

**Republic of Macedonia
Ministry of Health**

**HEALTH SECTOR AND SOCIAL PROTECTION PROJECT
Japanese Grant JPN 26814-MK**

Pharmaceutical Component

FINAL REPORT

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1. ABBREVIATIONS (Inception, Mid-Term, and Final Report)

CME	Continuing Medical Education
DUE	Drug Use Evaluation
EC	European Commission
EBM	Evidence Based Medicine
HI	Health Institution
HIF	Health Insurance Fund
HSSP	Health & Social Protection Project
IT	Information Technology
MMA	Macedonian Medical Association
MOF	Ministry of Finance
MOH	Ministry of Health
NDP	National Drug Policy
NDIC	National Drug Information Centre
PHC	Primary Health Care
PLD	Positive List of Drugs (HIF Formulary)
PSMAC	Public Sector Management Adjustment Credit
PSMAL	Public Sector Management Adjustment Loan
P&T	Pharmacy and Therapeutics (Committee)
RDU	Rational Drug Use
RRx	Rational Drug Prescribing
TOR	Terms of Reference

2. EXECUTIVE SUMMARY

This report is based on the findings presented in the Inception Report (Appendix I), as well as on various suggestions/options for improvements in the four key areas laid down in the Mid-Term Report. The stakeholders feedback was used to translate the initial findings and options into an implementation plan for all four areas of focus of this assignment: (i) Legislation on pharmaceuticals, (ii) Strengthening the capacities of the State Bureau for Medicines, (iii) Improvements in the capacities of HIF to monitor prescribing and drug use; and (iv) Adoption of transparent procedures and policies for maintenance of Formularies, including the development of a Hospital Formulary System. The implementation plan includes timetable for proposed activities and changes, assessment of required support, and allocation of financial resources.

In order to accomplish the desired long-term effects of the suggested reforms in all four key areas of the pharmaceutical sector two important efforts must take place: (1) significant information technology (IT) support must be provided, as well as (2) an appropriate education and training of a considerable number of health care professionals who will participate in and/or lead this process of pharmaceutical reforms. The above two efforts overlap in scope with similar efforts needed for successful implementation of objectives from other sub-components of the overall project (i.e., IT sub-component, Improving Services Delivery; Primary Health Care and CME). Both the IT support and education/training of health care professionals are of equally great importance to all four key areas in the pharmaceutical sector. As such, they are addressed separately in this report and included in the implementation plan.

The current Macedonian Law on Medicines should be harmonized to a greater extent with the European legislation. Nevertheless, the major weakness of the pharmaceutical legislation in Macedonia is not the “non-harmonized” Law on Medicines. It is rather the absence of dozens of essential by-laws, which should facilitate the implementation of the Law and provide effective legislature. Since the approval of the Law on Medicine in 1998, only a few by-laws have been adopted. Therefore, technical assistance is needed not only for the Law harmonization, but also for adoption of a series of essential by-laws. It is recommended to give priority to this objective and to accomplish the improvements in the pharmaceutical legislation in the first 6-9 months of the Project. It is recommended that foreign technical assistance is provided in the late phase of this activity, i.e. after local experts/working groups have prepared the draft versions of needed by-laws and changes in the Law on Medicines.

It is recommended that the by-laws regulating dispensing of prescription medications be changed so that it allows generic substitution and repeated prescribing/dispensing of medications. The current very common practice in Macedonia is that “by prescription only” (Rx) medications are dispensed without prescription. The current penalty provisions in the Law are unclear and ineffective and additional

measures should be introduced to assure strict adherence to the Law. It is recommended that the violations of the “by prescription only” rule are linked to the pharmacists’ licensing, and licence revocation be used as a corrective measure. Both MOH and Chamber of Pharmacists should be involved in revising the current legal framework and adopting by-laws that regulate drug dispensing.

This practice of approximately 50% of Rx medications being purchased without prescription poses a serious problem to the pharmaceutical system and makes it very difficult for MOH and HIF to monitor rational drug use in outpatient settings. Furthermore, the fact that more than 95% of general population are insured, makes the HIF forecasts for drug expenditures questionable, since the strict adherence to the Law may result with substantial increase in HIF’s expenditures for drugs on the outpatient positive list.

Under the current system of operations and organizational scheme, the Bureau is actually a division within the Ministry of Health. It is recommended that the current organizational structure be the starting point for the Bureau’s activities and capacities building. This needs to be paralleled with substantial administrative, personnel and technical strengthening. It is recommended that mechanisms (procedures and policy) be put in place, which would allow transparency and control over all phases of medication registration process. Increased accountability of the Bureau can be achieved only if the Bureau is in position to oversee all phases of the drug registration process. It is recommended that a high degree of administrative connectivity between the Bureau and the other participants in the registration process is established. This implies the feasibility of administering through the Bureau the requests for appropriate expert evaluations (e.g. quality control, pharmacological or clinical expert evaluation, bioequivalence studies, etc.).

The Bureau for Medicines does not have access to either the export-import information about the medications or their distribution in the country. Therefore, the strengthening of the Bureau’s administrative links with the Ministry of Finance (Customs), including the computerized network connectivity, is recommended, so that better monitoring of medications distribution is provided.

In Macedonia, there are currently two positive (priority) lists of drugs, i.e. Outpatient Formulary and Hospital Formulary, for which the HIF covers the cost. A 9-member committee appointed by the Minister of Health produces and maintains these lists. This committee should provide professional assistance to HIF with respect to the analysis of medications utilization and prospective follow-up of medication usage in outpatient settings and hospitals. However, the committee, both numerically and composition-wise, cannot meet the challenges of its activities as described above. It must be strengthened both numerically and in composition. It is recommended that two separate committees for outpatient and hospital positive drug lists are established and

that their professional composition reflects the list of drugs under their review. The efficiency and objectivity of the drug selection process for both drug committees may be increased by recruiting *ad hoc*/non-voting members, i.e. clinical pharmacologists, clinical pharmacists, specialists in pharmacoinformatics, and clinicians with focused interest and expertise in therapeutics. The committees for the HIF positive lists of drugs should expand their activities beyond the revision of lists of drugs and, by taking the role of Drug and Therapy (or P&T) Committees, should participate in the development of a “full” Formulary system. In addition to the priority drug list (Formulary), this system encompasses development of Formulary Manual, development of therapeutic guidelines, adoption of therapeutic protocols, development and implementation of drug use, evaluation programs and education of physicians and other health professionals in rational drug use.

In order to provide health professionals with easy access to unbiased information on therapeutics, it is recommended that National/HIF Drug Formulary Manual be developed. This activity should be a collaborative effort of Bureau for Medicines, HIF's Pharmacy Department and National Drug Information Centre. The Manual should include, but not be limited to: General Information section; Drug Information monographs, Special Information section, and Indexes to facilitate the use of the manual. Production of a hard copy and preferably electronic version of the manual and their distribution to health care professional should follow. Financial support is foreseen for development of the Manual.

The development of HIF positive (i.e. rationally-selected) list of drugs for outpatient and hospital use does not ultimately ensure that these drugs are prescribed and used correctly. Therefore, it is recommended that drug use evaluation (DUE) programs/protocols are developed and implemented as mechanism ensuring correct prescribing and rational drug use. Programs can be designed to monitor individual drugs, classes of drugs, or drug use in specified diseases. These programs should be initially developed at HIF level. Later, after introducing the formulary system and establishing the P&T committees in larger hospitals, DUE programs should be developed and implemented at the individual hospital level.

The analysis of drug use in hospitals indicates that 25 medications account for 80% of the total drug expenditure. It is recommended that for these high-volume/high-cost medications, DUE programs are developed and implemented. For high-cost medications (immunomodulators, anticancer drugs) therapeutic protocols should be also developed.

The analysis of usage of medications from the HIF outpatient positive list of drugs indicate that 50% of all medications are prescribed for the top 10 diagnosis. Likewise, the top 10 drugs that account for 40% of the expenditures are used for therapy of chronic cardiovascular disorders and acute infections of the upper respiratory tract.

Therefore, it is recommended that therapeutic guidelines for chronic cardiovascular diseases and rational use of antimicrobial agents, be the first developed.

In order for HIF to control the expenditures for prescribed medications in primary health care (PHC) settings, it is recommended that HIF introduce the system of indicators for rational prescribing, rather than to limit the number of prescription per PHC physician. On a long-term basis, the latter has been shown to be less cost-effective than use of indicators of rational prescribing. The indicators for the rational drug prescribing should be established based on information regarding the current (irrational) drug prescribing practice, especially for the most frequent diagnoses and high volume drugs. A system of incentives for rational prescribing should be developed and these indicators may be used when evaluating the quality of the PHC physicians' work.

One of the methods to promote rational drug prescribing and provide cost-effective treatments would be through the prescribing feedback system that informs physicians *which* medications they have prescribed and *for what* diagnosis. It is recommended that the HIF develop and implement a prescriber feedback program. The implementation of this program may include feedback information in the form of "Dear Doctor" letters or "Prescriber Reports."

Currently, HIF does not have in place a system for a continuous and timely monitoring of medications usage and no analysis is performed with respect to morbidity (diagnosis) and the overall cost of a certain treatment (cost-benefit analysis). The current system in place, that should be based on prescriptions and dispensed medication, monitor the outpatient drug use is outdated and has been rarely used at best. It is recommended that HIF be technically and personnel-wise equipped to continuously monitor and analyze the medication utilization in health institutions.

It is recommended that National Pharmaceutical Database (NPDB) be developed. It is suggested that this database is located at HIF. The HIF IT Department should be in charge with technical maintenance of the database. The development, management and update of the database should be a collaborative effort between HIF (i.e., Pharmacy Department) and Ministry of Health (i.e., Bureau for Medications). Both the stakeholders and this consultant agree that this database should be part of the integrative IT support to the pharmaceutical sector in the country. HIF and MOH should share the "ownership" and "control" over the database, yet limited access to different users should be provided. A unique identification number system for medications and medical devices should be introduced into and become an integral part of NPDB.

It is recommended that initially the larger hospitals, and ultimately all 36 hospitals in the country, are provided appropriate IT support (hardware/software), so they become the part of the integrated pharmaceutical information system. This would allow hospitals, in the upcoming decentralized health system environment, to (i) monitor

drug use, (ii) develop and implement drug use evaluation programs, and (iii) through therapeutic committees, facilitate hospital management teams in making rational (cost-effective) decision regarding drug expenditures and budgeting. Training of pharmacists, physicians and nurses will be required to support appropriate use of technology, monitoring of drug use and implementation of DUE programs.

Foreign consultancy is needed, to train health professional in using the pharmaceutical information technology and in development and implementation of DUE. It is recommended that initially, using the “teaching the teachers” approach, a pool of health professionals from larger hospitals (i.e., Skopje, Bitola, Tetovo, Kumanovo), are trained. Later they may serve as educators for training in other hospitals.

The sustainability of the implemented reforms in the pharmaceutical sector will depend upon significant future support from members of “various interest group”, i.e., retail pharmacists, clinical pharmacists, clinical pharmacologists, physicians, nurses, lawmakers. The group of health care professionals (a pool of 30-40 physicians and 20-30 pharmacists) who will participate in and/or lead the process of pharmaceutical reforms need to be appropriately educated/trained. The education should include but no be limited to:

- Courses/training in evidence-based medicine, clinical pharmacology, pharmaco-informatics, pharmaco-economics.
- Courses for preparation of therapeutic guideliness for most common diseases, therapeutic protocols for most expensive medications, and DUE programs for the high-volume/high-cost medications.
- Training on the usage/management of pharmaceutical information system/database.
- Education of pharmacists on generic substitution, repeated dispensing, and new models of payment.

It is recommended that with support from MOH and HIF:

1. Macedonian Medical Association (MMA) assumes the leading role in development of therapeutic guidelines and therapeutic protocols, and facilitate the training in evidence based medicine and clinical pharmacology; and
2. The National Drug Information Center (NDIC) and Chamber of Pharmacy assumes the leading role in development and implementation of DUE programs, courses in pharmaco-informatics, pharmaco-economics, and training in generic substitution.

Finally, it is recommended that the previously developed CME program in rational drug prescribing for PHC physicians continue and, along with the introduction of a physician-directed prescribing feedback system, is used influence physicians prescribing behaviour and promote rational drug use in outpatient settings.

3. IMPLEMENTATION PLAN SUMMARY

Participants	Activity	Time	Support	Cost
MOH - Bureau for Medicines	Law on Medicines harmonization with EU legislation and improvements in drug registration Adoption of essential by-laws	June-Sept 04	Local Consultants	\$14,000
		Oct - Dec 04	Foreign Consultants	\$30,000
MOH - Bureau for Medicines	Equipment, IT support, development of registers for medicines and medical devices	Sept 04-Mar 05	Local Consultants	\$14,000
			Goods	\$40,000
MOH - Bureau for Medicines HIF	National/HIF Drug Formulary Manual publication and dissemination (NPDB)	Sept-Dec 04	Local Consultants	\$8,000
			Publishing & dissemination	\$25,000
HIF with support from MOH Bureau for Medicines and NDIC	Development of National Pharmaceutical Database	Jun – Dec 05	Goods and IT training	\$300,000
HIF	Development of Drug Use Evaluation (DUE) Programs	Jun – Dec 05	Foreign Consultants	\$45,000
3 - 4 Larger/pilot hospitals	Establishing of therapeutic committees and development of DUE programs	Jan – Jun 06	Local Consultants	\$24,000
HIF Chamber of Pharmacy	Training in generic substitution, repeated dispensing and new models of payment	Jan – June 05	Local Educators/	\$12,000

			Consultants	
			Foreign Consultants	\$45,000
HIF	Development of prescribing feedback system and indicators of rational Rx for PCH settings	June - Dec 05	Local Consultants	\$8,000
			Foreign Consultants	\$30,000
Macedonian Medical Association; MOH; HIF	Development of therapeutic guidelines & therapeutic protocols, Training in evidence based medicine and clinical pharmacology		Local Consultants	\$24,000
			Foreign Consultants	\$24,000
Macedonian Medical Association; MOH; HIF	CME program in rational drug prescribing for 400 primary care physicians	Jan – Dec 05	Local Educators	\$40,000
Macedonian Medical Association; NDIC, Chamber of Pharmacy	Courses in EBM, clinical pharmacology, pharmaco-informatics and pharmaco-economics.	Mar – Sept 05	Foreign Consultants	\$40,000
HIF	Training in formulary system management	Mar – Sept 05	Local Consultants	\$8,000
			Foreign Consultants	\$45,000

4. INTRODUCTION

This report is a part of the preparatory project for the Health Sector Reform Project (HSRP) in Macedonia, which is supported financially by the World Bank. The key areas that have been addressed within this assignment include:

- The accountability, responsibilities and functions of the State Pharmaceutical Bureau in the Ministry of Health (MOH);
- A prescription and timetable for the necessary changes, clarifications, and amendments to the legal and regulatory framework governing the pharmaceutical sector;
- A prescription for the revision of the institutional arrangements and procedures used to produce and maintain the positive list system of pharmaceuticals, and to promote greater technical objectivity, transparency and governance in the process;
- An improvement in the capacities of HIF to monitor prescribing and consumption of pharmaceuticals at the operational level of the system, including the use of hospital formularies.

Concurrent with the beginning of this assignment, it was determined that additional support for the Drug Supply Management was needed and Preparation Project Unit was established, to seek technical assistance for this pharmaceutical subcomponent. The objectives of this component are:

- A prescription and timetable for the necessary changes, clarifications, and amendments to the legal and regulatory framework governing the pharmaceutical sector in the procurement, supply and distribution of drugs;
- Quality assurance and revision of the product licensing, registration and testing arrangements and processes to increase the use of the abridged procedure in order to facilitate increased competition among suppliers, produce closer harmonization with European procedures and increase activity in the area of pharmaco-vigilance;
- An improvement in the capacities of HIF to monitor prescribing and consumption of pharmaceuticals at the operational level of the system, including the rational drug use and international tendering of pharmaceuticals.

This Final Report is based on the findings presented in the December 2003 Inception Report, and is build upon the comprehensive review and analysis of various

previous and ongoing reports prepared by domestic and foreign consultants. These reviews and analysis were conducted between January-February 2004, and presented in the February 2004 Mid-Term Report. In this Report, the findings and recommendations of the Mid-Term Report, that were reviewed and accepted by Pharmaceutical working group and other stakeholders, are translated into an action plan that includes:

- Timetable for proposed activities and changes
- Assessment of required support, and
- Allocation of financial resources.

5. SUMMARY OF COMPLETED ACTIVITIES

Legal and regulatory framework	
	Activity
Law on Medications and existing by-laws regulating registration, quality control, distribution and prescribing of medications	Review of legal and regulatory framework of the pharmaceutical sector completed.
A review of and timetable for the necessary changes, clarifications, and amendments to the legal and regulatory framework governing the pharmaceutical sector	<p>Areas for improvement in the Law (harmonization with European legislation) and key by-laws that need urgent adoption identified, discussed and accepted by working group and other stakeholders.</p> <p>The Implementation Plan time-table, and assessments of required resources and technical assistance presented to and reviewed/accepted by working group and other stakeholders.</p>
State Bureau of Medicines	
Current organizational structure and activities of State Bureau for Medications	<p>Review of the Bureau for Medications structure and activities completed.</p> <p>Limitations and weaknesses in the Bureau's activities identified and areas of improvement and options for strengthening the capacity of the Bureau identified.</p>

	<p>Models of State Drug Agencies discussed and de-centralized model accepted</p> <p>Timetable for proposed activities (changes/improvements) presented to and assessments of required resources and level of technical assistance discussed and accepted by working group and other stakeholders.</p>
Positive list of drugs	
Review of the positive list of drugs	<p>The previous two and current HIF's positive list of drugs (i.e., outpatient and hospital formulary list) reviewed and compared.</p> <p>Weaknesses in the procedures and policy used to produce and maintaining the list identified.</p>
The institutional arrangements and procedures used to produce and maintain the positive list of pharmaceuticals	<p>The steps-wise activities required for strengthening institutional arrangements and procedures used to produce and maintain the HIF outpatient and hospital formulary (positive list of drugs) identified and discussed/accepted by working group and other stakeholders.</p> <p>Steps for developing Drug Use Evaluation (DUE) programs and monitoring the rational drug use presented to and discussed/accepted by working group and other stakeholders.</p> <p>Assessment of required technical assistance and timetable for implementation of the above activities presented to, and accepted by working group.</p>
Health Insurance Fund and Pharmaceuticals	
Improvement in the capabilities of the Health Insurance Fund (HIF) to monitor the prescribing and usage of pharmaceuticals	<p>Review of drug use and expenditure for outpatient and hospital medications in the period 2000-2003 and projected expenditure for 2004 completed.</p> <p>High cost/volume drugs in outpatient and hospital settings identified.</p> <p>List of high volume and/or high cost drugs that should be targets for DUE interventions proposed.</p>

	<p>The options of strengthening the capacity of the HIF Department of Pharmacy (including the introduction of Pharmaceuticals and Therapeutics (P&T) committees and clinical pharmacy services in larger hospitals) discussed by working group.</p> <p>Assessment of required resources and technical assistance presented to, and accepted by working group</p>
IT Support	
Integrated IT support for all four key areas	<p>The integrative links for development of comprehensive pharmaceutical information system at national level (National Pharmaceutical Database) identified and discussed by working group.</p> <p>The pharmaceutical databases to be upgraded/developed and their basic features (even though not a primary task for this component) discussed by working group.</p> <p>Assessment of required technical assistance presented and discussed with working group (This issue is more closely elaborated by the IT component of the Preparatory project; However, this working group should provide feedback for and have input into the part of the IT component that is related to the management of pharmaceuticals at the level of HIF, MOH, and large health institutions).</p>
Educational programs and training	
Educational programs and trainings in four key areas	<p>The following educational programs/training, necessary for successful implementation of reforms in the pharmaceutical sector, have been identified and discussed by the working group:</p> <p>Education programs/training of HIF Department of Pharmacy staff (PharmDs and MDs) and pool of doctors and pharmacists from larger hospitals in the following areas:</p> <ul style="list-style-type: none"> -EBM, clinical pharmacology, phamaco-informatics and pharmacoconomics; -development of formulary system and

	<p>drug utilization evaluation (DUE) programs and development of therapeutic guidelines</p> <p>Education/training of pharmacists in generic substitution, repeated prescribing/dispensing of drugs, and new payment models</p> <p>Training of primary care physicians in rational drug prescribing</p>

6. LEGISLATIVE AND REGULATORY FRAMEWORK IN THE PHARMACEUTICAL SECTOR

Both the working group members and other stakeholders agree that there is a need for improvements in the pharmaceutical legislation. Their opinions and suggestions are rather similar, in many cases identical. There is a consensus that the Law on Medications, Medicinal Products and Medical Devices should be harmonized with the European legislation. However, the immediate activities should be directed toward development of by-laws that will facilitate the implementation of the current law. The development of these by-laws should take into consideration the expected future Law changes and harmonize those with the European Union pharmaceutical legislation. The appropriate experiences from the countries in the regions, that have already harmonized their legislation and adopted those by-laws, should also be utilized.

Some of these by-laws are already in the process of adoption. The opinion of the working group is that these and other required by-laws should be prepared by local experts and MOH-appointed working groups. The same should apply to the preparation of the initial changes/amendments of the Law on Medications.

There is an agreement among the working group members that technical assistance by a foreign consultant would be necessary in the final phase of these activities. This foreign expert should have experience (active participation) in harmonization of pharmaceutical legislation in some of the Central/Eastern European countries. It is believed that this approach would be most effective.

With respect to by-laws regulating the dispensing of prescription medications, it is recommended that this regulation is changed so that it allows repeated prescribing/dispensing of medications. It is a common practice in Macedonia that “by prescription only” medications are dispensed without prescription. The Pharmaceutical Chamber of Macedonia strongly supports the position of the working group that this illegal practice should stop and that additional measures should be introduced to prevent

it. In this regard, violations of the “by prescription only” rule should be linked to the pharmacists’ licensing. More specifically, it is recommended that even licence revocation (temporarily, or permanently in case of repeated violation of the Law) should be used as a corrective measure. The current penalty provisions in the Law are unclear and ineffective.

The Pharmaceutical Chamber advocates strict adherence to the current Law which prohibits wholesalers, manufactures and physicians from owing retail pharmacies as well as from practicing retail pharmaceutical activities (apparent conflict of interest and risk of monopoly).

The development of the following by-laws was given priority and timeline for their adoption was determined:

- By-laws regulating registration of medications (marketing authorization)
- By-laws regulating bioequivalence studies
- By-laws regulating the information leaflet inserts in medication packaging
- By-laws regulating registration of medicinal products
- By-laws regulating registration of medical devices
- By-laws regulating registration of borderline products
- By-laws regulating clinical trials

The changes in the Law on Medications and its harmonization with European legislation, including the foreign technical assistance should be completed by December 2004.

Legislative and regulatory framework			
	Type of assistance	Timeframe	Comments
By-laws for registration of drugs (Marketing authorization)	Local Technical Assistance \$2,000	June – Sept 2004	» This document should include not only instructions for the documents required for the market-authorization application, but also the detailed description of the timeframe for the various steps in the registration process (i.e., submission of application, validation of the submitted documentation, request for additional information, issuing of marketing authorization, appeal process).

			<p>Activity to be conducted by MOF-appointed local working group</p> <p>» State Bureau for Medications should provide public access (Web site) to the list of all registered drugs, including the date when application was submitted and date when marketing authorization was issued.</p>
By-laws regulating bioequivalence studies	<p>Local Technical Assistance</p> <p>\$2,000</p>	June – Sept 2004	<p>» This document should include:</p> <p>(i) the list of referent/standard drugs to which all generic versions must be compared and shown to be bioequivalent</p> <p>(ii) List of referent countries from which studies of bioequivalence are accepted.</p> <p>This activity should be carried out by MOF-appointed working group that includes clinical pharmacologists</p> <p>Public (Web) access to the document)</p>
By-laws regulating registration of medicinal products and medical devices	<p>Local Technical Assistance</p> <p>\$2,000</p>	June – Sept 2004	<p>This activity should be carried out by MOF-appointed working group that includes clinical pharmacologists and pharmacists specialized in drug quality control</p> <p>Public (Web) access to the document</p>
By-laws regulating registration of Borderline products	<p>Local Technical Assistance</p> <p>\$2,000</p>	June – Sept 2004	<p>Activity to be conducted by MOF-appointed working group</p> <p>Public (Web) access to the document)</p>
By-laws regulating clinical trials	<p>Local Technical Assistance</p> <p>\$2,000</p>	June – Sept 2004	<p>Activity to be conducted by MOF-appointed working group that includes clinical pharmacologists, clinicians/sub-specialists, clinical pharmacists, and experts in medical ethics.</p>

			Public (Web) access to the document
Harmonization of Law on Medications with European pharmaceutical legislation	Local Technical Assistance \$4,000 Foreign Technical Assistance Two man/month \$ 30,000	Oct –Dec 2004	Activity to be conducted by MOF-appointed working group and foreign consultant with experience in harmonizing pharmaceutical legislation in some of the non-EU countries in the region.

7. THE STATE BUREAU FOR MEDICATIONS

An effective implementation of a National Medication Policy requires support from a well-organized and well-equipped agency for medications, staffed with trained pharmacists and physicians. The weaknesses in the current structure and activities of the State Bureau for Medications have been identified and discussed with the working group and other stakeholders.

Under the current system of operations and organizational scheme, the Bureau is actually a division within the Ministry of Health. Based on the current economic situation in the country with urgent need for investment in various high priority segments of the health care system, it is unrealistic to seek development of new centralized drug agency, similar to those in developed countries. This approach would require substantial financial and human resources, and time.

There is an agreement among the stakeholders that the current organizational structure should be the starting point for the Bureau's activities and capacities building, which needs to be paralleled with substantial administrative, personnel and technical strengthening.

The Bureau's administrative independence needs to be strengthened, resulting with a *de facto* professional independence, as defined in the Law on Medications.

Mechanisms need to be put in place that would allow transparency and control over all the phases of medication registration, starting with the request for registration submission, followed by initial validation of the submitted documentation, and ending with the final determination, which needs to be publicly displayed (Web site). Rules and regulations need to be established that would govern and clearly identify both the participants in and the timetable for each phase of the registration process.

A high degree of administrative connectivity between the Bureau and the other participants in the registration process needs to be established. This implies the feasibility of administering through the Bureau the requests for appropriate expert evaluations (e.g. quality control, pharmacological or clinical expert evaluation, bioequivalence studies, etc.)

As part of the Ministry of Health project for its computerized network connectivity with the electronic data archiving system, a development of a new program for medication registration is in progress. Appropriate training will be needed to implement it. At the present time, there is no electronic capacity in place for registration of medical devices and medicinal products. Appropriate software need to be fully developed and implemented.

The Bureau does not have access to either the export-import information about the medications or their distribution in the country. The strengthening of the Bureau's administrative connectivity with the Ministry of Finance (Customs) and the possible computerized network connectivity will enable better overview of the distribution of medications, medicinal products, medicinal devices, psychotropic substances and pharmaceutical raw materials. As part of their current practice, the customs authorities utilize five tariff numbers for import/export of medications. This system has proven less efficient for successful monitoring of the movement of medications in the country. Therefore, a new system/register needs to be devised, which would enable easy monitoring of the distribution of every single medication. Development of the nationwide unique identification number would facilitate this process.

Bureau for Medicines			
	Type of assistance	Timeframe	Comments
Development of electronic database (register) for all approved medications in the country and for medications on the outpatient and hospital HIF Formulary (Positive list of drugs).	Local technical assistance Financial support: (\$ 4000.00) 2 man/month	June - September 2004	» There should be Web access to this database/register. Printed version is also recommended, although, it may be a part of the printed version of the National/HIF Formulary Manual. Financial support is required. This activity should be carried out by Bureau for

			<p>Medicines and the HIF - Pharmaceutical Department.</p> <p>This database / register may be a part of the large National Pharmaceutical Database located at the HIF's IT Department.</p>
National/HIF Drug Formulary Manual publication and dissemination	<p>Local technical assistance</p> <p>\$8,000</p> <p>Financial support (\$ 25.000)</p>	September - December 2004	<p>The manual of registered drugs should be available in electronic (Web access) and printed form.</p> <p>Financial support is required for this activity</p> <p>This activity should be carried out by Bureau for Medicines, HIF's Pharmacy Department and National Pharmaco-information Center.</p>
Equipment for the Bureau	<p>Goods</p> <p>\$40.000</p>	September - December 2004	Computers (8-10), scanner, photo-copy machine, fax-machine, internet access; literature and PC software programs
<p>IT Support for the Bureau for Medicines:</p> <p>Registers/databases for medicinal products and medical devices, import/export</p>	<p>Local technical assistance</p> <p>Financial support \$ 14,000 7 man/month</p>	September 2004 - March 2005	<p>Registers and software programs should be developed for: (i) all approved medicinal products and medical devices; tracking the import/export and distribution of drugs, psychotropic agents, and raw medical materials; inspection reports for retail pharmacies, wholesalers, and manufacturers</p> <p>Public/restricted access to this information (Web site) to be provided</p> <p>Development of Web site for the Bureau and network</p>

			<p>connection with the National Pharmaceutical Database, HIF, Ministry of Finance (Customs)</p> <p>These activities to be conducted by the MOH and Bureau, local experts on medicinal products and medical devices with support from HIF's IT and Pharmacy Departments</p>
Bureau of Medicines: Improvements in personnel		2005-2006	Defined the needs for personnel improvements

8. POSITIVE LIST OF DRUGS -- FORMULARY SYSTEM

At the present time, Macedonia has a positive list of (priority) drugs. This list contains medications that are being prescribed in primary health care as well as in hospital settings. The HIF pays for these medications. A 9-member committee appointed by the Minister of Health determines this list and makes all necessary changes of it.

This committee does not have an established methodology for (1) evaluation of literature about the pharmacological group that a particular medication belongs to; (2) summation and presentation of data regarding a particular medication (monograph); and, (3) criteria and principles for medication selection. There is no established procedure to follow when adding to or removing a medication from the list. It is not standardized who can request whether a medication can be placed or removed from the list. Regulations must be put in place to define the methodology for addition or removal of a certain medication from the list. By the same rationale, a methodology must be put in place for evaluation of, comparison between, and selection of medications for this list.

This committee should provide professional assistance to HIF with respect to the analysis of medications utilization and prospective follow-up of medication usage in outpatient settings and hospitals.

The committee, both numerically and composition-wise, cannot meet the challenges of its activities as described above. It must increase in numeric terms as well as strengthen its professional composition. To increase its professionalism and

objectivity, it should be divided in two working groups (committees), one that would focus on the outpatient list of drugs and one on the inpatient list of drugs.

The first working group (committee) should be composed of physicians from the primary health care (PHC) sector, and -- given the type of the most frequently prescribed medications in the PHC -- physicians from the internal medicine group, clinical pharmacologists, microbiologists and pharmacists. The second working group (committee) should be composed of physicians from specialties or subspecialties in which the largest volume of or most costly medications are utilized. In addition, it should include clinical pharmacologists, clinical pharmacists or pharmacists from hospital pharmacies, pharmacists specializing in pharmacoinformatics, as well as nurses who have first-hand experience administering these medications.

The members of the above two committees will need a customized (basic) education in evidence-based medicine (EBM), clinical pharmacology, pharmacoinformatics and pharmaco-economy. There is a consensus that this educational activity (described below under *VII. Education*) will require special and financial support.

It is recommended that during 2004, MOH and HIF, in collaboration with the Clinical Center in Skopje, the Faculty of Pharmacy, the Macedonian Medical Association and other stakeholders, identify a larger pool of professionals from the above mentioned areas who would undergo the customized education program. This pool will serve as a membership basis for the future two working groups (committees) determining the positive lists of (priority) medications. The customized education program could be applied in educating an even larger group of physicians and pharmacists that would later be in a position to serve on hospital medical committees in the larger hospitals throughout the country.

The introduction of the system of priority medication lists (Formulary System) at the HIF level, and later at hospital level, requires support by well-educated clinical pharmacists. At the present time, none of the hospitals in the country has in place clinical pharmacy as a discipline and profession that is in charge of timely and regular distribution and usage of medications in these hospitals. The development of this discipline and profession is a requirement for the establishment and proper functioning of the P&T committees and the system of hospital formulary. This topic is further elaborated upon in Part V of this report, which deals with rational and safe medication usage in health institutions and advocates that clinical pharmacy should have an important role in carry out various therapeutics related activities in hospitals.

Formulary System (System of positive/priority lists of drugs)			
	Type of assistance	Timeframe	Comments
Strengthening the capacities of the HIF's Positive List of Drugs (P&T) Committee	Foreign technical assistance for management of formulary system (see educational activities part VIII)	September 2004	Committees for outpatient and hospital HIF formulary introduced
		June 2005	
	Foreign technical assistance for and introduction of Drug use evaluation programs for top 25 drugs 3 men/month 45,000	September 2004	By-laws regulating the formulary system management prepared and adopted
		March 2005	
Local technical assistance 12 men/month \$24,000	June - December 2005	Larger pool of physicians and pharmacists to be identified and trained in management of formulary system (see under VIII Education/training)	
	January - June 2005	Introduction of Drug Use Evaluation programs for top 25 drugs	
	January - June 2006	Development of P&T committees and DUE programs in 3-4 larger hospitals.	

9. THE HEALTH INSURANCE FUND AND CONSUMPTION/UTILIZATION OF MEDICATIONS

At the present time, HIF does not have in place a system for a continuous and timely monitoring of medications usage. Instead, it employs estimates for the each overall medication usage on the basis of a medication's usage in the previous year. These estimates are determined by the HIF Pharmacy Department. The parameters

used in these estimate analysis are the total medication volume and associated total cost during the previous year. No analysis is performed with respect to morbidity (diagnosis) and the overall cost of a certain treatment, which would include not only the medication cost, but also other possible costs associated with the therapeutic treatment (e.g. treatment duration, services provided by medical personnel, additional laboratory analysis, utilization of other medical accessory devices like syringes, infusion lines, etc.). In the PHC settings the medication utilization is associated with the diagnosis, but this is not necessarily the case with hospital-administered therapy. This presents a difficulty when attempting to monitor the medication utilization. HIF is currently not technically and personnel-wise equipped to continuously monitor the medication utilization in medical facilities.

The health care system in Macedonia is currently undergoing a decentralization marked with establishing contracts between HIF and particular hospitals (hospital contracting.) Given the fact that medication expenditures are a significant part of the hospital total expenditures, the hospitals will soon (2005) face the problem of having to control or even reduce their medication usage. They will have to develop strategies that will enable them to offer the same level of health care quality while reducing their medication expenditure.

This can be feasible only if: (1) hospital Pharmacy & Therapeutics committees are established; (2) both medication usage and medication expenditures are monitored; (3) programs are established to evaluate the usage of medications of particular interest (those with large volume and/or high cost); and (4) therapeutic guidelines/protocols are established for the most common and most expensive drug treatments. For these activities to take place an information system needs to be established, to monitor the hospital medication utilization. Of special importance is the further development of clinical pharmacy as a health care discipline, whose professionals would carry out these activities. The clinical pharmacy specialty exists as such in Macedonia. However, the hospitals do not have clinical pharmacists who would monitor the medication utilization.

It would be unrealistic to expect that in the beginning of the implementation of the health care sector reforms (2005-2008) all the departments at all the hospitals will be computerized, with all drug treatment information available in an electronic form (medications/diagnosis/patient). Likewise, it cannot be expected that clinical pharmacists will be educated, and employed, in all hospitals in the country, at a time when there is a pressure to reduce the number of health care workers in the public medical organizations. What is realistic is a gradual development of the clinical pharmacy service, first in the 3-4 largest hospitals, paralleled by functioning hospital P&T committees and systems for priority medications ("formulary system.").

First of all, an analysis is needed of the means of data collection and their flow as related to the distribution and utilization of medications in medical facilities. Also, it is

important to determine the steps and participants involved in the process of medication data collection, medication data entry as well as in their analysis. This will help in the design of the hospital/HIF information system. This issue has been addressed in the information technology (IT) subcomponent of the preparation project. Because of its importance for the pharmaceutical sector, it is also discussed in Part VII (Information Technology Support) of this report.

It is realistic to expect that during this project, at least the central hospital pharmacies in 3-4 of the largest hospitals (Skopje, Bitola, Tetovo, Kumanovo) will become technically equipped, while 15-20 clinical pharmacists will be trained to monitor the medication distribution and utilization (medications/diagnosis/patient) at hospital department level. This process will have to involve foreign technical assistance in the form of education and training. The employment of clinical pharmacists, at a time when new employment in the public administration has been ceased, can be justified with the multi-fold savings in the health care system that will be experienced in the event of timely and professional monitoring and analysis of medication utilization and consumption. An argument in support: at the University Clinical Center in Skopje, during 2000-2002 (Table 7), the expenditures for drugs have increased by 106% or \$8.5 million; if the above-recommended changes are implemented and bring about *only* a 10% savings, this will justify the economic expense for these employments.

An analysis of PHC usage in medications from the positive list shows that 50% of all medications are prescribed for therapy of chronic cardiovascular disorders and acute infections of the upper respiratory tract (Table 1).

Table 2: Top ten diagnoses in outpatient settings and projected number of prescription for year 2004

	ICD-10	Diagnosis	Number of Rx	%	Cumulative %
1	I10	Essential (primary) hypertension	810,869	12.33	12.33
2	J03	Acute tonsillitis	481,282	7.32	19.65
3	I20	Angina pectoris	455,706	6.93	26.58
4	I25	Chronic ischemic heart disease	374,575	5.70	32.27
5	E11	Type 2 diabetes mellitus	337,635	5.13	37.40
6	J02	Acute pharyngitis	263,153	4.00	41.41
7	I42	Cardiomyopathy	207,692	3.16	44.56
8	K29	Gastritis and duodenitis	192,608	2.93	47.49
9	J20	Acute bronchitis	162,854	2.48	49.97

The 10 most prescribed medications, accounting for 40% of the expenditures, are for the same diagnoses (Table 2). This information emphasizes that these disorders need to be a focus of attention, as well as their treatment based on rational prescribing of antibiotics and cardiovascular medications. PHC therapeutic guidelines for these disorders need to be the first established. The physicians need to be educated in rational prescribing of these medications.

Table 2: Projected expenditures for top ten drugs from out-patient positive list of drugs for year 2004

	Generic Name	Stickers per Year	Annual Price in \$	Price/ Sticker \$	Cumulative \$	%	Cum. %
1	Amox+Clav.Acid	357,359	2,191,671	6.13	2,191,671	8.7	8.7
2	Amlodipine	259,014	1,471,589	5.68	3,663,261	5.8	14.5
3	Enalapril	787,694	1,244,861	1.58	4,908,121	4.9	19.5
4	Azithomycin	64,263	1,148,249	17.87	6,056,370	4.6	24.0
5	Penicillin	143,530	1,037,921	7.23	7,094,291	4.1	28.1
6	Simvastatin	51,763	940,101	18.16	8,034,393	3.7	31.9
7	Lisinopryl	152,180	746,721	4.91	8,781,113	3.0	34.8
8	Cefalexin	271,727	689,351	2.54	9,470,464	2.7	37.6
9	Nifedipine	170,300	616,171	3.62	10,086,635	2.4	40.0
10	Cephachlor	104,028	565,469	5.44	10,652,104	2.2	42.2

The control of the volume of the prescribed medication in PHC should be conducted through introduction of indicators for rational prescribing in PHC, rather than through limitations on prescribing (as has been proposed by some stakeholders.) Given the most frequent diagnoses and the medications utilized for treatment in the PHC sector, the following indicators can be used to monitor the rational medication prescribing in PHC:

- Percentage of patients with essential hypertension who are treated with hydrochrolotiazide
- Percentage of patients with essential hypertension who are treated with a beta-blocker
- Percentage of patients with ischemic heart disease who are treated with a beta-blocker

- Percentage of patients with ischemic heart disease who are treated with low-dose aspirin
- Percentage of patients with acute pharyngitis or otitis media who are treated with an antibiotic
- Percentage of patients with acute bronchitis who are treated with an antibiotic
- Percentage ratio of prescribing amoxicillin vs. amoxicillin plus clavulanic acid
- Percentage ratio of prescribing amoxicillin vs. azithromycin

These indicators for rational prescribing may be used when evaluating the PHC physicians work, determining bonuses for quality work and contracting with HIF.

Rational drug prescribing assumes that the physicians are thought how they prescribe medications. One of the methods to influence (educate) rational prescribing is through providing feedback to the physicians informing them of the medications they have prescribed and for what diagnosis. The Health Insurance Fund should develop and implement prescriber feedback program. The HIF outpatient formulary committee may take a leading role in establishing this program. The implementation of this program may include feedback information in the form of “Dear Doctor” letters or “Prescriber Reports.” The HIF Pharmacy Department, supported by Macedonian Medical Association and local experts-educators in rational drug prescribing, should conduct this program.

It is recommended that HIF collaborates with the Macedonian Medical Association and the Chamber of Pharmacy in providing education and training for physicians and pharmacists on generic medications substitution and multiple prescribing of medications through a single prescription. This will enable an economically efficient therapy for the chronically ill, as well as relieve the general practitioners from repeated prescribing for these patients.

An analysis of the medication usage in hospital facilities (Tables 3-5) demonstrates that the majority of the funds (50% or about \$15 million) for hospital medication usage are spent on 15 medications. It also shows that about 80% of these funds (\$32 million) are spent on the 25 medication presented on Tables 3-5.

Table 3: Estimated expenditures for top 9 drugs in hospitals for year 2004

	ATC cod	Generic Name	Total in denars	Total in \$	%	Cum %
1	J01D A13	<i>Ceftriaxon</i>	56,834,102	\$1,136,682	11.21	11.21
2	H01A C01	<i>Somatotropin human</i>	52,963,639	\$1,059,273	10.45	21.65
3	B01A B00	<i>Ceptoparin (LMW heparin)</i>	51,056,023	\$1,021,120	10.07	31.72
4	A04A A03	<i>Tropisetron</i>	22,739,085	\$454,782	4.48	36.21
5	J01X A01	<i>Vancomycin</i>	19,785,734	\$395,715	3.90	40.11
6	J01D A10	<i>Cefotaxim</i>	16,180,490	\$323,610	3.19	43.30
7	H01B X01	<i>Methylprednisolone</i>	15,330,062	\$306,601	3.02	46.33
8	J01F F01	<i>Clindamycin</i>	14,831,823	\$296,636	2.93	49.25
9	M03AC04	<i>Atrakurium besilat</i>	14,546,469	\$290,929	2.87	52.12

5,285,348**Table 4: : Estimated expenditures for top 10 immnomodulators, blood substitutes, factors of coagulation and infusion solutions in hospitals for year 2004**

	ATC cod	Generic Name	Total in denars	Total in \$	%	Cum %
1	L03A B02	Interferon beta	131,267,448	\$2,625,349	21.71	21.71
2	B02B D02	Coagulat. factor VIII	88,500,000	\$1,770,000	14.64	36.35
3	J06A A	Imunoglobulin human	64,035,272	\$1,280,705	10.59	46.94
4	B02B D04	Coagulation factor IX	56,200,000	\$1,124,000	9.30	56.24
5	L03A A02	Filgastrim	52,533,600	\$1,050,672	8.69	64.93
6	B05A A01	Albumin human	49,352,800	\$987,056	8.16	73.09
7	B05B B01	Infusions: NaCL	35,840,000	\$716,800	5.93	79.02
8	L03A B04	Interferon alfa 2a	30,598,290	\$611,966	5.06	84.08
9	L04A A01	Ciclosporin	20,295,448	\$405,909	3.36	87.44
10	L03A B11	Peg interferon 2a	17,571,175	\$351,424	2.91	90.35

10,923,001**Table 5: Estimated expenditures for top six antineoplastic agents for year 2004**

	ATC cod	Generic Name	Total in denars	Total in \$	%	Cum %
1	L01C D01	<i>Paclitaxel</i>	132,982,560	\$2,659,651	33.35	33.35
2	L01B C06	<i>Capecitabine</i>	77,080,464	\$1,541,609	19.33	52.68
3	L01X X21	<i>Rituximab</i>	35,497,350	\$709,947	8.90	61.58
4	L01D B01	<i>Doxorubicin</i>	24,790,428	\$495,809	6.22	67.80
5	L01B C05	<i>Gemcitabine</i>	21,432,248	\$428,645	5.38	73.18
6	L01X X19	<i>Irinotecan</i>	20,260,932	\$405,219	5.08	78.26

6,240,880

Table 6: Drugs expenditures in University Clinical Center for year 2000-2002
(Medications distributed through central clinical pharmacy)

					% Increase <u>2001</u> 2000	% Increase <u>2002</u> 2000
	Currency	2000	2001	2002		
Medications	denars	328,071,195	384,932,478	510,482,586	117.3	155.6
	US dollars	\$6,561,424	\$7,698,650	\$10,209,652		
Antineoplastic	denars	98,505,509	180,253,647	346,421,636	183.0	351.7
drugs	US dollars	\$1,970,110	\$3,605,073	\$6,928,433		
TOTAL	denars	426,576,704	565,186,125	856,904,222	132.5	200.9
	US dollars	\$8,531,534	\$11,303,722	\$17,138,084		

It is recommended that very soon programs need to be developed that would monitor and evaluate the usage of these 25 medications (Drug Use Evaluation, DUE). Also, it must be pointed out that there are significant restrictions on the use of these medications, within the health care systems of the economically most powerful countries of the world, including the countries of the European Union and the United States. There is no reason why similar restrictions cannot be placed on the patients in Macedonia who are insured through HIF. There is a consensus between the working group members that these activities will require foreign technical help, including education for the participants in these activities.

Health Insurance Fund and Pharmaceuticals			
	Type of assistance	Timeframe	Comments
Development of National Pharmaceutical Database	Purchase of server, software, development of database for outpatient and inpatient drugs, and training for drug management; foreign technical	June – December 2005	The HIF should develop database that would primarily be used for management of outpatient and inpatient drugs. However, this database may be expanded to include all important information on pharmaceutical and to be shared with MOH and the Bureau for Medicines. Connectivity with the hospital electronic medical record system

	assistance Total \$ 300,000		should be provided, so drug and disease management programs may be implemented. This activity should be conducted by HIF's IT and pharmacy departments with support from the MOH, the Bureau and National Pharmacoinformation Center.
Generic drugs substations and Payment system	Local Technical Assistance \$14,000 Foreign Technical Assistance 3 men/month \$ 45,000	June – December 2005	Training of pharmacists and HIF's staff. This activity should be carried out by HIF Pharmacy department and Chamber of Pharmacists.
Development of prescribing feedback system and monitoring of targets for rational prescribing in PCH settings	Foreign Technical Assistance 2 men/month \$ 30,000 Local technical assistance 4 men/month \$ 8,000	June – December 2005	Physicians (irrational) prescribing behaviour should be monitored and corrected through prescriber feedback system. This activity should be conducted by HIF's pharmacy department and local experts involved in rational drug prescribing educational programs.

10. INFORMATION TECHNOLOGY SUPORT

The IT applications and the information systems support needed for the improvements in the pharmaceutical sector is more or less the same for all four key areas of this preparation project. There is a consensus among all stakeholders that an integrative approach must be utilized when addressing the IT needs in the pharmaceutical sector.

With this approach in mind, the need had been defined for establishing a uniform information system for monitoring and management of drugs (National Pharmaceutical Database, NPDB). The owners of this system would be the HIF and Ministry of Health (MOH). Different users of this system may have limited access to various parts of this database.

Apart from MOH and HIF, network connectivity to this system should be provided to: Bureau for Medicines, National Drug Information Centre, the institutions performing drug quality control, the Customs Department at the Ministry of Finance, and the clinical pharmacies at all 36 hospital facilities in the country. Limited public access to certain parts of this system should be provided to all health care workers, the insured – patients, the medication wholesalers and both the domestic and foreign drug manufacturers and their authorized representatives.

It is beyond the scope of this preparation project to define the structure of this information system. Its structure will be formulated in detail as part of the IT subcomponent of the preparation project. However, the type of information/data to be incorporated in the National Information System for Medication Monitoring and Management has been discussed by the working group and other stakeholders. The text attached as Annex I contains the key information and data, which should be included in this information system.

The need for introducing a unique identification number system for medications and medical devices was discussed and agreed upon. This unique medication number should include the ATC code and additional information related to dosage form, strength, manufacturer etc. It was recognized that for the hospital drug usage monitoring and evaluation, it is necessary that the unique medication number is linked to the patient and diagnosis.

11. EDUCATION/TRAINING OF HEALTH CARE PROFESSIONALS

The reforms in the pharmaceutical sector and their desired long-term effects, require that a significant number of health care workers, participants in these reforms, undergo appropriate education and training. At the present time in Macedonia, there is no system of continuing education on pharmacotherapy and pharmacy.

The upcoming changes in the pharmaceutical sector require activities that will result in:

- Development of a system for timely and continuous monitoring and analysis of medication use

- Introduction of a "fully" developed formulary system (system of positive list of medications) at the HIF level and at hospital level, including the introduction of hospital Pharmacy and Therapeutics committee
- Development and implementation of Drug Use Evaluation programs
- Introduction of a physician-directed system for feedback on prescribing of medications, aimed to provide rational prescribing of medications
- Generic medication substitution and multiple prescribing/dispensing of medication on a single prescription
- Introduction of therapeutic protocols and treatment guidelines for the most common disorders i.e. disorders requiring expensive medicamentous treatment
- Development of a clinical pharmacy system

The participants in the above-mentioned pharmaceutical sector reform changes will have to undergo appropriate education. To meet the needs of HIF and larger hospital P&T committees, the following coursework for 40-50 physicians and 20-30 pharmacists will be required:

- Courses, seminars and workshops in Evidence-Based Medicine
- Courses, seminars and workshops in the area of clinical pharmacology, pharmaco-informatics and pharmaco-economics
- Courses for preparation of Drug Use Evaluation programs (the 25 most commonly used/most expensive medications)
- Training of pharmacists and physicians on the usage/management of pharmaceutical information systems
- Training on introduction of prescribing feedback (educational) system informing physicians about their prescribing behaviour
- Education of pharmacists on generic substitution, multiple prescribing and repeated dispensing, and new models of payment.

There is a consensus among the working group members and the other stakeholders that the educational activities should begin as soon as possible, to parallel the other reform activities. They should take place in the first 6-18 months of the implementation of the health care reforms. Financial assistance in the form of foreign technical assistance will be required. It is estimated that for educational activities not covered in the previous sections of this report (i.e, preparation of therapeutic guidelines, CME in rational drug prescribing) would require an additional \$100,000-\$150,000.

It is recommended that the above activities are coordinated by the Ministry of Health, in collaboration with the Macedonian Medical Association and the Chamber of Pharmacy. The logistical support should be provided through the MOH centers for

continuing education, the National Drug Information Center, as well as through the Macedonian Medical Association and its specialty sections.

To provide for the introduction and normal existence of the system of clinical pharmacy, the related educational activities should be implemented over a longer time span (3-5 years). The long-term support for these activities should come from MOH, HIF and the Faculty of Pharmacy – and not as part of this project. It is recommended that all stakeholders, determine their realistic needs and capabilities for developing this system. It is apparent that a clinical pharmacy system is needed in order to support the long-term economic effectiveness of the pharmaceutical system in Macedonia. The sooner this system is defined and the plans for its development are in place, the longer-lasting and sustainable the positive effects of the planned reforms in the pharmaceutical sector will be.