine and famotidine were often unaffordable because of high cost.

M-Cholenergic blockers:

Pirenzepine—as non-efficacious drug.

Gastroprotectants:

Some hospitals deleted Bismuti Subcitrate (De-Nol) as a non-efficacious costly drug.

Laxatives:

Senosides were deleted as unavailable from suppliers. Picosulfate Sodium and Extractum Frangulae were deleted as duplicative drugs. Phenolphthalein was deleted as a low efficacy drug. Olium Vaselini was excluded as it is not included in the treatment guidelines.

Antiflatulent drugs:

Polyphepan (Lignin) was deleted as low efficacious.

Enzymes:

The most commonly deleted enzymes were Panzimorm (Lipase 6,000 IU, Tripsine 450 IU, Chemotripsine 1,500 IU, Amylase 7,500 IU, Acidum Holicum 0.0135 g, Pepsin 50 IU, Eminoacids 0.1 g, Acidum Hydrochloridum 100 MEQ) as drugs of low efficacy, and often costly

Pancreatin was deleted as a duplicative drug. Acidine Pepsine (Bethain Hydrochloride 0.4 and Pepsine 0.1) was deleted as non-efficacious drug.

Local antimicrobial agents:

Chinioform (Enteroceptol) and Intestopan (Dibrom-8-Oxichinolin 0.2, Dibrom-8-Benzailoxichinaldine 0.04) were deleted as non-efficacious drugs.

Drugs affecting intestinal microflora:

Lactose, Bificol (Bifidum Bacteria plus E. Coli), Chilac (Lactates) were deleted as unavailable from suppliers. Gastropharm (Lactobacilus) was deleted as a non-efficacious drug.

Choleretic drugs:

Many choleretic drugs were deleted in almost all the hospitals. Those are: Liobil (Bovine bile), Flaminum (Extractum Folium Chelidori Areolaris), Cholosas (Extractum Fructus Rosae), Oximethyl Amide Nicotinate (Nicodine), Cholenzym (bovine dry bile 0.1, dried pancreas 0.1, dried intestinal mucose 0.1) Tanacechol (Extractum Flores Tanacetii), Osalmid (Oxafenamid), Hydroximethylnicotinamid (Nicodin). They were deleted as low efficacy drugs.

Cholagol (Extractum Radicis Curcumae 0.0225, Extractum Frangulae 0.009, Magnesium Salicylate 0.18, etheric oils 5.535, Ethanol 0.8, olive oil and Olimetin (Oleum Mentae Piperita 8.5 mg, Oleum Terebinthinae Rectificatum 17 mg, Oleum Calamae 12.5 mg, Olive oil 0.46 g, Serum Depuratum 1.7 mg) were deleted because of high cost.

Hepatic Protectants:

Essentiale (essential phospholipids and multivitamins) and Silibicon were deleted because of high cost. LIV-52" (extracts of different plants) and Sirepar (Bovine liver extract) were deleted because of their low efficacy.

### **Antiallergic drugs**

H<sub>1</sub>-blockers:

In different hospitals different H-1 blockers were deleted. The most commonly excluded were Mebhydrolin (Diazolin), as unavailable from suppliers, Cyproheptadine (Peritol) as rarely used and non-efficacious, and Clemastine Fumarate (Tavegil) as expensive.

### **Drugs affecting bronchopulmonary functions**

Bronchodilators:

The most commonly deleted were Orceprenallin Sulfate (Alupent) (low safety and high cost), Theophylline (Theopec) unavailable from suppliers, Ipratropium and Berodual (Phenoterol 0.05 mg, Ipratropium 0.02 g) not included in the treatment guidelines.

Expectorants and mucolytics:

The most commonly deleted were Acetylcystein (Mucosolvin) and Radex Glycyrrhae as they were not included in the treatment guidelines.

Antitussive drugs:

The most commonly deleted were Oxeladin (Tusuprex) and Stoptussin (Butamerat 0.04, Guaifenasine 1.0) as duplicative drugs. Glauicine was deleted as rarely used. Codeine and multicomponent drugs containing codeine (Codterpine, Cottermopsis, Antitussive tablets, etc.) were deleted as unsafe drugs.

**Drugs affecting renal function**

Antiurolitics and nitrogen expelling agents:

Lespenephriol (Extractum Lespedesae Capitatae), Lespephlan (Extractum Lespedesae Capitatae), Cyston (Different Plant Extracts), Cystenol (Different Plant Extracts), and Urolesan (Different plant extracts and oils) were all deleted as low efficacy drugs.

**Hormones, their analogs/Drugs affecting metabolic processes/Hypoglycemic drugs**

Drugs stimulating tissue metabolism:

Many hospitals deleted drugs in this group mainly for the reason of their low efficacy: Inozine, Rumalon (cartilage bovine extract), Humisol (mud extracts), FIBs (mud extracts), Befungin (extract Inonotus Obliquus), Plasmol (human blood extract), Corpus Vitreum (bovine corpus vitreum extract). Actovegin (Deproteinated calf blood extract) and Solcoseryl (Deproteinated calf blood extract) were deleted as expensive.

Insulins:

Among insulins, insulin aminochinuride, insulin actrapide NM were deleted as not readily available from suppliers, and insulin lente for its low efficacy.

Oral hypoglycemic agents:

The most commonly deleted were tolbutamide (Butamid), Carbutamid (Bukarban), Buformin as not included in the treatment guidelines. Chlorpropamide was deleted as a low efficacious and low safety drug.

Corticosteroids:

Triamcinolon was deleted because of its high cost. Dexamethasone was deleted as unsafe.

Androgens:

Testosterone Propionate was deleted as non-efficacious. Methyltestosterone was deleted as rarely used.

Estrogens:

Allylestrenol (Turinal) was deleted as unsafe, Hexestrol (Synestrol) was deleted as non-efficacious.

Anabolic Steroids:

Methandriol (Methylenandrostendiol) was deleted as rarely used.

Drugs used for the treatment of hypothyroidism:

Triiodthyranin was deleted as rarely used, Thyreoidine (T4+T3) and Thyreotom (T4+T3) were deleted for the reason of low efficacy.

Drugs used for the treatment of hyperthyroidism:

Diodthyrosine was deleted for the reason of low efficacy.

Drugs improving bone and cartilage metabolism:

Chonsuride (Cartilage extracts of young animals) was deleted due to its low efficacy.

Anticoagulants, thrombolytics and antiplatlet drugs:

Pheninindandion (Phenellin) was deleted as unsafe drug. Fibrinolysine was deleted as low efficacious, Dipyridamol was deleted as non available.

Hematopoietic agents:

Iron Salts. The most frequently deleted was long acting Ferrum Sulfate (Ferrogradument) and Hemostimulin (Dried blood 0.123, Ferrum lactate 0.246, Cuprum Sulfate 0.005) due to their low efficacy. Ferrum Saccharate (Ferrum-lek) was deleted due to its low safety.

Drugs stimulating erythropoiesis:

Eritropoietin was deleted due to its low efficacy.

Drugs stimulating leucopoiesis:

Methyl-oximethyluracil (Pentoxil) was deleted as a low efficacy drug.

Among drugs affecting homeostasis different hospitals deleted different drugs. It is hard to identify the most frequently deleted drugs. The same is true for vitamins. Mainly multivitamins were deleted.

Drugs affecting uterine motility:

Three drugs were deleted from this group: Dinoprost (Oxytocin and Vasopressine), Pituitrine (Oxytocin and Vasopressine) and Hyphotocine. All these drugs were deleted because they are not available from suppliers.

### **Drugs affecting immunologic process**

Immunocorrectors:

In the majority of hospitals two drugs containing the extract of thymus were deleted: Tactivin, as an available from suppliers and duplicating, and Thymoptin as not included in the treatment guidelines and duplicative. Levamisol was deleted for safety reasons.

Immunosuppressants:

Azathioprine was deleted in some hospitals as a low efficacious drug and unavailable from suppliers.

Antineoplastic agents:

In some hospitals, an insignificant number of drugs in this group was deleted.

### **Dermatological drugs for topical use**

In various hospitals, various drugs were deleted from the formulary lists, especially ointments and creams containing glucocorticosteroides, antifungal drugs and antimicrobial drugs. Dermatological drugs were mainly reduced as duplicative drugs.

### **Drugs for topical use in otolaryngology, stomatology, ophthalmology**

In some hospitals xylometazoline hydrochloride was deleted from the formulary list as a rarely used and duplicative drug. Some hospitals significantly reduced the number of different solutions for mouth and throat wash for various reasons.

In ophthalmology, among the drugs used for treatment of glaucoma, many hospitals deleted timolol because of its high cost. For the same reason, two drugs used for cataract treatment were deleted from the formulary list: Ophtan Catachrom (Citochrom C 0.675 mg, Sodium Succinate 1 mg, Adenosine 2 mg, Nicotinamid 20 mg), and Retinol pamitate (Vitadral).

Among mydriatics, some hospitals deleted tropicamid (Mydriacil) as an expensive drug.

**Drugs used in surgery, anaesthesiology, proctology and urology**

Drugs for general anaesthesia:

Among them Ether Anaesthetic was excluded as low efficacious and unsafe.

Topical enzymes for treatment of wounds:

Trypsin and Hymopsin (Alfachymotrypsin and Trypsin) were deleted because of their low efficacy.

Antidotes and chelating agents:

Unithiolum, Penicillamin and EDTA were deleted due to their low efficacy.

Radiopaque diagnostic agents:

Indigobissulfonate (Indigocarmin), Iopamid and Acidum Iopanoicum (Iopagnost) were deleted as not readily available from suppliers.

### ANNEX 3: DRUGS ADDED TO FORMULARY LISTS

In the initial formulary lists development, 98 drugs were added to the formulary lists in the surveyed hospitals, among them:

#### **Cardiovascular drugs**

ACE inhibitor Enalapril was added due to its high efficacy and safety.

#### **Beta-blockers**

Acebutolol and atenolol were added due to their efficacy and adoption of new treatment schemes.

#### **Calcium channel blockers**

Long-acting nifedipine and Amlodipine besylate were added due to their good patient compliance. Diltiazem was added because of its high efficacy

#### **Antiarrhythmics**

One hospital added Amiodaron and Ethacizine for the reason of high efficacy.

#### **Diuretics**

One hospital included Indapamid for the reason of high safety. One hospital added Triresid K (Dihydralazin Sulfate 0.01 g, Reserpin 0.0001 g, Hydrochlorthiazide 0.01g, Potassium Chloride 0.35g). They were added as readily available from suppliers, and in high demand.

#### **Drugs affecting gastrointestinal functions**

H<sub>2</sub> blockers: Ranitidine was added as a more efficacious and safer drug.

H+K+ATP-ase inhibitors: Omeprazol was added as highly efficacious, and included in a new ulcer treatment scheme.

Gastroprotectants: one hospital added Bismuti Subcitrate (De-Inol) due to its high efficacy.

#### **Antimicrobials**

Penicilline group: Amoxicillin was added as a more efficacious drug, and as a drug included in a new treatment scheme. Augentine (Amoxicillin and clavulanic acid) was added because of its high efficacy. Azlocillin was added as highly efficacious.

In some hospitals, cephalosporines were added, all of them because of their high efficacy: Ceftazime, Ceftriaxone, Cefalixine and Cefamandol.

Some hospitals added Imipenem because of its high efficacy.

**Fluoroquinolone**

Ciprofloxacin was added due to new STG development. Norfloxacin and Ofloxacin were added as highly efficacious drugs.

Some hospitals included in the formulary list modern macrolides: Azithromycin and Midecamycin. Azithromycin was added as highly efficacious, and Midecamycin was included in newly developed STG.

**Aminoglycosides**

Amikacin was added for the reason of high efficacy, and as an element of a new treatment scheme.

Among the 98 drugs added to the formulary lists, the main reason for the addition was high efficacy. About 10% of the drugs were included as safer drugs. Ten percent of the drugs were added as new treatment schemes including these drugs were adopted in the hospitals. One of the 98 added drugs was included for the reason of ready availability from the suppliers. Ten percent of the drugs were added as they were in demand. One drug out of the 98 was added because of its high quality. Four percent of the drugs were added because of the STG changes. Two drugs were added due to good patient compliance.

The cost of the drugs did not affect the additions at all. Four drugs were not used for treatment even though they have been added to the list: those are Ceftriaxone, Simvastatin, Ambroxol and Ipratropium. Along with high efficacious and safe drugs, some hospitals added to the formulary lists obsolete, less efficacious, and narrow therapeutic index drugs: Triresid K, Orale (enzymes of *Aspergillus Oryzae*), Ketorolac, and Ethacizine.

**ANNEX 4: RECENT CHANGES MADE TO EXISTING FORMULARY LISTS  
(DATA FROM 12 FACILITIES)**

**Drugs Recently Deleted from Formulary Lists**

<b>DELETED DRUG</b>	<b>REASON</b>
<b>CARDIOVASCULAR DRUGS</b>	
ACE inhibitors:	
Captopril	Low compliance
Diuretics:	
Oxodoline (Chlortalidone)	Not readily available from suppliers
Antiarrhythmic drugs:	
Chinidine	Not readily available from suppliers
Sympathomimetics:	
Dobutrex 25.0 vials (Dobutamine)	Not readily available from suppliers
<b>DRUGS ACTING ON THE CENTRAL NERVOUS SYSTEM</b>	
sedatives:	
Sodium bromide	Low efficacy
Herba Leonuri	Low efficacy
Adonis-brom (Extr. Adonidis 0.25, Kbr 0.25)	Not included in STGs
Valocordin	Low efficacy
Radix Valerianae 20.0	Low efficacy
Droperidol	Low efficacy, rarely used
Anxiolytics:	
Tofizopam	Low efficacy
Drugs for general anesthesia:	
Sombrevine (Propanidid)	Unsafe
Analeptics:	
Camphora 20%-2.0	Low efficacy
Nicethamide (Cordiamin)	Low efficacy
Antiparkinsonic drugs:	
Nacom (Levodopa+carbidopa)	High cost

DELETED DRUG	REASON
Opioid analgesics:	
Fortral (Pentazocine)	Not readily available from suppliers
Nonsteroidal anti-inflammatory drugs:	
Piroxicam	Unsafe
Phenylbutazone	Unsafe
Aspizol (Lysine acetylsalicylate)	Not readily available from suppliers
ANTIMICROBIAL DRUGS	
Sulfadimethoxine 0.5 N	Low efficacy, unsafe
Anti-TB drugs:	
Pasomycin inj. 0.5 (Dihydrostreptomycin paraaminosalicylate)	Not manufactured
Florimycin inj. 0.5	Not manufactured
DRUGS AFFECTING GASTROINTESTINAL FUNCTION	
H <sub>2</sub> -blockers:	
Cimetidine	Low efficacy, unsafe
Gastroprotectants:	
Bismuthi subcitratris (De-nol)	High cost
Antacids:	
Vicair (Bismuthi subnitras 0.35, MgCO <sub>3</sub> 0.4, NaHCO <sub>3</sub> 0.2)	Not readily available from suppliers
Enzymes:	
Lecozym (proteolytic enzymes)	Not readily available from suppliers, high cost
Drugs for parenteral nutrition:	
Vamin (aminoacids)	Not readily available from suppliers
Intralipid (lipid emulsion) 500.0 sol. for infusions	Unsafe
HORMONES	
Testosterone	Low efficacy
Synestrol (Hexestrol)	Low efficacy
Marvelon (Desogestrel 0.15+ethynylestradiol 0.03)	Not used for treatment
Dexamethasone	Unsafe

DELETED DRUG	REASON
HYPOGLYCEMIC DRUGS	
Insulin lente	Low efficacy
Chlorpropamide	Unsafe
DRUGS STIMULATING TISSUE METABOLISM	
ATP	Low efficacy
Mucopolisaccharidi-polisulfas (Artaparon)	Unsafe
ANTICOAGULANTS	
Phenilline (Phenindione)	Not readily available from suppliers
BRONCHODILATORS	
Theophylline (Teopek)	Rarely used
ANTINEOPLASTIC DRUGS	
Sarcolysine	Rarely used
ANTISEPTIC AND ANTI-INFLAMMATORY DRUGS FOR TOPICAL USE	
Tinct. Calendulae	Not included in STGs

#### Drugs Recently Added to Existing Formularies

ADDED DRUG	REASON
CARDIOVASCULAR DRUGS	
Nitrates:	
Isosorbide mononitrate (Elantan)	Efficacy
ACE inhibitors:	
Captopril (Tensiomin)	Efficacy
Enalapril (Enap)	Efficacy
alfa and beta sympathomimetics:	
Epinephrine (Adrenaline)	Efficacy
Drugs improving microcirculation:	
Troxerutin (Troxevasin) gel	No other drug in the formulary for the treatment of the disease
Thrombolytics:	

ADDED DRUG	REASON
Streptokinase 100000IU	Efficacy
DRUGS ACTING ON THE CENTRAL NERVOUS SYSTEM	
Antiparkinsonic drugs:	
Madopar (Levodopa+Benseracid) tab. N 100	Often used, low cost
Opioid analgesics:	
Morphine (Morphilon)	Efficacy
Nonsteroidal anti-inflammatory drugs:	
Indometacin	Often used
Ketorolac (Ketorol)	Efficacy
Hormone-containing anti-inflammatory drugs for topical use:	
Diprogent (Bethametasone dipropionate 0,0005 gentamycin sulfate 0,001) ointment	Efficacy
Diprosalic (Bethamethasone dipropionate 0,0005, Ac.salicylici 0,03)	Efficacy
ANTIMICROBIAL DRUGS	
Amykacin	Efficacy
Ofloxacin	Efficacy
Amykacin 0.5	Efficacy
Ceftazidim	Efficacy
Antifungal drugs:	
Levorin 500000IU tab.	Efficacy
DRUGS AFFECTING GASTROINTESTINAL FUNCTION	
H <sub>2</sub> -blockers:	
Ranitidine	Efficacy, safety
Antidiarrheal agents:	
Diocamedric smectite (Smecta) 3.0 N 30	Included into STGs
Drugs for parenteral nutrition:	
Infesol (amino acids, salts)	Efficacy
Blood volume expanders:	

ADDED DRUG	REASON
Rehydron	No other drug in the formulary for the treatment of the disease
Gelatinol	No other drug in the formulary for the treatment of the disease
Rehydron (NaCl 3,5, Na citrate 2,9, Kcl 2,5, dextrosa 10,0) N 20	Good quality, included into STGs
Polyvynilpirolidon (Hemodese)	Efficacy
Neuromuscular blocking agents:	
Pipcuronium bromide (Arduan)	Efficacy
Antitussive drugs:	
Prenoxdiazin hydrochloride (Libexin) 0,1 N 20	Efficacy, safety
Drugs affecting bone metabolism:	
Clodronate (Bonefos)	New method of treatment

## **ANNEX 5: REPORT OF RYAZAN STATE MEDICAL UNIVERSITY ON RATIONAL PHARMACEUTICAL MANAGEMENT PROJECT (1995–1998)**

(Excerpts from the full report)

### **I. ACTIVITIES ON PRACTICAL IMPLEMENTATION OF FORMULARY SYSTEM**

Formulary system concept received complete understanding and support from the administration and the rector of the University academician RAMS Ye. A. Stroev, which has served as a foundation for the active work of RSMU on practical implementation of formulary system in Ryazan oblast.

The main areas of this work are the following:

1. Participation in development of the first formulary in Ryazan oblast—the formulary of Ryazan Oblast Clinical Hospital (ROCH). Four university staff-members were included in the Formulary-therapeutic committee (FTC) of that health-care facility.
2. Participation in development and revision of the first Formulary Manual of OCH. Among the authors of the formulary manual are two faculty members of the University, including the rector of RSMU, academician of RAMS Stroev Yevgenii Alexeyevich. The reviewers of the formulary manual were the senior deputy rector of RSMU, the head of the Department of Pharmacology with the course on pharmacotherapy at the Department of Post-graduate education, professor Makarova Valentina Grigorievna, and other faculty members from the University.
3. Work as a member of the Oblast Formulary Committee on development of Oblast Formulary and Formulary Manual.
4. Participation and consulting assistance in development of formularies of a number of health care facilities in the city and oblast. The faculty members of the University are also the members of FTC of Oblast Pediatric Hospital, Oblast Cardiological clinic, etc.

### **II. DEVELOPMENT AND INTRODUCTION OF EDUCATIONAL PROGRAMS ON RPM PROJECT**

The university capabilities allow to successfully deal with the educational objectives of the project due to the fact that here we have the opportunity both to employ highly qualified faculty members and have a broad audience—there are 11 teaching departments for students and the Department of Post-graduate education, where physicians and pharmacists improve their knowledge and skills.

The priority issues for education are the issues on those areas of RPM project that are being implemented in Ryazan Oblast. They include the following:

- principles of rational drug use,
- formulary system and drug use evaluation,
- unbiased therapeutic and drug information.

The staff members of the center provide training:

- 1) for students—both within curriculum, as well as during extra-curriculum classes;
- 2) for interns, physicians, pharmacists—within training at the Department of Post-graduate education;
- 3) for teachers of nursing colleges; and
- 4) for post-graduate students and faculty members of the University.

## 2.1. Activities with students

The university started from the lecture on formulary system issues for students of therapeutic department. That lecture was presented by the Director of the RPM project in Russia, Anthony Savelli. Later on the audience, topics and methods of training were constantly expanded.

### 2.1.1. Program on RPM project in the curriculum

We have developed and included in the curriculum (on pharmacology and pharmacotherapy) for the third and fourth year students an interactive program on the RPM project.

The most comprehensive training is conducted at the Therapeutic and Pharmacy Departments. The program includes both lectures and practical sessions.

#### PROGRAM "RATIONAL PHARMACEUTICAL MANAGEMENT" LECTURES

YEAR/DEPARTMENT	LECTURES
3rd year	
therapeutic department pharmacy department therapeutic and preventive medicine department dentistry department department of management (lectures 1, 2, 4)	<ol style="list-style-type: none"> <li>1. Principles of rational drug use.</li> <li>2. Unbiased drug information.</li> <li>3. Importance of drug information for patients.</li> <li>4. Concepts of cost-effective drug selection. Generic drug names.</li> <li>5. Principles of drug formulary development and maintenance.</li> <li>6. Concepts of drug use evaluation. ABC- and VEN-analysis.</li> <li>7. New drugs, evaluation of justification for prescribing.</li> </ol>
4th year	
therapeutic department pharmacy department	8. Concepts of P-drugs

#### PRACTICAL SESSIONS

YEAR/ DEPARTMENT	PRACTICAL SESSIONS
3rd year	
therapeutic department pharmacy department therapeutic and preventive medicine department dentistry department	<ol style="list-style-type: none"> <li>1. Patient drug information.</li> <li>2. Formulation of solid and soft drug dosage forms, patient counseling on their use.</li> <li>3. Formulation of liquid and gas drug dosage forms, patient counseling on their use.</li> <li>4. Basic principles of working with drug data bases.</li> </ol>

YEAR/ DEPARTMENT	PRACTICAL SESSIONS
4th year	
therapeutic department pharmacy department	5. Cost-effective drug selection. ABC- and VEN-analysis. 6. New drugs: evaluation of justification for prescribing. 7. Concepts of P-drugs (WHO, Groeningen University, Netherlands). 8. Basic principles of operating computer drug data bases—30 min. for each student on every practical session. 9. P-drug selection and principles of their prescribing for certain indications (IHD, heart failure, arterial hypertension, bronchial asthma)—2 hours for each practical session.

### 2.1.2. Lectures by RPM specialists

It was planned by the project to include lectures of the American specialists in curricula. The following lectures were presented:

1. December 15, 1995. Rational drug use. Anthony Savelli, Director of RPM Project in Russia.  
Attended by: 241 students from therapeutic, dentistry, pharmacy, and therapeutic-preventive medicine departments.
2. April 22, 1996. Unbiased drug information. Keith Johnson, Director of Drug information department, USP convention.  
Attended by: 193 students from therapeutic, dentistry, pharmacy, and therapeutic-preventive medicine departments.
3. October 1, 1996.
  1. Rational Pharmaceutical Management Project. Anthony Boni, Cognizant Technical Officer of RPM Project, USAID.
  2. First results of RPM project in Russia. Anthony Savelli, Director of RPM project in Russia.
  3. Pharmacoeconomics. A.V. Bykov, consultant from MSH Moscow office, candidate of medical sciences.  
Attended by: 203 students from therapeutic, dentistry, pharmacy, and therapeutic-preventive medicine departments.
4. February 10, 1997. Therapeutic and economic aspects of formulary system. Anthony Savelli, Director of RPM Project in Russia.  
Attended by: 206 students from therapeutic, dentistry, pharmacy, and therapeutic-preventive medicine departments.

### 2.1.3. Testing on RPM project issues

Taking into account the present importance of rational drug use and formulary system implementation, the department of pharmacology has included a number of questions, related to the project, in the examination on pharmacology, and also has developed and included in test on pharmacotherapy a testing-training computer program on RPM issues.

The training on RPM program was provided for:

- The year of 1995–1996, 599 students
- The year of 1996–1997, 765 students
- The year of 1997–1998, 779 students

## **2.2. Training for the Department of Post-graduate education**

Training was provided for interns, physicians of all specialties, pharmacists, teachers of nursing colleges, and faculty members of the university as part of training at the Department of Post-graduate education.

### **2.2.1. Training programs for interns**

Starting from 1996, the university has been conducting a two-week specific course for interns “Selected issues of rational drug use,” which includes the topics related to the RPM Project and rational prescribing of several drug therapeutic classes. The main topics of lectures and seminars on the project are the following:

Lectures:

- Rational drug use
- Formulary system and drug use evaluation
- Unbiased drug information
- New drugs: evaluation of justification for prescribing
- Clinical aspects of VEN-analysis in formulary development
- Specifics of USA health care system
- Concepts of P-drugs

Seminars:

- Rational drug use. Formulary system and drug use evaluation
- Unbiased drug information. New drugs: evaluation of justification for prescribing
- Principles of P-drug selection and prescribing for treatment of hypertension
- Topics of essays for interns:
  - ▶ Principles of formulary system implementation and maintenance
  - ▶ ABC- and VEN-analyses, their purpose and methods of performing
  - ▶ Concepts of drug use evaluation, goals and principles of performing
  - ▶ Concept of P-drugs, its advantages

The training on this course was provided to the following number of interns:

- 1996, 105 interns
- 1997, 113 interns
- 1998, 115 interns

### **2.2.2. Educational programs for physicians and pharmacists**

The training on the main issues of the RPM Project was also provided for physicians of various specialties and pharmacists, both on the university grounds and through visiting the facilities. The most common style of working with physicians and pharmacists from the Department of Post-graduate education are one-day workshops, that include lectures and practical sessions.

The main topics of lectures:

- Formulary system: methods of implementation and maintenance. Introduction to drug use evaluation.
- Unbiased drug information. Importance of drug information for patients.

The main topics of practical sessions:

- Principles of drug formulary development. The role of a physician (a pharmacist) in a health care facility in formulary development.
- New drugs: evaluation of justification for use.

The training was provided to the following number of specialists:

1996: 48 physicians (therapists, pediatricians)  
12 pharmacists

Regions: Ryazan, Ryazan Oblast (Rybnoye), Kurgan, Novosibirsk, Chelyabinsk, Magnitogorsk.

1997: 98 physicians (therapists, pediatricians, health care administrators)  
18 pharmacists

Regions: Ryazan, Ryazan Oblast (Mikhailov, Miloslavka, Kasimov, Korablino, Ryazhsk, Yermish, Rybnoye, Scopin, Shatsk, Klepiki, Starozhilovo, Pronsk, Gus'-Zheleznyi), Oryol, Saransk, Tambov, Novosibirsk, Novokuznetsk, Yaroslav', Yekaterinburg, Kharkov, Nizhnii Novgorod, Tula.

1998, January–February:

50 physicians (pediatricians, therapists, health care administrators);  
14 pharmacists

Regions: Ryazan, Ryazan Oblast (Scopin, Klepiki, Chuchkovo, Miloslavka, Korablino, Kasimov, Sarayev), Tula, Tula Oblast (Novomichurinsk), Perm, Yekaterinburg.

All the lectures for interns, physicians and pharmacists include pre- and post-testing, as well as evaluation through questionnaires; for this purpose special test and questionnaires were developed. Each trainee receives a package, developed by the department, of information documents on the topics of the lectures, including the information on formulary system and unbiased drug information.

### **2.2.3. Training for the faculty of the Medical College and nursing schools in the Oblast.**

Training for the faculty of the Medical College and nursing schools in the Oblast is conducted in the way of an annual workshop that includes lectures and practical sessions on RPM Project. The workshop conducted in January 1998 included the following lectures and practical sessions:

- Results of formulary system implementation in health care facilities in Ryazan Oblast. First Formulary manual, its structure and contents (lecture).
- New drugs: evaluation of justification for prescribing (lecture).
- Introduction and basic principles of working with computer drug data bases (practical session).

Training was provided for:

1996, 8 faculty members;

1997, 8 faculty members;

1998, 8 faculty members.

#### 2.2.4. Training for faculty members of RSMU on RPM Project issues

The workshops on the project were conducted in January 1997 and January 1998 for assistant lecturers and assistant professors of clinical departments in the university. These workshops included both lectures on formulary system and unbiased drug information, and practical sessions on working with computer drug data bases, including Medline, which is necessary for the faculty members of the University.

The training was provided to:

- 1997: 13 assistant lecturers of clinical departments; 11 assistant professors of clinical departments;
- 1998: 12 assistant lecturers of clinical departments; 12 assistant professors of clinical departments.

#### 2.3. Sources of information used in training

The information sources provided by MSH and USP are of great assistance in preparing for the lectures and practical sessions on RPM project. This assistance is considered to be of great importance, because there is practically no local information on the issues discussed. The main sources used are the following:

1. *Manual for the Development and Maintenance of Hospital Drug Formularies*. Savelli, A., Schwarz, H., Zagorski, A., Bykov, A. MSH, 2nd edition. Arlington/Moscow: 1996.
2. *Ryazan Oblast Hospital Formulary Manual*, Voronkov, D. V., Stroeve, Ye. A., et al. Ryazan: 1997.
3. *Guidelines for Implementing Drug Utilization Review Programs in Russian Hospitals*. Moore, T., Bykov, A., Savelli, A., Zagorski, A. 2nd edition. MSH, Arlington/Moscow: 1997.
4. *Guide to Good Prescribing: Practical Manual Based on WHO Publication*. de Vries, T. P. G. M., Henning, R. H, Hogerzeil, H. V., Fresle, D. A. WHO/MSH, Arlington/Moscow: 1997.
5. Drug information for health care specialists. Vol. 1, 2/Under revision of M. D. Mashkovski. Moscow, 1997.
6. USP DI, Volumes 1, 2.
7. *Martindale Extra Pharmacopeia*.
8. RPM Project. *Assessment of pharmaceutical sector in Ryazan Oblast* (MSH).
9. Materials of RPM Project workshops.
10. Formulary manuals from hospitals in the USA.

#### 2.4. Educational-methodological materials, developed by faculty members of the University, on RPM Project issues

The faculty members of the university have developed methodological guides for practical sessions, that contain the list of test questions and assignments for individual work in the format of schemes, tables, case examples.

The following methodological guides, approved by scientific-methodological council of the University, were published in 1998:

1. Semenchenko, M. V. *Rational Drug Use: Drug Formulary Development. Methodological Guide for Physicians*. Under revision of prof. V. G. Makarova, Ryazan, 1998.
2. Semenchenko, M. V. *ABC- and VEN-Analyses For Drugs, Goals, Methodology. Methodological Guide for Interns*. Under revision of prof. V.G. Makarova. Ryazan, 1998.
3. Semenchenko, M. V., Ryabkov, A. N., Savilov, K. V. *Pharmacotherapy of Hypertension. Principles of P-drugs Selection and Prescribing. Methodological Guide for Interns (According to the Methodology of Problem-Based Education)* Under revision of prof. V. G. Makarova, Ryazan, 1998.

The following materials were prepared for publication:

1. Yakusheva, Ye. N. *New Drugs: Evaluation of Justification for Prescribing. Methodological Guide for Students*. Under revision of prof. V. G. Makarova, Ryazan, 1998.
2. Semenchenko, M. V. *Concepts of P (personal)-drugs. Principles of P-drugs Selections and Prescribing. Methodological Guide for Practical Sessions on Pharmacotherapy for Students of Therapeutic Department (According to the Methodology of Problem-Based Education)*, Under revision of prof. V. G. Makarova, Ryazan, 1998.

The following RPM publications are widely used as training guides:

- *Manual for the Development and Maintenance of Hospital Drug Formularies*
- *Guidelines for Implementing Drug Utilization Review Programs in Russian Hospitals*, also recommended by WHO for medical education institutions.
- *Guide to Good Prescribing* (WHO, adapted and translated into Russian by RPM)

## 2.5. Interdepartmental program “Rational Drug Use. Basic Principles of Pharmaceutical Management”

Development and implementation of the interdepartmental program “Rational Drug Use. Basic Principles of Pharmaceutical Management” has become a new step in the further development of the activities within the project, with drawing in the leading University departments and faculty members, who have undertaken training in the USA as part of the Project. The program has united both the departments that provide the education to students and the Department of post-graduate education (DPGE). the topics of the main lectures are presented in table below:

### Topics of the Lectures Within the Interdepartmental Program “Rational Drug Use. Basic Principles of Pharmaceutical Management”

TOPIC OF LECTURE	DEPARTMENT, LECTURER
The role of the Information-Educational Center of Ryazan State Medical University in implementation of the Program “Rational Drug Use. Basic principles of pharmaceutical management”.	Department of Pharmacology with the course of pharmacotherapy, prof. Makarova V.G.
Cost-effective drug selection. DUE.	Department of Pharmacology with the course of pharmacotherapy, assistant professor Semenchenko M. V.
Unbiased drug information.	Department of pharmacology with the course of pharmacotherapy, assistant professor Yakusheva Ye. N.
Clinical aspects of VEN-analysis in formulary development.	Department of hospital therapy with the course of functional diagnostics and out-patient therapy, professor Yakushin S. S.
Basic principles of management: philosophy, functions.	Department of pharmacy, DPGE, assistant lecturer Moshkova N. A.

TOPIC OF LECTURE	DEPARTMENT, LECTURER
Specifics of the U.S. health care system.	Department of social medicine, organization and economics of health care, assistant professor Popov Yu. Ye.
Drug therapy in medical insurance system (local and foreign experience).	Department of social medicine, organization and economics of health care, professor Ponomaryova G. A.
Pharmaceutical sector in the USA.	Department of pharmacy, DPGE, assistant lecturer Zdanovich L. A.
Pharmacy services and drug quality control.	Department of pharmaceutical chemistry, assistant professor Platonova N. A.
Development of new drugs according with GMP standards in the USA. Validation. United States Pharmacopeia, its role in drug standardization. Structure of USP.	Department of pharmaceutical technologies, assistant professor Pakhomova M. V.
Rational drug use: drug interactions.	Department of pharmacology with the course of pharmacotherapy, assistant professor Ryabkov A. N.
Principles of rational antibacterial therapy.	Department of therapy, DPGE, professor Abrosimov V. N.
Rational antibacterial therapy in pulmonology.	Department of hospital therapy with the course of functional diagnostics and out-patient therapy, professor Yakushin S. S.
Individualized therapy of angina pectoris.	Department of hospital therapy with the course of functional diagnostics and out-patient therapy, assistant professor Okorokov V. G.

## 2.6. Conferences on the issues of rational drug use.

Annually the Department of Pharmacology conducts several conferences on rational use of drugs from various therapeutic classes for students and interns, physicians and pharmacists of DPGE. These are the examples of the topics of the conferences:

- December 1996: “Basic principles of rational use of certain psychotropic agents” for the students.  
 May 1997: “Principles of rational selection and use of antibiotics” for the students, therapists and pediatricians from DPGE.  
 January 1998: “New drugs. Principles of rational use” for interns, therapists, pediatricians, and pharmacists from DPGE.

## III. SHARING THE EXPERIENCE OF WORKING WITH RPM PROJECT

### 3.1. Presentations on congresses, workshops, conferences

April 10–15, 1995, Moscow. 2nd All-Russian Congress “Man and Drug”.  
 Presentation “Educational Center of Drug Information”.

February 15–23, 1996, Moscow. Program “Rational drug selection. Drug formulary development”.

Presentation “Rational Pharmaceutical Management and Drug Information System in Ryazan Medical University”.

April 16–19, 1996, Moscow. 3rd All-Russian Congress “Man and Drug”.

Presentations: “Information Development for the Formulary Manual”, “Organization of Information-Educational Center in RSMU”.

May 28, 1996, Ryazan. Oblast seminar “Drug Provision Policy in RPM Project”.

Presentation: “Information for Formulary Manual Development”.

October 15, 1996, Moscow. Russian-American Conference on the issues of providing health care specialists with professional information.

Presentation: “Information-Educational Center in RSMU”.

November 21–24, 1996, Moscow. Russian-American Conference “Health Care reforms: experience of the program “Zdravreform”.

Presentation: “The Role of Ryazan State Medical University in implementation of RPM Project.”

April 8–12, 1997, Moscow. 4th All-Russian Congress “Man and Drug”.

Presentations: “Educational aspects of RPM Project in Ryazan State Medical University”, “Experience of the Information-Educational Center in Ryazan State Medical University”.

June 8–11, 1997, Moscow. International scientific-practical conference “Drug information for professionals”. Participation as a moderator in the section on formulary system.

October 14–16, 1997, St.-Petersburg. International scientific-practical conference “Health care system reforms in Russian Federation: problems and solutions.”

Presentation: “Experience of the Information-Educational Center of Ryazan State Medical University within the RPM Project.”

November 4, 1997. Ryazan Oblast conference of cardiologists.

Presentation: “On Rational Pharmaceutical Management Project in Ryazan Oblast.”

### **3.2. Publications**

1. Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N. Educational Center of Drug Information Service. Main Points of the Presentations on the 2nd Russian National Congress “Man and Drug”.-Moscow, 1995, p.327.
2. Semenchenko, M. V., Makarova, V. G., Savelli, A. Experience of Drug Monographs Development for Formulary Manual. Main Points of the Presentations on the 3rd Russian National Congress “Man and Drug”. Moscow, 1996, p.321.
3. Stroeve, Ye. A., Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N., Johnson, K., Savelli, A. Regional Model of Information-Educational Center. Main Points of the Presentations on the 4th Russian National Congress “Man and Drug”.- Moscow, 1997, p.342.
4. Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N. Integration Course on the Rational Pharmaceutical Management Project in Ryazan State Medical University. Main Points of the Presentations on the 4th Russian National Congress “Man and Drug”. Moscow, 1997, p.330.
5. Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N., Savelli, A. Methodological provision of

- educational programs within Rational Pharmaceutical Management Project. Main Points of the Presentations on the 4th Russian National Congress “Man and Drug”. Moscow, 1997, p.330.
6. Stroeve, Ye. A., Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N. Russian-American Information-Educational Center: experience of creation, and perspectives.//Russian Medico-Biological Herald named after acad. I. P. Pavlov. 1996. ##1–2. pp.114–116 (Attachment 5).
  7. Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N. Formulary System as the Basis for Rational Pharmacotherapy in Geriatrics. Main Points of the Presentations on the 2nd International scientific-practical conference “Elderly Patient. Quality of Life”. Moscow, 1997, p.36.
  8. Makarova, V. G., Yakusheva, Ye. N., Semenchenko, M. V. The Role of Drug Information Centers in Rational Pharmacotherapy of Elderly. Main Points of the Presentations on the 2nd International scientific-practical conference “Elderly Patient. Quality of Life”. Moscow, 1997, p.183.
  9. Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N. Formulary System- New Approach to Rational Drug Provision. “Diagnostics and Rehabilitation of Physical Status of a Man”. Compilation of scientific articles/Under revision of acad. MAI professor Sautkin M.F. and candidate of medical sciences Proshlyakov V. D. V.3.- Ryazan, 1997, pp. 29–31.
  10. Makarova, V. G., Semenchenko, M. V., Yakusheva, Ye. N. Formulary System Implementation on Regional Level. Main Points of the Presentations on the Regional Scientific Conference “Problems of Pharmacology and Pharmacy on Far East”. Part 2. Khabarovsk: October 1997.

Another six presentations outlines have been submitted for publication for the 5th National Congress “Man and Drug” (Moscow), for the International Conference (Samara) and for the Inter-regional Conference (Saratov).

#### **IV. INFORMATION FOR THE FORMULARY SYSTEM**

Taking into account the importance of unbiased drug information, the university considers the information function of the Information-Educational Center (IEC) to be one of its main purposes. The Center’s information function is in organization of reference-information fund, in publication and distribution of newsletters.

##### **4.1. Reference-information fund**

The university’s IEC has developed the reference-information fund, in creation of which MSH and USP have provided assistance. These organizations have provided worldwide known publications, that contain unbiased drug information (in English).

## LIST OF FOREIGN MEDICAL LITERATURE

1. Remington's Pharmaceutical Sciences, 1995.
2. AMA Drug Evaluation Annual, 1995.
3. Martindale The Extra Pharmacopeia, 1993, 30 ed.
4. USP Dictionary of USAN and International Drug Names, 1995.
5. Poisoning and Drug Overdose, 1994.
6. Trissel's Handbook of Injectable Drugs, 1994.
7. Physicians' Desk Reference, 1995.
8. Meyler's Side Effects of Drugs, 1992.
9. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk, 1994.
10. Hansten's Drug Interactions & Updates, 1995.
11. AHFS Drug Information, 1995.
12. Clinical Pharmacokinetics: Concepts and Applications, 1005.
13. Merck Manual, 1992.
14. Harrison's Principles of Internal Medicine, 1994.
15. Index Nominum, 1995.
16. Goodman & Gilman's The Pharmacological Basis of Therapeutics. New edition, 1995.
17. Drugs and Renal Disease. 1986. Bennett W.N. New edition.
18. Effects of Drugs on Clinical Laboratory Tests. 1990 Yiung D. S.
19. Guide to Antimicrobial Therapy Sanford J. P., 1995.
20. Handbook of Pediatric Drug Therapy, 1990.
21. Clinical Guide to Laboratory Tests, 1990. Tietz N. W.
22. USP DI, Volumes 1 and 2, 1994, 1995, 1996, 1997.

The University also has the following information software:

1. MEDLINE data base (provided by USP)
2. USP data base
3. Drug data base of drug reference developed under revision of M. D. Mashkovski
4. Data base of VIDAL reference, etc.

The reference-information fund is regularly updated with new local and translated manuals, references, and periodicals.