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Assessment of regulatory impacts on pharmaceutical promotion

Bishkek, 2015

This paper represents the evaluation of the nature, scale and impact of regulation on the pharmaceutical promotion. The methodology of the evaluation followed the guidelines named 'Promotion of medicines: the evaluation of nature, scale and impact of regulation', which was prepared under the guidance of international experts supported by the Health Action International (HAI), with funding from the 'Medicines Transparency Alliance' (MeTA) and the Global Program of HAI.

The research team acknowledges the cooperation of managers of health organizations in Bishkek, of oblast and territorial hospitals, and of family medicine centres in Osh, Issyk-Kul, and Chui oblasts, as well as health professionals of these institutions. We are also grateful to all interviewees: officials, pharmaceutical business representatives, managers and representatives of pharmaceutical manufacturers, media, and non-governmental organizations. Their comments significantly contributed to this evaluation.

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CONTENT

1. Executive summary

The pharmaceutical advertisement and promotion has increasingly influenced the public policies and efforts to provide people with good quality, safe and affordable medicines. It also affects the rational prescriptions and has implications for pricing of medicines.

In recent years, in Kyrgyzstan, the relationships between healthcare professionals (doctors and pharmacists) and pharmaceutical companies have been heavily discussed. In particular, the focus has been on the possible influence of the pharmaceutical industry on decisions to prescribe and dispense medicines through a variety of promotional tools[1]. These tools can affect the treatment choices and, therefore, lead to sub-optimal choice of medicines, sometimes to the detriment of the patient's health.

HAI Global, jointly with the WHO have developed an evaluation methodology named as the 'Promotion of medicines: the evaluation of the nature, scale and impact of regulation', which can help countries to analyze their national legal and regulatory frameworks and to assess how key stakeholders perceive the situation with regulation of pharmaceutical promotion. This methodology includes a section of literature review and the survey of respondents using semi-structured questionnaires. They are designed to evaluate the characteristics, scope and impact of regulation of pharmaceutical promotion.

Using this methodology, the research team reviewed the legal and regulatory acts, and reviewed the literature describing and assessing regulatory practices of pharmaceutical promotion in foreign nations. For data collection purposes, the interview guides were reviewed and adapted to the context of Kyrgyzstan, using methodology developed by the HAI and Meta in their guideline 'Promotion of medicines: the evaluation of the nature, scale and impact of regulation'. The survey was conducted with interviews of health care professionals, patients, pharmacists, representatives of pharmaceutical companies, professional associations, experts and public officials. Additional tools were developed for the analysis of advertising materialы found in health care organizations during the study visits.

The evaluation reviewed the key issues of pharmaceutical promotion relevant to public health and healthcare system in Kyrgyzstan. Likewise in many other countries, the pharmaceutical promotion's role was found significant in the increased out-of-pocket costs due to medicines and gaps in rational prescriptions. The qualitative data suggested that the continued violations of the rules of prescribing and dispensing of prescription medicines, poor generic substitution practices, and corruption in the pharmaceutical sector were found to factor the increased OOP costs and rational use of medicines.

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[1] 'Forgotten morals and shame, or Glory of 'unethical marketing', Kyrgyz Tuusu News Agency, 17.11.2013, see at http://www.gezitter.org/society/23775_zabvenie_sovesti_i_styida_ili_protsvetayuschiy_neetichnyiy_marketing/

Although this study did not seek to measure quantitatively the scales the pharmaceutical promotion, it managed to describe the mechanisms of unethical marketing, which are important to discuss solutions to better regulate the pharmaceutical promotion, to fight corruption, and to enforce legislation as a whole. Particular attention shall be required to the facts of the bonus schemes present in the medicine prescriptions, collusions between advertisers and service providers, the relationships between healthcare managers and medical personnel that facilitate the unethical pharmaceutical promotion, as well as the potentially unethical presentations of medicines to the medical professionals and pharmacists in cases when capacities to critically evaluate the promotional materials are limited. There are also complex schemes of legal registration in the country of medical representatives of pharmaceutical producers, which potentially contribute to their limited liabilities in disputed cases or cases of consumer complaints.

Finally, the review of the international literature highlighted the existing regulatory practices, of which for the first time the options to embrace the business self-regulation in Kyrgyzstan were discussed. The interviews confirmed that involving business associations was identified as the main mechanism for implementation of the self-regulation practices, whereas the businesses, in addition to public regulation, will be directly involved in the regulation of the pharmaceutical promotion.

2. Study aims and objectives

Aim:

To assess the nature, extent and impacts of the regulatory system on the pharmaceutical promotion in the Kyrgyz Republic.

Objectives:

- Review the pharmaceutical promotion and advertisement practices in Kyrgyzstan;
- Review the content and implementation of legislation and regulations of the pharmaceutical promotion and advertisement in Kyrgyzstan;
- Review the awareness, opinions and solutions offered by informants on issues in the field of pharmaceutical promotion and regulations;
- Develop, discuss and propose practical recommendations to improve the regulation of the pharmaceutical promotion and advertisement. Particular attention is paid to options to embrace and implement the industry self-regulation.

3. Methodology

This section presents the evaluation phases, approaches to the development of research tools, stages of data collection, regions where data were collected, and the list of informants.

The evaluation was conducted in three phases:

Phase 1: Development, consultation and agreement of evaluation tools and the list of informants;

Phase 2: Desk review and field data collection;

Phase 3: Processing and analysis of the data collected, report preparation, discussion of the evaluation results, and development of final recommendations.

3.1 Study tools

1. The list of questions for review of legislative and regulatory documents related to the pharmaceutical promotion. This list of questions was developed based on the literature review and MeTA and HAI Guideline 'Promotion of medicines: the evaluation of the nature, scale and impact of regulation'. The scope of documents reviewed included those related to the healthcare sector in general, pharmaceutical regulations, regulations of advertisement, and other documents.

2. Five questionnaires for individual interviews with key informants. These questionnaires were the function of the semi-structured questionnaires recommended in the HAI and MeTA Guideline 'Promotion of medicines: the evaluation of the nature, scale and impact of regulation', which were discussed in the team of researchers and adapted according to the needs and the situation in Kyrgyzstan. The questions in this instrument were adapted in line with the results of the preliminary desk review and literature review and discussions in the team of researchers.

i. Questionnaire for interviews with key individuals in the regulation of pharmaceutical promotion;
ii. Questionnaire for interviews with managers and medical professionals in the healthcare organizations;
iii. Questionnaire for interviews with representatives of civil society, patients' organizations and representatives of international organizations and donor agencies involved in the import of humanitarian aid to Kyrgyzstan;

iv. Questionnaire for interviews with representatives of the pharmaceutical industry, business, and the media;

v. Structured questionnaire for clinicians and pharmacists

3. Blank forms for review of advertising materials (leaflets, brochures, etc.) and presentations of pharmaceutical companies. For the analysis of promotional materials and presentations, the evaluation used the WHO's Guide 'Understanding and responding to pharmaceutical promotion' and the Health Action International. The criteria for the review of the advertising materials largely drew from this document and the requirements to the content of advertisement provided for by the Technical Regulations.

3.2 Data collection and selection of informants

The data collection followed the results of the preliminary review of legal documents and the literature review on topics related to advertising and promotion of pharmaceutical medicines.

The data were collected using individual semi-structured interviews with key informants, structured interviews with healthcare professionals (doctors, pharmacists) and patients, analysis of advertising materials and observations of promotion activities (conferences, presentations in the healthcare organizations).

The advertisement materials were reviewed on the basis of pre-set criteria. The review covered all advertisement materials presented by the interviewed healthcare professionals, who, in turn, received them from representatives of a variety of pharmaceutical companies. Review of the presentations at the conferences held in the organizations on the basis of criteria developed.

The data collection was carried out in four regions of the country:

- Bishkek;
- Chui (Jaiyl rayon and Tokmok town);
- Issyk-Kul oblast (Karakol town, Ton rayon, and Cholpon-Ata town);
- Osh oblast (Osh city, Karasu rayon and Nookat rayon).

In each region, the interviews were held with the heads of two primary healthcare facilities and two territorial hospitals.

The interviews with key informants in the regulation of the pharmaceutical sector, regulation of the pharmaceutical promotion, pharmaceutical business, representatives of pharmaceutical companies, the media, NGOs and others were held in Bishkek.

Visitors of primary healthcare organizations were also interviewed on their awareness of the medicines, their relation to medicine advertising. In total, 95 visitors were interviewed, 40 of them women (42.1%), 55 men (57.9%), who attended the PHC organizations for acute and chronic diseases or other reasons. In terms of education, most interviewed visitors had higher education - 36.8%, with 25.3% having secondary vocational education, 28.4% having secondary school education, and 9.5% having incomplete higher education.

3.3 Data processing and analysis, synthesis of information and report formulation

Data obtained from the desk review, individual interviews and quantitative surveys, as well as observations and review of advertisement materials, were initially reviewed to isolate the issues/topics of particular importance and concern among informants. Individual opinions, data from reviewed documents and publications, as well as the observations of promotion activities were subjected to critical analysis, with the triangulation of data from different sources. Finally, the results of such exercise were synthesized into information covering the situation relevant to the aims and objectives of the evaluation.

The results obtained in the structured interviews (survey) of service providers were processed using SPSS 16 software.

4. The pharmaceutical market in the Kyrgyz Republic

At the moment, the pharmaceutical market in Kyrgyzstan is one of the most dynamic sectors of the national economy. According to the Report of the pharmaceutical industry evaluation in Kyrgyzstan[2], imports of pharmaceutical products in 2012 amounted to 9.7 bln Kyrgyz Soms, the annual growth rate of medicine imports over the past 5 years made 30% an average. The annual volume of domestic production of pharmaceuticals and medical devices is 280 million Kyrgyz Soms. Within 2003-2013, the volume of production in Kyrgyzstan increased 20 folds, with the number of pharmaceutical companies grown by 64% and the number of registered pharmaceutical products increased by 5 folds.

Kyrgyzstan's market is heavily dependent on imports, with 97% of medicines being imported from the CIS and far abroad. The share of pharmaceuticals manufactured in Kyrgyzstan remains insignificant, not exceeding 2.5-3% over the past decade. Medicinal herbs and preparations prevail in the national manufacturing. As of 2009, according to MoH data, 40% of the imported medicines are generics with trade names[3].

At the moment, there is no public regulation of medicines pricing. The Government's policy on medicine pricing provides for free market driven pricing for medicines, and the threshold fixed add-ups to wholesale and retail sales not apply. The average total margin on the price of imports to the end user is an average of 55%. The expensive medicines have been actively promoted, with the final price including the costs of the promotion. The promotion costs include the costs of all marketing tools. According to the monitoring undertaken by the MoH Department of Pharmaceuticals and Medical Devices (III quarter 2013), the average wholesale add-up for 8 medicinal products across different pharmaceutical companies was found at 23%, the average retail add-up was 26 %, and the total margin of import prices to the end customer was 55%.

There are 1,200 businesses operating in the pharmaceutical market. The majority of businesses (around 60%) are corporate entities (Ltd., JSC, Inc.), and the rest operate in the form of individual entrepreneurs. These entities are licensed to operate over 3,500 pharmaceutical sale companies, of which about 300 wholesalers entitled to import medicines and medical devices. Currently, in the Kyrgyz Republic there are more than 7.200 items of medicines registered and around 400 manufacturers[4].

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[2] 'Assessment of the pharmaceutical sector in the Kyrgyz Republic', Academy of Public Administration under the President of the Kyrgyz Republic, Institute of Public Administration Studies, Bishkek, 2014

[3] Health Policy Paper №67 'Factors contributing to the use of generic drugs', CPAP, Bishkek, 2009

[4] Unofficial data, the Register of medicines available at the website of the Department of Pharmaceuticals and Medical Devices of MoH cannot be downloaded or opened, see at http://www.pharm.kg/ru/registry

5. Impact of pharmaceutical promotion on public health

In general, the pharmaceutical industry plays a central role in the development and manufacturing of medicines. However, there may be trade-off between the business interests through the product promotion and the public health interests. In fact, the World Health Organization called it 'an inevitable conflict of interest' between the legitimate economic goals of manufacturers and the social, medical and economic needs of service providers and the community as much as possible rational selection and use of medicines[5].

Systematic reviews and studies of the impact of medicine promotion on the behavior of physicians have suggested that physicians prescribing medicines who rely on advertising as their main source of information often practice inappropriate prescriptions; they prescribe more often and tend to quickly adopt new products in practice. In many developing countries, the promotional activities of the pharmaceutical industry become the main, if not the only source of medicine information for physicians and consumers[6].

Excessive, inadequate or incorrect use of medicines can result in health risks, more adverse reactions, and more costs. To illustrate, the WHO estimated the costs of medicines make a quarter to two-thirds of the national healthcare budgets in developing countries and the out-of-pocket costs for medicines can become an unbearable burden for households, in particular to poor households[7].

In Kyrgyzstan, the public has recently been aware and discussed the problem of unethical marketing in general, and communications of healthcare professionals with pharmaceutical companies in particular[8]. Influence of businesses on decision-making in public procurement, prescriptions and dispensing of medicines have been of particular attention. These debates have also involved the parliamentarians and government officials. Public concerns have been around several facts.

Growing healthcare expenditures for medicines, growing prices, and self-medication have been identified as the most significant challenges to consider. This has been confirmed in review of studies, interviews, the media reports, which are described below.

[5] WHO, Clinical and pharmacological assessment of the pharmaceutical regulation. WHO, 1993
[6] Norris et al. 'Drug promotion: what we know, what we have yet to learn' Reviews of materials in the WHO/HAI database on drug promotion. BO3, HAI, 2005 г.
[7] WHO: 10 facts of essential medicines. 2009 г.
[8] S. Mosieeva, Vecherniy Bishkek News Agency, 'Distributors called for boycott unethical pharmaceutical companies', see at: http://www.vb.kg/doc/219530_distributorov_prizvali_boykotirovat_neetichnye_farmacevticheskie_kompanii.html

The Kyrgyz Integrated Household Survey demonstrated that over the past 10 years, the out-of-pocket healthcare expenditures increased by 3.5 folds, from 1.5 bln Kyrgyz Som in 2000 to 5.6 bln Kyrgyz Soms in 2009, with 60% comprised of expenditures to medicines[9].

There is a growth of self-medication in Kyrgyzstan[10]. This undermines the government's efforts to establish and enforce rules of appropriate prescriptions and dispensing of prescription medicines. In this evaluation, 26.3% of respondents reported that, when in need, they do not seek care from the family doctor but take medicines on their own. Besides, interviewed pharmacists reported that the majority of pharmacy clients ask for medicines of particular trade names. Of these, about one-quarter (23%) explained their choice with the advertisement of the sought medicines (on TV, newspaper).

The obvious factor of the prevailing self-medication is the free sale of medicines in pharmacies. In pharmacies, almost any medicine can be bought without a medical prescription. Failure to comply with the established rules of prescription in respect of certain medicines contribute to increased public health risks, of which many respondents considered the risks of antimicrobial resistance were found particularly crucial.

Interviewed officials, experts, and activists reported that the role of pharmaceutical marketing has significant role in the growing household expenditures for medicines, growing process for medicines, and prevailing self-medication. Concerns were expressed in relation to the pharmaceutical promotion prevailing in areas of subsidized medicines (e.g. public provision of free insulins, where there is active promotion by pharmaceutical companies, including through engaging active patients and support by doctors). Often there is a complete lack of information and access to medicines for cancer and rare diseases, which contributes to medicine smuggling in bags, referred also as 'sumochnyi business', that is when the doctors themselves import small portions of these medicines from neighboring countries and sell them to their patients on higher prices.

Positive impacts associated to the pharmaceutical promotion were also noted. Factors such as perceived contribution to more competition and, thus, potential for reduced prices, as well as extended information sources for doctors and the public were noted as important. Indeed, information presented during the promotion activities will currently represent the only major source of information for doctors. This strengthens the position and credibility of pharmaceutical companies among medical professionals, because the government currently is unable to provide extensive information on existing and new medicines.

[9] Source: 'Access to medical care and out-of-pocket expenditures in Kyrgyzstan: integrated household survey, 2001-2010'.
[10] Evidence-based medicine unit of MoH pf the Kyrgyz Republic http://arch.24.kg/community/164481-v-kyrgyzstane-vnov-podnyali-problemu.html

Following a number of heavily debated events related to medicine procurements and activist campaigns against unethical marketing, the National Program of Pharmaceuticals for 2014-2020 was adopted, which provides for the revised legislation in the field of medicines. The unethical marketing practices, growing prices for medicines, growing consumption of medicines both due to medical prescriptions and as a result of self-medication have been among challenges to address under the Program. Implementation of the Program provides for a series of measures to strengthen the regulation of pharmaceutical promotion.

6. Legislation on pharmaceutical promotion

In the international practice, there are 5 principles of regulation of the pharmaceutical promotion (L. Ziganshina and J. Lekschin., 2004):

1. National laws and regulations;
2. Law enforcement through application of practice codes and other standards;
3. Monitoring of the pharmaceutical promotion to ensure compliance with laws and regulations;
4. Adequate sanctions to prevent violations;
5. Evaluation of the regulation effectiveness.

As pointed by L. Ziganshina and J. Lekschin (2004), even countries with adequate resources for regulatory oversight vary enormously in the extent to which they carry out any or all of these steps. There may be a law and a national code, but little enforcement and no sanctions for violations are in place. In other cases, a functioning regulatory system is in place but no evaluation of regulatory effectiveness, for example, in ensuring that promotional claims support rational medicine use and public health goals. Ideally regular or ongoing evaluations should lead to changes in standards and the process of regulation, and these changes should, in turn, be evaluated. In practice, this rarely happens.

This section describes the purpose and roles of several relevant laws and regulatory documents in the regulation of pharmaceutical advertisement and promotion. This is followed by the definition of the pharmaceutical advertisement and promotion in these documents, the regulatory approaches, and the review of particular regulatory issues.

6.1 Key legislation and regulatory acts for pharmaceutical advertisement and promotion

The main legislative and regulatory documents in the field of pharmaceutical advertisement and promotion are as follows:

- The ‘Advertisement Act’;

- The ‘Administrative Responsibility Code Act’ dated October 17, 2008 N 214 (hereinafter referred to as the ‘Administrative Code’);

- The Technical Regulations of ‘Safety of medicines’ by the Government of the Kyrgyz Republic dated 06.04.11, № 137 (hereinafter referred to as the ‘Technical Regulations’).

The Advertisement Act

The objective of the Advertisement Act *is to protect against unfair competition in advertisement, prevention of inappropriate advertisement that can* be misleading or cause *harm in relation to health, property of individuals or legal entities, environment, or harm the honor, dignity or business reputation of these individuals, as well as detrimental to the public interest, principles of humanity and morality.*

The Technical Regulations

In addition to other requirements for safety of medicines, *the Technical Regulations set requirements for advertisement and promotion of medicines, medical devices, dietary supplements, homeopathic medicines,* which are used in the traditional and alternative medicine. In contrast to the Advertisement Act, provisions in the Technical Regulations are more detailed.

The Administrative Code

The Administrative Code is part of the legislation of administrative responsibility[11]. All new laws providing for administrative responsibility shall be included in the Administrative Code. Among others, the legislation on administrative responsibility aims to protect the individuals, the protection of rights and freedoms, health, sanitary and epidemiological protection of people, protection of the state powers and governance, public order, rights of legal entities and their associations from the administrative offenses and the timely and objective consideration of administrative violations and their prevention.

In the general provisions part, the Administrative Code operates such concepts as intentional and reckless violation/offence, presumption of innocence, responsibility for administrative offense, administrative sanction/penalty. The special part of the Administrative Code describes specific issues, including advertisement in general and advertisement of medicines and medical devices.

6.2 General issues in legislation of the pharmaceutical advertisement and promotion

The Advertisement Act covers all promotional activities, including the pharmaceutical advertisement. The advertisement is defined as the 'information (advertisement information) disseminated in any form and about physical or legal entities, goods, ideas and undertakings, which is intended for unspecified persons, designed to build and maintain interest in these individuals and legal entities, goods, ideas and

[11] Legislation of administrative responsibility comprised of the Constitution, law, President resolutions, Government resolutions, common principles, norms of international law and the current Administrative Code

undertakings, as well as to promote the sale of goods, ideas and undertakings'. This is followed by definitions of **direct** and **indirect advertising**. The definition of direct advertising for regulatory purposes operate with what is called the content of pharmaceutical advertising. The definition of indirect advertising covers activities that correspond to promotion of medicines and medical devices. These are sponsorship, organization of cultural and sporting events, public events and competitions, price discounts by coupons and vouchers, use or display of goods and services, their logos, trademarks.

Requirements for the ***content of promotional materials*** in the Kyrgyz Republic are regulated by the the Technical Regulations. They should contain the following information:

- The name of the active ingredient, with the use of the international nonproprietary name (INN) or commonly understood names of approved medicine;
- trade name;
- The content of the active component at a dose necessary for reception;
- Approved by the authorized body of the indications for use;
- Dosage and procedure;
- Side effects and major adverse reactions;
- Information on the contraindications, warnings and cases where the medicine should be used with caution;
- Other components of the medicine, which are known that they can cause side reactions;
- Interaction with other medicines;
- The name and address of the manufacturer or distributor;
- A reference to the relevant scientific sources.

Apart from the reference to the contents of advertisement materials, the definition of advertisement in the Advertisement Act also covers the **communication activities of advertisers with advertisement users.** While the Advertisement Act provides definitions of advertisement, its text does not provide definition or any reference to the promotion of medicines and medical devices. However, the concept of advertisement refers a variety of advertising information such as booklets, posters, presentation slides, sponsorship activities, organization of cultural events, social events and competitions. These activities the what referred to as promotional activities, i.e. communication of the advertisers, which are mostly pharmaceutical companies, to users of advertisement, which are mostly doctors, pharmacists, healthcare facility managers, and people. These activities are also referred to as promotion of medicines in the Technical Regulations that defines it as 'a set of measures to advertise and motivate, undertaken by pharmaceutical companies to encourage prescriptions, offers of medicines, sales and / or use of medicines.

Regulation of the pharmaceutical advertisement and promotion is closely related to the national permitting system and legislation of administrative responsibility. Clause 16 paragraph 4 of the Advertisement Act and Clause 318 of the Administrative Code ban the advertisement of medicines and medical devices in the absence of permission of the Ministry of Health to produce, sell or provide medical and diagnostic services. Violation of the requirements results in administrative sanctions in the form of fine valued as five to ten calculation indices, and for officials valued ten to twenty calculation indices. The relation of the regulation of pharmaceutical advertisement to the permit system and legislation on administrative responsibility represents a major item for discussion of solutions to improve the regulation of pharmaceutical advertising and promotion.

With respect to the pharmaceutical advertisement and promotion, the **legislation stipulates to protect both the public health and the pharmaceutical business interests.** Information and promotional materials are required to be reliable, up-to-date, evidence-based, and / or have appropriate illustration of the advertising text, and apply national and / or official languages. The information and advertising materials should not compare a medicine with other medicines to enhance the advertising effect and should not undermine the reputation of manufacturers of medicines, consumer confidence in the effects of medicines.

The Technical Regulations requires that the promotion of medicines should '... take into account the ethical criteria established in this Regulation'. However, the Technical Regulations does not mention any ethical criteria in the text. **Despite the fact that the legislation provides a space for the introduction of the ethical criteria in the regulation, there is a need for further improvements in this part of the Technical Regulations.**

6.3 Individual topics in the legislation

This section covers several individual topics in the legislation related to the advertisement of prescription medicines, company representatives, and activities of pharmacists.

6.3.1 Promotion of prescription medicines

By law, **the advertisement of the prescription medicines is banned.** Such ban is consonant with the health policy objectives in Kyrgyzstan to promote the rational use of medicines, to reduce out-of-pocket expenditures, and to control the prevalence of resistance to antimicrobial medicines. In 2014, the

Ministry of Health approved a list of medicines dispensable in pharmacies based on medical prescriptions. These include antibiotics, narcotics, and other potent medicines. The legislative ban on advertising and promotion of prescription medicines refers to those lists issued by the Ministry of Health.

Clause 16 paragraph 4 of the Advertisement Act provides for the advertisement of prescription medicines and medical devices is allowed only in printed publications designed for medical and pharmaceutical professionals. The Technical Regulations also extends the platform for the advertisement of prescription medicines intended for professionals, as it allows it '... in specialized publications, through information centers, conferences, symposiums, exhibitions and other events that are not prohibited by national legislation'. **When comparing the Advertisement Act with the Technical Regulations for provisions on advertisement of prescription medicines and medical devices among healthcare professionals, the former looks more stringent than the Technical Regulations. This difference requires the harmonization of these laws.**

6.3.2 Inappropriate and unethical promotion of medicines and medical devices

In particular cases, however, the **risk of inappropriate advertisement to healthcare professionals should be considered a significant issue for regulation**. The 'inappropriate advertisement' is prohibited by Advertisement Act and is defined as '... the unfair, unreliable, unethical, apriori false or other information that breaches requirements to content, time, place and method of distribution as established by the legislation of the Kyrgyz Republic'.

The risk of inappropriate advertisement is particularly important in respect of advertising the prescription medicines to healthcare professionals. The law protects the people from any advertising of prescription medicines through banning. However, the **proper perception of the pharmaceutical advertising by healthcare professionals would involve certain skills of critical assessment of the content of presentations and other forms of advertising.** Indeed, according to some respondents, complex charts and statistical calculations in promotional materials, gaps in knowledge of language used in the presentations or of the concepts (glossary) can undermine adequate perception of advertisements by health professionals.

According to the Technical Regulations, the 'company representatives should provide pharmacists and doctors who prescribe medicines with complete and unbiased information on each of the considered medicines, similar to that provided in the approved scientific data sheets or other similar sources of information'. However, in cases ***gaps present in the knowledge of used glossary, language of***

presentations, understanding basic statistics, epidemiology, and pharmacology among the healthcare professionals, the inappropriate advertisement of medicines (e.g. of antimicrobial medicines) 'can mislead or may mislead consumers with respect to the advertised goods ... through abuse of trust of individuals or lack of experience ... '. In this case, the criteria for the definition of 'unfair advertising' in the Advertisement Act shall be met.

In cases of gaps in monitoring by the regulatory authority, the advertisement of medicines to healthcare professionals may be 'unreliable advertising', if it contains false information on the results of research, scientific terms, quotations from technical, scientific and other publications; or the statistical data presented that exaggerate their validity, refer to any recommendations, or to the approval by individuals and legal entities, including obsolete data; or use terms of superlatives, including through the use of the words 'best', 'single', 'only', 'absolute', 'unique', etc., if they cannot be documented.

Awareness and mindfulness of the concept of 'inappropriate advertisement' is important in an environment where some companies advertise and promote their products bypassing the approval of the regulator authority. They occur more in regions far from the central city, where the regulator and executive bodies' chances are limited. These facts were confirmed by respondents and observations by the research team in the selected health organizations.

The Technical Regulations provide for procedures for obtaining prior approval of the advertisement materials, filing complaints on the promoted medicines, sanctions and their enforcement, rules and conditions of information and promotional materials, requirements for advertising to healthcare specialists. These requirements apply to manufacturers, distributors, company representatives, suppliers, healthcare workers, medical and other academic institutions, professional associations, patient groups and consumers, professional and public media. The high risks of the inappropriate advertisement should be properly assessed by the executive authorities, with emphasis to their prevention.

6.3.3 Pharmaceutical company representatives

The Technical Regulations sets requirements to pharmaceutical companies in relation to the functions of their representatives, their skills and knowledge, need of their continuous education. During their visits to healthcare facilities, the company representatives shall, among other functions, collect information on adverse reactions associated to the medicines advertised, with further transmission of this information in the company's headquarters or to the manufacturer. The pharmaceutical companies shall appoint a person who, among other things, shall be responsible for training of staff involved in the promotion of products. The pharmaceutical company representatives should have appropriate medical

education background and be adequately trained. They should possess scientific data in the amount sufficient to present accurate and complete information on the promoted medicines.

The legislation does not clearly articulate responsibilities of the company representatives for their behavior and statements. According to the Technical Regulations, the managers of pharmaceutical companies shall be responsible for instructing the company representatives on ethical conduct. The managers of pharmaceutical companies are also responsible '...for the statements and activities of their representatives in the promotion of medicines in the Kyrgyz Republic'. However, the Technical Regulations do not provide any responsibilities to the company representatives.

This is found important for the context of Kyrgyzstan, as there are **gaps with legal registration of some company representatives of pharmaceutical manufacturers that represents a barrier to responding to patient complaints related to the use of promoted medicines.** In Kyrgyzstan, there are numerous pharmaceutical company representatives with various forms of work organization and legal registration. Approximately 12 manufacturers have official representations in the country. Some other companies are represented by individuals employees of offices in neighboring countries such as Kazakhstan – they work in Kyrgyzstan as travelling office workers. Another part of the individual representatives work as individual entrepreneurs, paying taxes on the basis of eased taxation (referred as patents) or on labor contracts with local distributors and wholesale pharmaceutical firms. This situation is set to bear negative implications for taxation and the possibility of prosecution in cases of violation of the advertisement legislation.

6.3.4 Ethical code of pharmacists

In addition to other relevant legislation, the activities of pharmacists are regulated by the Moral and Ethical Code of the Pharmacist, which was adopted on the 1st Congress of Pharmaceutical Workers in Kyrgyzstan. This document is a set of moral and ethical standards of pharmacist activities.

In relation to the advertisement, the Moral and Ethical Code requires that the pharmacists shall work in the interest of public health, ensure quality, safety and efficacy of medicines; keep principles of ethical competition, ethical marketing and advertising; should not replace physicians in choosing medicines or offer medicines to patients on own discretion. Entering into cooperation with the manufacturers and middlemen companies, the pharmacists shall be free from economic interest. However, **to enforce its provisions, the Moral and Ethical Code of Pharmacists relies on the existing legislation, as if the violations of ethical standards at the same time relate to provisions of the legislation of the Kyrgyz Republic, the pharmacist is responsible, in accordance with applicable law.**

Interviews as part of this study showed that there are numerous instances of collusion of pharmacists with pharmaceutical company representatives to advance sales of the supplied and promoted medicines. Many pharmacists are directly involved in the sales of medicines using prescription forms provided by pharmaceutical companies, keeping records on the number of sold medicines, and contacts of prescribing doctors, in order to subsequently transmit the data to pharmaceutical company representatives. These data then are used to assign payments to the prescribing doctors. As some respondents told, normally the prescribing doctor will receive 10-20% of the amount paid by the patient at the pharmacy for the prescribed medicine.

These facts represent violation of several laws, including antitrust and administrative responsibility legislation. To build formal evidence of these facts would require the involvement of the executive bodies with appropriate powers.

7. Public authorities in the regulation of pharmaceutical promotion

In the implementation of the existing legislation the leading role is assigned to two agencies - the State Agency of Anti-monopoly Regulation under the Government and the Ministry of Health. This section describes functions and powers of these agencies, and discusses the impact of their work on advertising and promotional activities of pharmaceutical companies.

7.1 State Agency of Anti-monopoly Regulation under the Government

The State Agency of Anti-monopoly Regulation is the main executive body responsible for implementing the legislation on advertisement and consumer protection in general, including pharmaceutical advertising. According to the Regulations on this agency (hereinafter referred to as the 'Anti-monopoly Agency'), its purpose is to protect and develop the competition, and to implement the state anti-monopoly policies. The Anti-monopoly Agency has a number of tasks appropriate for the topic of interest of the study: i) prevention of monopolistic activity and unfair competition, and ii) protection of consumers of advertisement.

The Anti-monopoly Agency's functions, among others, are as follows:

- ✓ control over compliance with legislation on advertising and consumer protection;
- ✓ decision making on the imposition, collection and enforcing of fines and economic sanctions for violation of legislation;
- ✓ response to complaints and claims of individuals and legal entities for non-compliance with the legislation on consumer rights protection and advertisement;
- ✓ examination of cases of violation of the legislation on consumer rights protection and advertising, conducting inspections on compliance;
- ✓ consultations and practical training courses on the application of the legislation on consumer protection and advertisement;
- ✓ interaction with public organizations (associations) on the protection of consumer rights and advertisement.

The Anti-monopoly Agency consists of the central office and regional offices. Its structure includes the Department of Advertisement that supervises issues of compliance with legislation. The functions are carried out using the staff in the central office and in the field.

Functions of the Anti-monopoly Agency are in fact focused on compliance with the requirement to present the permitting documents on the advertisement materials. As stated by the interviewed officials, Anti-monopoly Agency controls the **content** of advertising materials; promotional activities of pharmaceutical companies are not subject to inspections, monitoring, complaints response and other functions of the agency. The Anti-monopoly Agency only controls the availability or presence of reference to registration (marketing authorization) in the advertisement. These data are subject to verification upon forma request by the Anti-monopoly Agency to the Department of Pharmaceuticals and Medical Devices of MoH. The rest of the content of the pharmaceutical advertising (indications, adverse reactions, etc.) is subject to the Public Health Agency, i.e. Ministry of Health.

Controlling the content of pharmaceutical advertising by the Anti-monopoly Agency largely assumes that the presence of reference to the marketing authorization for the advertised medicine or medical device is a kind of guarantee that the advertiser is acting within the law. In this situation, the question arises: to what extent the reference to the registration certificate in promotional materials is sufficient to well regulate pharmaceutical advertising?

Such a narrow function of the Anti-monopoly Agency in regulating the pharmaceutical advertising would imply wider functions of the Ministry of Health. As review of the advertising materials found, the risk of inappropriate advertisement is very high. Despite the available rules of the content of advertising materials, there are materials that contain unreliable information. In addition, there are facts of spreading promotional materials amongst healthcare professionals without prior approval by the DPhMD MoH. This is particularly common in regions. To improve its awareness of the situation and better coordination with the Ministry of Health, the Anti-monopoly Agency could exercise its right to carry out surveys among buyers and sellers.

Finally, **while the Anti-monopoly Agency has actively monitored the advertising billboards, banners, leaflets in pharmacies and the like, it is unclear how this agency responds to advertisement of prescription medicines in media such as TV, radio, newspapers, and websites not designed for use by medical and pharmaceutical professionals.** Observations of the study team and the interviews found that the advertisement of prescription medicines is still practiced in the media, although with recent trend towards downgrade. This is an obvious violation of the Advertisement Act. The advertisements of prescription medicines can be observed both in domestic and in some foreign television channels. In many ways, this is facilitated by the spread of cable television, whereby the regulation of advertisement apparently has a number of legal difficulties.

The Department of Advertisement of the Anti-monopoly Agency related this situation to the lack of technical capacity, i.e. lack of professionals with expertise in the regulation of pharmaceutical advertising, and lack of communication around technical information, such as the list of prescription

medicines. Interviewed employees of the Anti-monopoly Agency do not have a list of prescription medicines and do not use the concept of prescription medicines and over-the-counter medicines. This is despite the fact that the DPhMD MoH fairly regularly publishes the lists of prescription medicines and over-the-counter medicines using both trade names and names of manufacturers.

When carrying out on-site inspections or monitoring, the Anti-monopoly Agency do not have the permission by MoH for advertisement as a subject of inspections or monitoring. The review of official documents did not find regulations providing that the inspections should be guided by the presence of permissions for advertising issued by the competent authority (the Commission under DPhMD MoH). On the other hand, the Commission under DPhMD MoH does not have any significant powers to respond to violations of advertising.

7.2 Ministry of Health

The Ministry of Health has recently established a unit responsible for policy making in the field of pharmaceuticals. The establishment of this unit aims to separate the policy formulation from regulation, assigning the former to the Ministry of Health and the latter to the DPhMD MoH.

Under coordination by the named unit of MoH and support by the MeTA project, the new Pharmaceutical Act has been drafted, whereas the medicine promotion are paid more attention than the current legislation. This has been perceived one of successes by many interviewed experts. However, **in general, the function of pharmacovigilance in the Ministry of Health needs strengthening through improved technical expertise**. This would expand the possibilities of the Ministry of Health to actively engage with regulation of pharmaceutical advertising.

The Ministry of Health fulfills the following functions of interest for this study:

- Policy formulation of the pharmaceutical supply;
- Development of clinical guidelines and protocols
- Selection of essential medicines;
- Public procurement of medicines and medical devices;

7.2.1 Clinical guidelines / clinical protocols

At the moment, the development of clinical guidelines and protocols is implemented using the platform of the Department of Evidence-based Medicine of the Ministry of Health, with significant role given to

professional medical associations. Many associations already have rich experience in drafting guidelines and protocols. However, their coordinating role is not supported by sufficient power. The working groups are established by the MoH orders and include experts from different fields. The drafting of the guidelines and protocols is not funded by the MoH budget. For certain conditions/ diseases, the guidelines and protocols are funded with support by international organizations (e.g. Tuberculosis, HIV, viral hepatitis, childhood diseases).

To date, the implementation of the clinical guidelines and protocols has remained a challenge, exacerbated by the lack of resources for regular monitoring and evaluation of the implementation. The lack of monitoring results in physicians to divert from treatment standards as established by the guidelines and protocols, which contributes to more influence by the pharmaceutical marketing. Many interviewed doctors believed the guidelines and protocols are not always applicable, do not provide for individual characteristics of patients. In such events, to meet requirements of the Mandatory Health Insurance Fund monitoring, many doctors would choose not to adhere with the standards while keeping the medical records compliant with the standards.

Prescriptions deviating from standards was named as one of the reasons for not prescribing recipes using the prescription forms. According to many doctors interviewed, this reduces responsibility in case of inspections by MOH or MHIF. Interviewed managers pointed that one of the challenges is the frequent facts of inappropriate prescriptions of unjustified numbers of medicines. Despite the internal controls through the Quality Committee, which function in every healthcare organization, the violations of medicine prescriptions rules and compliance with clinical guidelines and protocols have continued. The managers state that this is largely driven by the information received from pharmaceutical companies.

Within 2008 – 2014, 41 clinical guidelines and 118 protocols have been approved for common diseases (obstetrics, cardiology, tuberculosis, HIV etc.). Most of the standards have been designed for primary healthcare. During focus group discussions, many doctors suggested that very little has been developed for in-patient conditions/diseases, which results in bottlenecks in prescriptions compliant with the standards; this is exacerbated by the often poor efficacy of medicines purchased by healthcare organizations.

7.2.2 Selection of the essential medicines

Medicines in the list of essential medicines have advantages over other medicines in terms of preferential taxation and priority in public procurements at central level by the Ministry of Health and health organizations at all levels. In addition, the currently available programs of guaranteed coverage with medicines and care (the Additional Package, Medicine provision under the State Guarantee

Program) are designed with preference of essential medicines (80% of medicines are from the essential medicines list). These conditions predispose to lobbies around the selection of medicines for inclusion into the List of Essential Medicines.

To date, the selection procedure of essential medicines involves the survey of clinicians throughout the country. Interviews revealed examples of pharmaceutical companies having closely worked with physicians to influence their responses to the survey, with a view to include certain medicines in the List of Essential Medicines. In addition, the pharmaceutical companies have cooperated with the managers/heads of healthcare organizations towards submitting formal requests to include certain medicines in the List. For example, the Ministry of Health central office has received a number of letters from various health organizations to include a particular medicine in the List, with the same justifications of those requests and the same texts of the letters. The investigation of that fact found that a pharmaceutical company had distributed a text of the letter to the healthcare organizations so that they on their behalf sent requests to MoH to include the medicine in the List.

The existence of such practices was confirmed by managers/heads of healthcare organizations. The interviewed respondents also noted that the pharmaceutical companies have attempted to exert influence on the individual members of the commission for selecting essential medicines (members of the Pharmaceutical Committee).

The interviewed experts suggested that the unregulated and sometimes corrupt lobbying practices in relation to the List of Essential Medicines are primarily facilitated by unclear procedures for selection of essential medicines, unclear inclusion / exclusion criteria of medicines, unclear procedures of preparation and updating the lists with account for the healthcare priorities, pharmacovigilance data, cost-effectiveness data, evidence-based medicine, and others.

7.2.3 Department of Pharmaceuticals and Medical Devices of the Ministry of Health

At the moment, the role of the DPhMD MoH in the regulation of pharmaceutical advertisement and promotion is implemented through several functions:

1) Review and agreement of the content of promotional materials for medicines;

2) Coordination of promotional actions and materials with healthcare organizations (conferences, presentations, training, etc.);

3) Monitoring of advertising and promotional activities;

4) Development of legal documents;

The first two functions, that is review of content of advertisement materials and coordination of promotional materials and actions, are fulfilled by the Commission for Review of Promotional Materials under the DPhMD MoH that was established by the MoH order. The Commission meets regularly, following the accumulation of applications from advertisers. Its composition varies depending on the needs and consists of representatives from various departments and offices of DPhMD MoH. The Commission reviews the following:

1. Content of advertising materials (leaflets, brochures etc.);
2. Content of promotional materials (presentations to healthcare professionals, videos and printed materials for advertising in the media, etc.)

The decisions of the Commission for Review of Promotional Materials are of purely consulting nature. The review of promotional materials use provisions of the Chapter 12[12] and Chapter 13[13] of the Technical Regulations as the review criteria. If the promotional material are compliant with the requirements of the Technical Regulations, the DPhMD stamp is placed on the sample of the promotional materials. This copy is kept by the advertiser (pharmaceutical companies) and can be presented to the State Agency of Anti-monopoly Regulation, if needed.

The study team **identified gaps in conveying information about the decisions of the Commission for Review of Promotional Materials to users of advertisement.** These are gaps in communication between the DPhMD and the State Agency of Anti-monopoly Regulation and service providers, as well as between the advertisers (pharmaceutical companies) and end-users.

Firstly, **the Commission's decisionы of the review of the promotion materials are not reported to the State Agency of Anti-monopoly Regulation on systematic basis.** Consequently, during inspections or monitoring visits to pharmacies and healthcare organizations, the employees of the State Agency of Anti-monopoly Regulation may not be aware of whether a particular advertisement material has been approved by the Commission. This information becomes available either from the advertiser when they provide a copy of the approved materials or upon a request to the DPhMD. The lack of feedback and gaps in communication between the two agencies result in such cases when a pharmaceutical company, having approved advertisement materials, is still fined by the State Agency of Anti-monopoly Regulation for illegal advertising campaign.

Secondly, **the review status of advertising materials by the Commission does not becomes available to the service providers and end users**. Many interviewed doctors and pharmacists stressed the inability to

[12] Глава 12 Техрегламента “Требования безопасности при рекламе лекарственных средств”
[13] Глава 13 Техрегламента “Требования к продвижению лекарственных средств”

recognize the review status of individual promotional materials presented to them by the pharmaceutical companies. The advertising materials distributed to the service providers and the public do not have any signs or codes pointing to their review status and approval by the Commission. As noted above, the stamp of the Commission is placed on one copy, which is then kept by the pharmaceutical companies, while the printed copies do not have these stamps or codes. When reviewing the advertisement materials presented by the interviewed doctors, the research team could not determine which of the promotional materials had been approved by the Commission.

On the ground, these deficiencies in the accounting of the approved promotional materials often lead to controversies between the service providers and the DPhMD MoH. When inspecting the healthcare professionals and pharmacists for involvement in unethical marketing practices, there have been instances when the DPhMD MoH employees took the advertising materials received by physicians and pharmacists during **formally approved presentations of medicines**. Doctors and pharmacists were not able to recognize the approved materials and distinguish them from materials that have not been reviewed or had been rejected by the Commission. Subsequently, the DPhMD made inspection acts to which the healthcare organizations had to respond through penalties to individual physicians, in the form of deprivation from salary bonuses, reprimand etc. As noted by a facility manager,*'…if a pharmaceutical company was given a permission to advertise, then it will clearly use its promotion materials in the form of booklets and brochures, pens and calendars with the company logo attached etc. Why can doctors not openly use the information materials and stationery that we need?'.*

The **capacity of the Information Unit of the DPhMD MoH as a leading unit in regulation of the pharmaceutical advertisement needs to be constantly strengthened**. With the current emphasis on the government regulation, the number of the DPHMD employees (4 people) involved in the monitoring of advertising campaigns is insufficient for adequate coverage of places and the means by which the pharmaceutical promotion is conducted. According to DPhMD MoH, in 2013, 626 advertisement materials were submitted by advertisers for approval, of which the Commission agreed with 421 materials and rejected 205 materials. To illustrate, in the US, the Department of Marketing, Advertising and Communications of the Food and Medicine Administration (FDADDMAC) has 40 employees. By law, the Department cannot require pre-approval of advertisements, but companies need to provide their ads when they start advertising campaigns. In 2005, the DDMAC assessed 53,000 promotional materials.

8. Interaction of pharmaceutical companies with service providers

8.1 Forms of marketing interactions with healthcare professionals

The study to assess the implementation of the National Pharmaceutical Program, it was noted that 90% of surveyed physicians met with representatives of the pharmaceutical companies in the previous year, with about half noting that the frequency of contacts was at least once per month. Interviews with facility managers and healthcare practitioners in this study confirm the facts of the interaction of physicians and the pharmaceutical industry. Observations and interviews in this study identified the following forms of marketing used by pharmaceutical companies when interacting with doctors:

1. Regular presentations of medicines to medical weekly meetings in healthcare organizations (once per week for 10-15 minutes). In all visited healthcare organizations, the presentations of medicines take place on weekly basis during medical meetings, by pharmaceutical companies upon agreement with DPhMD MoH and management of the organizations. Attendance of these medical meetings is mandatory for all doctors. In each healthcare organization, there is a person in charge of arranging such presentations (mostly deputy head in charge of clinical work), who interacts with the company representatives and agree on the terms and order of presentations.

It is worth noting that all healthcare organizations in Bishkek and Chui region allowed the presentations based on agreement with DPhMD and facility management. However, the interviewed heads of rayon healthcare organizations in Osh and Issyk-Kul oblasts noted that they were not aware of the requirement of written approvals of presentations by the DPHMD MOH. The presentations in these organizations are carried out only by oral agreement with the facility management.

Some healthcare organizations used registers for scheduling the presentations by pharmaceutical companies. Interviewed facility managers emphasized that the medical meeting allowed the presentation of only one medicine. Presentations at medical meetings are typically conducted by company representatives, sometimes by invited local lecturers from academia (professors, associate professors). Facility managers and doctors stressed that the information provided by the lecturers was more convincing and useful, because they provide data on the general principles of diagnosis and treatment of diseases in addition to the presentation of individual medicines.

2. Organization of conferences on significant issues of healthcare and diseases (normally on quarterly basis), with use of key opinion leaders. These conferences are mostly organized by the pharmaceutical companies outside healthcare institutions, in special conference halls or prestigious hotels in Bishkek and regional centers, often with trips for several days to prestigious hotels in the recreation areas on the

shores of Issyk-Kul Lake. These conferences cover all costs for invited doctors. The pharmaceutical companies involve prominent experts in the health system as lecturers.

As part of these conferences, the so-called satellite symposia take place. It is a common practice that the program notes that the symposium is held with support of a pharmaceutical company, and then the most lectures and presentations focus on medicines of that company. There is also a plenary program that is mandatory and completely independent from the influence of any manufacturers, despite the fact that all the conference is paid by the pharmaceutical company.

The majority of interviewed pharmaceutical companies reported the lecturers are paid for delivery. Representative of one pharmaceutical company, referring to the IFPM code and UK Antibribery Code, reported that their parent company recently banned payments to lecturers. Therefore, this company has abdicated holding such conferences and is planning to deliver information to doctors on medicines using on-line tools, such as webinars, Skype and other resources online communications.

3. Sponsorship of participation of clinicians and facility managers in conferences and seminars abroad. The companies sign a declaration with the clinicians and facility managers that the sponsoring the trip imposes no obligation to promote the company's medicines.

It is worth noting that the sponsorship covers mainly in-patient clinicians. None of the interviewed facility managers and doctors of primary healthcare organizations gave examples of pharmaceutical company sponsoring such events for them, while nearly all in-patient institutions confirmed such sponsorship, including employees of the regional level hospitals.

4. Campaigns for general public, including 'disease focused' campaigns. Such campaigns are often held in conjunction with events and actions undertaken by the Ministry of Health with the participation of the medical community (non-governmental organizations and professional medical associations). For example, the day of Fight Hypertension, Healthy Heart, Fight Diabetes and others. These campaigns are accompanied by active dissemination of informational materials and brochures on medicines to the general public.

5. Building relationships with doctors through personal contacts. It is the most common type of marketing activity of the company representatives. While previously the company representatives went directly to doctors' offices, recently the company representatives wait in queues along with other patients and enter the doctor's office as a 'patient'. As noted by the interviewed doctors, the representatives do not take time longer than the patient appointment (20-25 minutes). During those visits, the representatives tell the doctor about the advertised medicines and leave promotional materials.

Nearly all interviewed facility managers reported they prohibit personal contacts of company representatives with doctors. However, they cannot constantly follow them. At the moment, due to increased control by the DPhMD MoH that prohibits personal contacts of company representatives during medical appointments, these meetings are often held outside the healthcare organizations. The company representatives have recently pursued a tactic of gathering the meetings in cafes and restaurants outside of working hours. The facility managers stated that they clearly cannot influence this kind of contacts. *None of the managers gave examples of any administrative measures in cases of identified personal contacts.*

Over a half of company representatives visited healthcare organizations on monthly basis. Most often they visited doctors in Bishkek, and less frequently they visited doctors in Osh, Chui, Issyk-Kul oblasts.

The interviewed doctors named the following incentives provided by company representatives: provision of demonstration materials for the patients, sponsorship of participation in conferences, congresses, symposia, gifts in the form of uniforms and stationery, providing cash bonuses, provision of free samples of medicines. In addition, one-third of physicians pointed they attend the company representatives to address emerging issues related to the use of medicines.

It should be noted that almost all of the above forms of incentives applied to nearly all physicians attended by company representatives, except for accrued bonuses. Bonuses paid to doctors in all regions were mentioned only in relation to several pharmaceutical companies. At least four companies were named to practice bonuses. These companies have recently been operating in Kyrgyzstan and do not have official representations in the Kyrgyz Republic. The research team attempted to meet with these companies, but these companies did not want to be interviewed.

6. Provide free samples of medicines. Many doctors have a positive attitude to free medicine samples and many healthcare organizations have a practice of doctors receiving free samples of medicine to dispense them to patients. As noted by some interviewed doctors, the free samples of medicines are often given to patients who cannot afford buying those medicines. Most physicians welcome the practice of receiving free samples of medicines. During focus-group discussions, doctors reported they an example of the distribution of free samples of two types of medicines last year. One of the medicines was for treatment of bronchial asthma, which is not a first-line medicine according to the approved clinical guidelines. Doctors noted its high effectiveness which they observed on the example of improved conditions of their patients. As found by the study team, the pharmaceutical companies do not inform the regulator authorities about the distribution of these medicines, such as the Ministry of Health and the DPhMD. The company representatives personally hand over the medicines to doctors for the purpose of prescriptions, without appropriate labeling that the medicine is free.

'... The pharmaceutical companies provide doctors with free samples. But when you ask doctors, they deny it. Companies usually do not inform us about to whom they distribute the medicines. We have not had experience that we officially received the free samples to the institution and distributed free to all'. (Extract from interview with a facility manager).

According to paragraph 261 of the Technical Regulations, the free samples shall be provided to persons authorized to prescribe medicines, in limited quantities, once a year, only after a written request of the recipient, with signature and date indicated on the request. Each sample shall be labeled as a free sample of medicines, and cannot be used for resale or other personal objectives.

7. Information on medicines and their rational use. This study, as well as other studies around rational prescriptions (HPAX, 2009), indicate that the information on medicines presented by pharmaceutical companies remains one of the most common sources of information about medicines to doctors. The interviews with doctors found that the main source of information on medicines were the booklets and seminar materials from pharmaceutical companies, medical web sites, package inserts, Formulary, and tips from colleagues.

Interviewed doctors in Bishkek and Osh region reported they preferred using information provided by the pharmaceutical companies, Internet resources, and package inserts. For doctors in Chui and Issyk-Kul oblasts the main sources were materials provided by the pharmaceutical companies, with other sources used only in a few cases.

The interviewed doctors reported that, when due to workload it is not possible to devote a few hours a week to reading articles about medicines, the company representatives with medical education can deliver the same information in a more concentrated and accessible form. Review of the reasons why most physicians prefer information from pharmaceutical companies found that there are no other available sources.

Doctors who were found to prefer the information provided by the pharmaceutical companies explained that this information was more reliable and trustful. Other reasons were ' do not have time to read other literature', 'no time to search for information', 'there is no other source', and 'no one else will provide such information'.

Extract from the focus group discussions with doctors:

'*We trust the data that pharmaceutical companies present to us. If their products were of bad quality, they would probably be not registered here in Kyrgyzstan. Apart from the pharmaceutical companies,*

nobody *gives us the updated information on medicines. We cannot afford searching in the Internet and do not know how to search it'.*

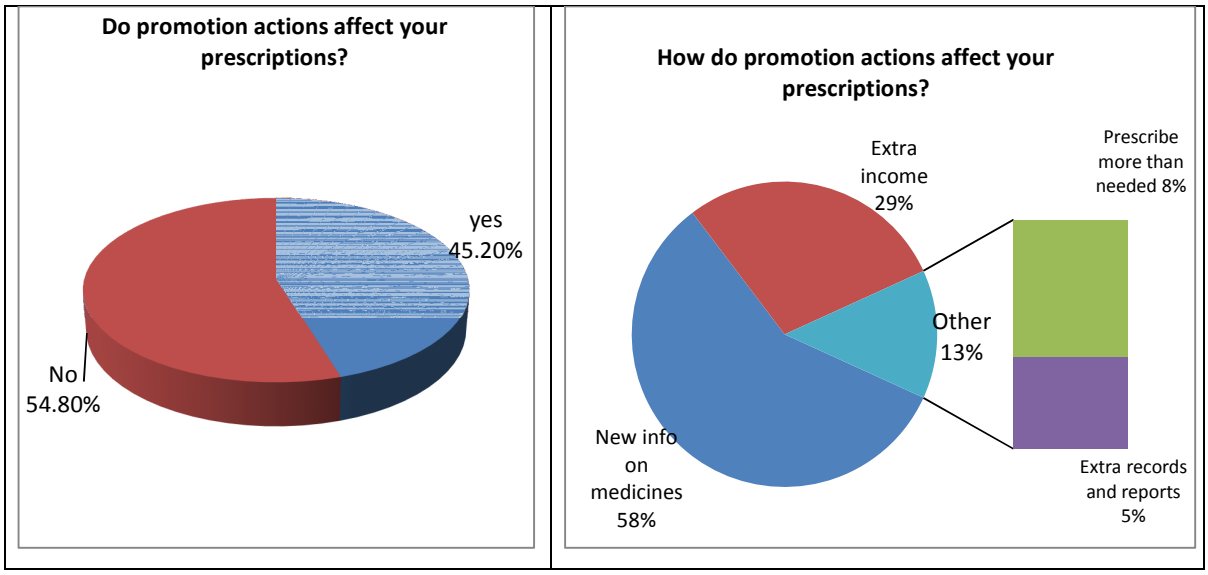
'Information provided by the pharmaceutical companies is more updated, covers the latest developments. During the CME courses, which we take in the Kyrgyz State Medical Institute of Continuous Medical Education, we mainly cover essentials of diagnostics, and treatment issues are provided in the old-fashioned manner. Information on medicines is often outdated. The pharmaceutical companies provide more necessary information both on medicines and diagnostics. They provide lectures that are delivered by professors and associate professors invited by the pharmaceutical companies'.

Extract from an interview with a Deputy Director of FMC:

'I am the Chairman of the Committee for Quality and I regularly run audit of medical records of patients. Seeing solely the cards, I can judge what company made a presentation this week and what medicine was presented. Following the presentation, all doctors start prescribing exactly the medicine that had been presented, even with no [clinical] indication'.

8. Clinicians and facility managers. One of the questions in this study was whether the advertisement materials and promotion actions of medicines affect the doctor's work with patients. The interviews with doctors found that over a half of the doctors did not see any effects of promotional activities on their routine work. In focus groups, the doctors noted the provision of information about medicines was a good practice as the advertised medicines were more effective compared with medicines recommended under clinical guidelines and protocols. Among those physicians who recognize the impact of advertising on their routine activities, 58% reported the advertising of medicines was a source of information about new medicines, 29% reported that promotion activities represented a possibility to earn additional money, and 14% of doctors confirmed that they prescribed medicines more than necessary and make records and reports for the pharmaceutical companies (Fig. 3).

Fig. 1. Effects of promotion on medical prescriptions Fig. 2. Consequences of promotion actions



9. Material incentives to prescribing doctors. As noted above, there are doctors in healthcare organizations who practice prescriptions using templates with logos provided by manufacturers or distributors. The prescription forms that are part of an established system with account of sales through pharmacies and bonus payments in the form of gifts or monetary compensation. It is worth noting that the focus group discussions none of doctors denied the fact of personal contacts with company representatives and receipt of bonuses for the prescriptions.

The interviews of doctors found that some companies provide doctors with prescription forms for them to use for prescribing the company medicines. Although these data do not claim to representativeness, it is worth noting that 7.6% of the interviewed doctors confirmed they used prescription forms from the companies, 48.4% reported having only official prescription forms, and 27.4% reported use of both the official prescription forms and forms provided by companies.

The interviewed facility managers confirmed that in their organizations there is a practice of prescriptions on letterheads of pharmaceutical companies. Almost all managers said they forbid doctors to interact with pharmaceutical companies and to receive any payments for prescriptions on company forms. Despite these efforts, many doctors continue cooperating with companies and receive payments. Management is unable to track down all appointments with doctors and company representatives. Managers themselves periodically inspect the workplaces to identify prescription forms from companies. There were facts when doctors were found with prescription forms of companies, which were then withdrawn with formal warnings given to doctors. Managers mentioned no examples of any more stringent measures for these violations. Only in visited healthcare organization, the manager reported that 2 doctors were deprived from 1 month bonuses as a penalty for violations of the rules.

During the focus group discussions with doctors, when the question of why they receive and agree to receive the company bonuses, one of the family doctors reported: *'This for us is a source of additional income, as our salaries are low. Our children need education, clothes, food. I do not have additional sources of income. Some doctors, who do not want to receive bonuses from the sale of medicines, can make money from referring to particular private labs and receive bonuses once a month. This is a necessary measure as long as salaries stay the same low. Many are engaged in this, but do not admit, they fear to admit'.*

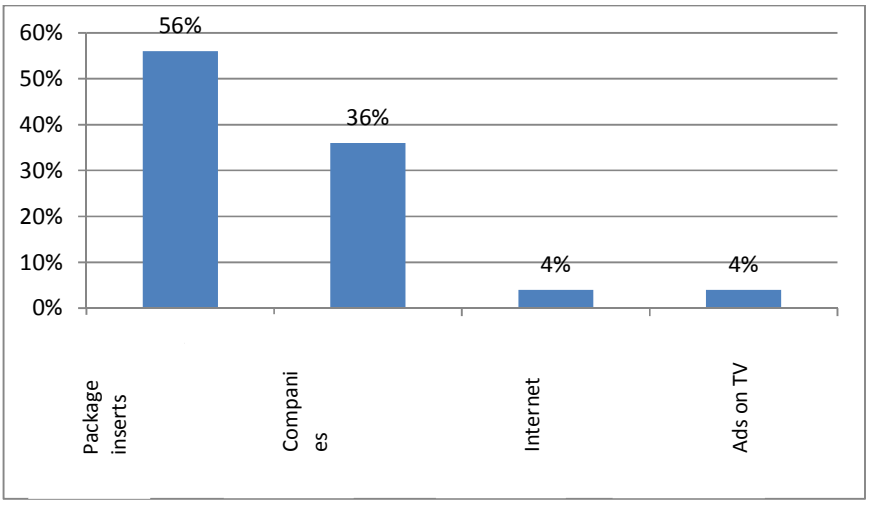
Finally, **the interviewed facility managers, referring to low salaries of doctors, noted these payments were a kind of additional motivation of doctors work and, sometimes, of improved functions of the healthcare organizations.** The deputy head of one healthcare organization stated: '... the pharmaceutical companies support us with printing paper that is always short. We do not have extra funds from the government budget to buy the printing paper. They also distribute calendars, and we need them for work too as these also cost money. We, doctors, are in such situation that we take anything free of charge. For example, when we were running the vaccination program against measles, it was difficult to attract parents to bring their children for vaccination. We asked the pharmaceutical companies to help us, and they bought a variety of stationaries for children such as books, coloring books, crayons, balls, paint, and albums. And we gave them to the children who came to the vaccination. It worked like a 'word of mouth' - that is if you go for vaccination, the children shall be handed out free gifts. This action stimulated many parents bring their children for vaccination. This turned out way out for us too'.

The study observations, interviews, and focus group discussions with doctors found that the practice of company bonuses has been spread mainly among doctors at the primary healthcare organizations, while at the hospital level there was more common practice of financing study tours to overseas.

8.2 Promotion of medicines among pharmacists and generic substitution practices

The interviews with pharmacists found out their main sources of information about medicines (Fig. 10). For 56% of interviewed pharmacists, the main source of information was package inserts, and for 36% - information provided by the pharmaceutical companies.

Fig. 3. Sources of information on medicines for pharmacists



82% of interviewed pharmacists reported that the company representatives carried out at least 1 visit to their pharmacy points per month. When visiting the pharmacy points, the company representatives provided information materials, gave invitations to seminars, provided gifts (robes, stationery), and visited to provide bonuses.

Nearly all interviewed pharmacists stressed that they sold to patients only medicines recommended by their doctors. That contrasted to the responses of PHC visitors, of which 66.3% responded their pharmacists offer replacing the medicines with others. Moreover, 34.7% of PHC visitors reported the replaced medicines were more expensive than the prescribed, while 65.3% reported replaced medicines were cheaper than the prescribed.

Extract from an interview with a PHC visitor: '... *The doctor prescribed medications that I needed to buy in a certain pharmacy point near the hospital. He noted all his prescriptions in a piece of paper. The pharmacist gave me all the prescribed medications, but the amount was too high for me and I could not buy everything at once. I asked to replace some of the prescribed medications with something cheaper. The pharmacist said that she cannot replace, the prescribed ones were the best. She explained to me the more expensive is the medication, the better it is'.*

Under this study, all visitors of PHC were asked to answer questions on the sources of information about medicines. The family doctors, pharmacists, package-inserts, and friends and neighbors were main information sources. However, when questioned about the content and meaning of those information sources, half of respondents confessed that **doctors often do not provide information on the effects of medicines, and for many the information from media was more significant and meaningful**.

9. Review of the advertising materials and promotional activities

The WHO Ethical criteria for medicine promotion offer the types of information that, as a minimum standard, should be contained in the advertising through magazines (WHO, 1988). Their objective is to ensure the essential information for decision making on prescriptions of medicines is available. The International Non-proprietary Name of the medicine (INN) is a must information to be included. The INN help doctors and pharmacists to determine the medicines class and, thus, ensure the erroneous prescription of several medicines of the same class.

The WHO requirements and the national legislation have been used for the review of advertisement materials and presentations in the selected healthcare organizations.

9.1 Findings of review of promotional materials and presentations in the selected healthcare organizations

The following criteria for the review of promotional materials and presentations were chosen:

- whether INN or trade names of medicines were used in the promotion pomaterials;
- whether data on efficacy and safety of medicines as confirmed with relevant referrals to results of trials (RCTs and meta-analyzes) are available;
- whether the indications for use are supported by the evidence-based medicine or recommended under the clinical guidelines / protocols. The search of information was held in international databases on the use of medicines, namely in PubMed, NICE, SIGN, BNF, Medscape;
- whether information on adverse reactions, precautions, contraindications and warnings, food and medicine interactions is available.

The review of the advertisement materials covered all materials availed by the interviewed healthcare professionals in the visited healthcare organizations - brochures, leaflets, presentation materials. The reviewed brochures and leaflets did not have any marks of an agreement or permission of authorities that the information was compliant with the legislation requirements of the Kyrgyz Republic.

Eventually, 52 leaflets and brochures were reviewed. Of all reviewed advertising leaflets and brochures, the most common were advertising of antimicrobial agents - 45%, vitamins - 16%, neuroprotection agents - 10%, non-steroidal anti-inflammatories - 8%, and probiotics - 5%, herbal and dietary

supplements - 16%. Only 6% of the reviewed materials listed INN in addition to the trade names of the advertised medicines. The other 94% of materials used only trade names of medicines.

30% of the reviewed materials provided the indications for use with no evidence supported by international clinical guidelines and databases. None of the advertisement materials had references to the scientific literature and links to familiarize with the original sources, with 9.6% advertising materials providing references to opinions of prominent experts.

15.3% of the reviewed materials did not provide formulations and administration routes of the advertised medicines. 35% of the materials did not provide information on possible adverse reactions, 23% did not specify precautions, 50% did not indicate the food and medicine interactions.

According to the Technical Regulations, the promotional information on medicines should contain information of the manufacturer and its legal address in the Kyrgyz Republic. Only 57.6% reviewed materials had information of the manufacturer, and only 14 advertising materials (26.9%) had the legal address in the Kyrgyz Republic.

In 78, 8% of the reviewed materials, the advertised medicines were positioned as unique for treatment of particular diseases, and used misleading terms, such as ‘shaping the future of the joints’, ‘the apparent protection against invisible enemies’, ‘fortress of your nerves’, ‘for those who choose the most useful’, ‘saves lives’, ‘robust measure to fight infections’, ‘a single strike victory’, and others. 27% of the promotional materials used the words ‘new’, ‘powerful’, ‘unique’.

The reviewed promotional materials was loaded with information that exaggerates benefits and downplays the negative effects of the promoted medicines. To illustrate, one-third of the studied advertising materials (32.7%) were overwhelmed by the graphic information on the efficacy and safety of the medicines.

As required by the Technical Regulations, any promotional media should contain the registration (market authorization) number, date of registration, and the expiry date of registration in the Kyrgyz Republic. Only a quarter of the studied advertising material contained this information (25%).

9.2 Findings of the review of presentations in selected healthcare organizations

As provided by the Technical Regulations, the healthcare professionals can provide services to pharmaceutical accompanies as consultants, based on labour contract in writing signed by the two parties, to hold presentations during information and educational events organized by the pharmaceutical companies (seminars, conferences, round tables, and so on). These activities may be conducted in healthcare organizations, medical educational institutions, conference centers, etc.

As part of this study, the research team visited two scientific conferences with the Conference Program and List of participants agreed with MoH, and 4 medical conferences in the selected healthcare organizations, which are held on a regular basis upon consultation with facility managers and DPhMD MoH.

These conferences were observed to find out financial support by pharmaceutical companies, the availability of the approved Conference Programs, gifts and 'free lunches and receptions'. In addition, the content of the presentations at these events were reviewed using the following criteria:

- Names of medicines (under the trade or under INN);
- Indications and contraindications;
- Notes on possible adverse reactions, precautions and medicine interactions;
- Sources of information (references);
- Focus on a particular disease and comparison with other medicines and outdated medicines.

The two visited conferences were held in Bishkek on the basis of the MoH Order, with the approved Program and List of participants. Both events were carried out with the financial support of the pharmaceutical company. All the participants were given handouts, including information and promotional materials and stationery (calendars, notepads and pens with the logo of the a pharmaceutical company). For some of the participants (following the list), the medical clothing (gowns and surgical suites) and medical instruments (stethoscopes and blood pressure) were prepared. At these events, the free coffee-breaks were organized for the participants. Some of the participants were given invitations to the dinner (following the list). Presentations at these conferences were conducted by healthcare professionals working in healthcare organizations and medical educational institutions.

The four visited presentations of the pharmaceutical companies, which were held during medical meetings with the selected healthcare organizations, were held at the beginning of meetings. Their length was 15 - 30 minutes. These presentations were made by company representatives and were devoted only to a particular medicine. At the end of the presentation, the doctors were given information leaflets.

In summary, 8 medicines were presented in the conferences and medical meetings visited by the research team. The observation of the presentations at these events found that the presentation texts used only trade names of medicines, and INN were not pointed in none of the cases and not mentioned by the lecturers.

Of 8 medicines presented in the visited events, for 4 medicines the indications for medical use were not justified. For them, the presented indications for medical use in certain diseases were not approved by clinical guidelines and protocols. These presentations referred to data on the efficacy and safety of

medicines from the randomized clinical trials and meta-analysis, but pointed to only surrogate points (change in behavior, memory, etc.), while the endpoint results were absent (improved quality of life, survival rates, etc.). The references to the scientific literature were rather outdated (over 7-15 years).

The presentations of 6 medicines did not point the possible adverse reactions and contraindications. None of the presentations contained safety information, food and medicine interactions. The presentations of 4 medicines compared them with other peers and outdated medicines.

10. Practice of industry self-regulation

Over the past decades, the pharmaceutical promotion has changed significantly. Laws and regulations are also significantly changed over this period, but in many countries the research pharmaceutical industry has made a number of mechanisms of self-regulation of information and educational and promotional activities. These activities not only cover, but sometimes go beyond the requirements of the legislation. For example, many pharmaceutical companies have significantly expanded the functions of standards compliance, so that communicationы with healthcare professionals and patients follow relevant order. *The purpose of self-regulation is to provide healthcare providers with threshold information needed for informed decision-making in the treatment of patients.*

The self-regulation delegates the regulation to the pharmaceutical or advertising companies, or to organizations with represented stakeholders. These associations adopt their own codes of standards. They are authorized to issue permits for advertising and have established responding to complaints.

This section provides an overview of the content and standards of self-regulation, mechanisms of enforcement of the principles of self-regulation with a focus on the role of pharmaceutical associations. These issues are discussed with a focus on 1) regulation of the content of advertising materials and 2) interaction of pharmaceutical companies with service providers and other parties (promotional activities). These discussions are supplemented with data from the interviews and review of the national legislation in Kyrgyzstan.

10.1 Industry Codes of Practice and Conduct

Below are the **main provisions and requirements of international and national codes**[14] as summarized by Jeffrey F. et al. (2014):

- Fundamental requirements for ethical and professional behavior, putting patients first, compliance with regulations etc.
- Standards for interactions between companies and healthcare professionals
- Sponsorship or support for healthcare professionals' attendance at meetings and continuing medical education
- Acceptability of venues and locations for meetings
- Fees for service for engagement of healthcare professionals
- Providing promotional aids, samples etc.

[14] In certain countries, these provisions can be in legislation and not in codes

- Hospitality limitations
- Standards for promotional information – accuracy, balance, substantiation etc.
- Essential information for advertisements (e.g. prescribing information)
- Prohibition of promotion of unlicensed products and uses
- Electronic communications
- Interactions with patient organizations
- Clinical research and transparency
- Company procedures and responsibilities, including approval and certification arrangements, staff training
- Complaints handling and enforcement arrangements

Additional coverage of these areas is provided in all European and some other national codes:

- Expanded requirements of the above areas
- Prohibition of direct to consumer advertising for prescription-only medicines
- Specific requirements for representatives
- Requirements for public listings of support and/or engagement of healthcare professionals and/or patient groups
- Donations and grants
- Non-interventional studies
- Aspects of market research activities
- Providing educational and support services e.g. therapy review and nurse services

Additional coverage of these areas occurs in one or more individual codes:

- Expanded requirements of the above areas
- Standards for non-promotional medical information to healthcare professionals and/or patients
- Non-promotional information for patients and the public; disease awareness activities
- Interactions with the media, press releases etc.
- Specific requirements for websites, social media etc.

In addition to the main requirements, such as the *basic information required tha*t must be included in advertising (prescription information, etc.), the code provisions cover the other two main areas:

- Promotional claims about products (for example, the requirements for information on the effectiveness and tolerability) and
- Interaction with healthcare professionals (e.g., the requirements for sponsorship and benefits)[15].

10.1.1. Self-regulation of advertising claims on products

All the codes maintain the assertion that the **advertising claims must be of high quality and meet the prescription information, which shall be approved by regulators.**

Generally speaking, the IFPMA Code of Practice and national codes require that product claims relating to prescription medicines be **accurate, balanced, and up to date. Material must be truthful and not misleading, including misleading by omission and half-truths. For example, claims must strike a balance of the available evidence and cannot provide only 'half the picture'.** If challenged, a company is obliged to provide data to substantiate its claims.

The IFPMA Code includes the concept that material must be "sufficiently complete to enable the recipient to form his or her own opinion of the therapeutic value" of the product. Materials should also "encourage appropriate use" of medicines by presenting information objectively and without exaggeration. These and other requirements also apply to the comparative nature of advertising claims.

Direct to consumer advertising (DTCA) is prohibited in most countries that regulate prescription medicines, although the United States and New Zealand are major exceptions. Although the IFPMA Code of Practice sets global standards, it remains silent on DTCA because the code cannot preempt national laws and regulations. At a national level, codes of practice reflect the local legal situation and usually detail the rules and standards for non-promotional communications concerning prescription medicines that companies can make direct to the public or patients. PhRMA in the US has promulgated a set of voluntary standards regarding DTCA, including appropriate risk communication and timing of certain advertising (PhRMA, 2009).

A universal and important prohibition relates to advertising a medicine, or a new use of an existing medicine, before regulatory marketing authorization is received. Legislation and codes share similar

[15] PhRMA, Руководствопопрямойрекламерецептурныхлекарств (PhRMA, Guiding Principles on Direct to Consumer Advertising about Prescription Medicines). 2009.
http://phrma.org/sites/default/files/pdf/phrmaguidingprinciplesdec08final.pdf

wording on this point; however, distinguishing promotional and non-promotional information remains complicated. Moreover, at least one appeal court in the United States has recognized the right of companies to provide truthful and non-misleading information about unapproved uses of approved medicines (US v. Carolina, 2012 in Jeffrey F. et al. (2014). Other bodies may react differently to the case, as happened in the UK, where in one case the sponsorship material about the medicine, the code resolution was stricter than regulatory decisions (Pharmaceutical Journal Insert - 20 January 2007. 2007).

10.1.2. Self-regulation of the interactionы with healthcare professionals

In many countries, the relationship between pharmaceutical companies and healthcare professionals are regulated by both the legislation and self-regulatory codes. In addition, **national legislation on bribery and corruption, such as the US Foreign Corrupt Practices Act in the US and UK Bribery Act in the UK may have potential application if certain inappropriate interactions with healthcare professionals in other countries were suspected.** Ensuring compliance with the Code of IFPMA and its affiliated national codes helps ensure compatibility with the relevant sections of the anti-corruption legislation. In fact, **the requirements of national codes prohibit improper personal benefits offered to healthcare workers, and can often go beyond the requirements of anti-corruption legislation (**Jeffrey F. et al., 2014)**.**

One of the questions around the national codes - can companies support visits of healthcare professional to conferences. **Codes in many countries find acceptable to sponsor the attending to conferences, coverage of costs for travel, accommodation and meals. However, these codes also make a few precautions.** In particular, the main objective of the conference or meeting should have a scientific and professional nature, any food and drinks should be connected to this end. Venue must conform to the scientific or educational purpose, and the international travel should be justified by the international nature of the conference, or other considerations of logistics or security.

Sponsoring the participation of healthcare professionals in the meetings, however, remains a matter of debate. Some countries (e.g., the United States and Norway) do not permit the direct sponsorship of participation in scientific meetings (with the exception of medical students in the United States), while others (such as France) require review of agreements by an independent body. Some countries have introduced other measures such as co-payment charges. International companies can also apply the sponsorship policies of healthcare professionals who are outside the scope of external regulations (Brennan D., 2011). This underlines the sensitivity of the perception of the companies financing visits to international educational meetings. However, **the prohibition of sponsorship can lead to prevention of**

healthcare workers from access to sufficient funding and the opportunity to learn and interact with world leaders in their chosen field, if no developed alternative funding mechanisms or digital educational services are in place. This is especially important for healthcare workers from developing countries, where alternative sources of funding may be unavailable.

Providing branded low cost advertising media (pens, notebooks, tongue holders, antiseptic wipes, etc.) has long been a tradition of pharmaceutical and other advertising. International rules still allow the low-cost advertising materials, if they are relevant to the practice of healthcare professionals. However, there is a trend to ban advertising means in general. Recently, the US (PhRMA, 2009) and the United Kingdom[16] have prohibited the provision of branded promotional tools. At least one global company has ceased to provide such products all over the world (Brennan D., 2011). **The reason for the prohibition of advertising through branded low cost means is not that these promotional tools represent gifts that affect the healthcare workers or purchasing decisions, but that these items do not contribute to a new relationship built on mutual professional respect.** In addition, industry leaders seek to establish relationships with healthcare professionals to exchange educational information and not to provide items that can be seen as gifts.

In most parts of the world it is allowed to provide samples of medicinal products to healthcare professionals and such samples can improve patient care. However, the situation varies considerably between countries according to local factors. In some countries, the samples are not allowed at all, while a number of industry codes limit their numbers, frequency and period after launch during which they may be provided[17,18].

10.2 WHO Ethical Criteria

The WHO Ethical Criteria have been developed as the result of a consensus between healthcare professionals, regulatory agencies, consumers and the pharmaceutical industry, and thus represent a broader view on the good marketing practices, rather than codes developed by the pharmaceutical industry and its professional associations.

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[16]Clause18. Association of the British Pharmaceutical Industry: ABPI code of practice for the pharmaceutical industry 2011. London: ABPI; 2011.

[17]Статья 17. Association of the British Pharmaceutical Industry: ABPI code of practice for the pharmaceutical industry 2014. London: ABPI; 2014.

[18] European Federation of Pharmaceutical Industries and Associations: EFPIA Code of Practice on the promotion of prescription-only medicines to, (EfpiaCodeondisclosureoftransfersofvaluefrompharmaceuticalcompaniestohealthcareprofessionalsandhealthcareorganizations). [http://www.efpia.eu/]

The main objective of Ethical criteria is to support and encourage the improvement of the quality of healthcare through the rational use of medicines. The Ethical criteria have no legal status, but are designed for use as general principles that should be adapted by national governments in the development of legislation, as well as a standard for the creation of voluntary codes. They also provide international ethical standards with which to compare the regulation of promotion activities and procedures.

10.3 Internal operational standards (SOPs) of pharmaceutical companies

The compliance departments of many companies develop internal standard operational procedures (SOPs), which guide employees in the advertising and communications activities, and employees are trained to these internal requirements on regular basis.

According to the heads of several companies, **in Kyrgyzstan, the SOPs within several pharmaceutical companies impose strict requirements for the content of advertising and communications with healthcare professionals, sometimes surpassing the national legislation.** In addition, several companies are parties to the UK Antibribery Code which transcends to operations in overseas and also impose stringent requirements on pharmaceutical advertising and communications.

To review the relationships between legislation and self-regulatory codes, the Table 1 provides the content and regulations of certain areas of pharmaceutical promotion.

Table 1. Control systems for prescription medicine advertising (adapted from J. Francer и др., 2014).

	IFPMA affiliated industry codes of practice[19]	**Independent local industry codes of practice**	**Professional bodies' codes of practice**	**Regulatory authority activities**	**Legal actions**	**Company standards**
Description	National codes incorporate and expand on the IFPMA Code	National codes, developed independently	International or national medical, pharmacy, and nursing bodies have professional behavior codes. Employers may also have codes of conduct	Regulatory authority interprets and applies law and regulations. Can include pre-approval and post-hoc enforcement	Possible breaches of laws and regulation pursued through court action	Companies have codes of conduct and internal compliance and audit organizations to enforce them
Applicability	International pharmaceutical member companies wherever they operate. Includes local companies in a few countries	Local companies belonging to sponsoring trade associations or agreed to comply with the Code	Applied nationally by the professional body	All sectors within the scope of the legislation. Applied nationally	All sectors within the scope of the legislation. Applied nationally	All countries where the company does business
Comment	National codes often detailed & subject to national laws&regulations. Some states embrace code based actions more readily than others	Variable in scope and application	Professional codes may include requirements on interactions with commercial organizations	Some regulatory authorities are more active than others	Actions may be brought by government bodies or competitor companies. Some countries resort to legal action more readily than others	Internal standards are usually broader in scope than external codes and legislation

[19] Codes affiliated to IFPMA, local company codes, and codes of professional associations all are industry codes

10.4 Mechanisms of self-regulation implementation in practice

This section reviews the conditions and mechanisms of enforcing the industry codes. Among the specific questions, the practice of sanctions and complaint response are outlined.

Various pharmaceutical industry codes have been around for decades. However, since 2002, there has been a shift in the industry with respect to advertising and communications, which requires a regular review of international codes, updating and expansion of all affiliated national codes (J. Francer и др., 2014).

The key question in the system of self-regulation is whether the violations under voluntary codes represent violations under the legislation? From this comes one of the problems that often the codes are not technically laws.

Companies' standards and operating procedures relating to communications often go beyond the requirements imposed by laws and regulations. However, no compliance documentation can cover all possible situations. **Corporate culture is a key aspect of successful self-regulation. When employees understand that communication activities are for the benefit and welfare of patients, the rules governing these activities are put in context.** Compliance departments can thus play a critical role in educating and shaping a company's values and culture (J. Francer и др., 2014).

National codes of practice are generally managed by local industry associations. They are implemented in the developed countries and many developing countries. Furthermore, the **industry codes of practice are tiered.** National codes must be consistent with the international IFPMA Code of Practice. In Europe, national associations that are members of the European Federation of Pharmaceutical Industries and Associations (EFPIA) must ensure that their codes are consistent with EFPIA Codes[20]. National association codes, in turn, require member companies to follow complementary baseline standards and procedures. Because each level sets minimum requirements, national codes are generally more detailed than international codes. Company standards are even more detailed, often reflecting corporate cultures as well as incorporating international and national codes.

[20] Source: European Federation of Pharmaceutical Industries and Associations: EFPIA Code of Practice on the promotion of prescription-only medicines to, and interactions with, healthcare professionals'; 'EFPIA Code of Practice on relationships between the pharmaceutical industry and patient organizations'; Efpia Code on disclosure of transfers of value from pharmaceutical companies to healthcare professionals and healthcare organizations. http://www.efpia.eu/,

Member companies of the IFPMA and its agents shall comply with the provisions of the IFPMA Code and national codes of member associations, if there are any. Nevertheless, the global network of affiliated IFPMA codes of practice that apply to international pharmaceutical companies do not necessarily apply to the other participants and healthcare organizations, such as doctors, local producers, suppliers of generic medicines and medical devices. Pharmaceutical companies are covered by the same codes and standards of practice only if they are members of the national association affiliated to IFPMA, and thereby agree to comply with the relevant rules (as is the case with international pharmaceutical companies).

At the national level, the requirements of codes and laws usually widely overlap. The advertising statement or activity that is illegal according the law will also violate the local code of practice. In many countries, the code requirements are normally broader than in the legislation and / or provide more information about what is acceptable and what is not.

In some countries, particularly in the United States, the **competition laws or antitrust policies may limit the ability of companies and national associations to dictate the joint rules of marketing** (J. Francer et al., 2014). Accordingly, in such markets, the marketing codes may not include formal procedures for dispute resolution through the courts. Instead, the rules on advertising of pharmaceutical products are widely covered in the laws and regulatory documents of the United States.

10.4.1. Sanctions in the codes of practice

Codes of practice operate on a fundamentally different basis to legislation. They do not rely merely on the threat of punitive fines for their effectiveness. Rather, the **sanctions represent a collective commitment of member companies to behave in a responsible manner**. Deviations from the code requirements are dealt with in a variety of ways that must always be consistent with local laws, including anti-trust and anti-competition provisions (J. Francer et al., 2014). Below is the table summarizing the types of sanctions as outlined in the international literature.

Table 2. Summary of code of practice sanctions and provisions

(adopted from J. Francer et al., 2014)

Sanction or requirement	**Comments**
Requirement to cease non-compliant activity	A universal requirement. Often associated with a written undertaking not to repeat the non-compliant or similar activities, claims etc. The

Sanction or requirement	Comments
	company may be required to recover and destroy offending material. Repetition may result in severe penalties.
Publication of the outcome or public reprimand	Undertaken if local legal considerations allow. May consist of detailed reports or more concise summaries. Offending company is usually identified. In some countries, serious offences may be publicised in the medical press.
Monetary penalties	The amount is usually graded according to the number and/or seriousness of the offences, generally from thousands to hundreds of thousands of dollars.
Additional pre-screening requirements	In countries where pre-screening is optional.
Requirement for a formal audit of company procedures	This is particularly useful if a company's procedures or training may be the cause of a serious or repeated shortcoming.
Suspension or expulsion from membership of the local trade association	Expulsion may mean that the code regulatory system will not apply to the company and external legal and regulatory controls will therefore take effect routinely. Suspension may mean that the company is still required to comply with the national association code.
Issue a corrective communication	This provision is particularly useful if recipients of the material may have been misled. It will be at the expense of the company.

In many countries, fines or administrative fees may be levied and there are requirements to cease the activity that caused the breach. However, the **effectiveness of sanctions is mainly based on actions that support the voluntary commitment to good behavior, such as public disclosure of the details of the breach, where local laws permit.** In circumstances where companies appear not to have demonstrated the necessary commitment to code compliance, or where the breach is particularly serious, they may be suspended or expelled from membership of the local association that administers the code. The self-regulation system therefore relies on a genuine commitment by companies to take the rules seriously. For international companies, this commitment is reflected in their internal control systems governing promotional activities (J. Francer et al., 2014).

10.4.2 Corporate mechanisms for the enforcement of codes of self-regulation

Companies also set out approval procedures for their communications. Prior to use, materials and activities are approved by designated individuals who are responsible for checking acceptability against all applicable laws, regulations, and codes. In Europe and several other countries, there must be a final approval of advertising by a designated doctor or pharmacist. In France and Belgium, the "responsible pharmacist" has a legally constituted responsibility for such approvals. In addition to ensuring compliance with regulations and codes, the physicians and pharmacists who certify promotional activities also have a responsibility as healthcare professionals to patient welfare and are of course subject to the codes of conduct of their professional bodies. *Compliance with rules and ethics are not always synonymous; an activity can be legal but not ethical, or considered ethical by many but not legal. What is ethical is open to interpretation and the concept of appointing doctors and pharmacists to approve company outputs reflects a responsibility to patient welfare that goes beyond compliance with written standards* (J. Francer et al., 2014).

The pharmaceutical companies can themselves initiate greater transparency between companies and healthcare professionals, as it was in the United States and Europe. Often this is followed by the adoption of these rules by other companies or industry codes of practice. The example of acceptance of these rules by the entire industry can be seen in the recent adoption of the European Disclosure Code relating to the transmission of values from the company to healthcare workers[21] (J. Francer et al., 2014).

10.4.3 Complaint procedures

Codes and company procedures at all levels, with rare exceptions include complaint procedures in which information may be provided to companies or associations to address the alleged violations of the code. Since the legislation and regulatory mechanisms are reflected in the codes of practice, some countries have expressed concerns that the full transparency of codes can lead to a 'double jeopardy' (i.e. a second case concerning the same matter) which in turn might inhibit the utility of the code adjudication process.

There are several options of involving codes of business practices in the event of complaints or other concerns as summarized J. Francer et al. (2014):

[21] European Federation of Pharmaceutical Industries and Associations: EFPIA Code of Practice on the promotion of prescription-only medicines, and interaction swith, health care professionals'); 'EFPIA CodeofPracticeonrelationshipsbetweenthepharmaceuticalindustryandpatientorganizations'; EfpiaCodeondisclosureoftransfersofvaluefrompharmaceuticalcompaniestohealthcareprofessionalsandhealthcareorganizations [http://www.efpia.eu/]

1) Appeal to the company can be a quickest way to resolve issues of concern. People with complaints or questions may contact the local affiliates and / or international offices. The compliance departments of companies usually welcome the communication of problems and many companies run 'hot lines', often on their websites. If the company disagrees with the applicant, the applicant may resort to other methods as detailed below. *Complaints are usually kept confidential and will not be disclosed to public*, which means that other companies cannot derive lessons of the case. Nevertheless, th*e simple issues communicated to the company can find a quick and efficient resolution*. The dialogue between the companies can also be the first line, when one company is concerned about the activities of the other, and can lead to quick resolution of issues. *While such dialogue is encouraged, caution is needed with regard to compliance with competition laws.*

2) Contact national code of practice body. Almost all codes of practice have an associated complaints resolution process. This usually involves detailed consideration of the complaint by a panel of people independent of the company concerned, sometimes including practicing healthcare professionals and/or regulatory body representatives. In some cases, the process is overseen by lawyers. Code adjudication processes will lead to a judgment on the matter by reference to the relevant code, which will often be broader in scope than the law and regulations. The process for adjudicating complaints varies between countries and the details are often dependent on local legal and regulatory constraints. Where possible under local legislation, full transparency is encouraged by making public details of the complaint and the company concerned. Local codes often cover a wider spectrum of activities than regulations and the IFPMA Code.

3) Contact IFPMA. When national codes cannot be applied; for example, when the company involved is not subject to the local code or no IFPMA-affiliated association exists in the country concerned, and providing the company involved is a direct member of the IFPMA or belongs to an IFPMA-affiliated association in at least one country, the complaint can be processed by the IFPMA. It will be adjudicated under the IFPMA code operating procedure (Article 13), assuming of course that the subject of the complaint is within the scope of the code. The IFPMA Code does not, however, operate as a higher authority that could overturn a decision made under a national code of practice process.

Although the pharmaceutical industry advocates using the available self regulation options there may be occasions when this is not an option for example if a local company is not covered by the various codes (see Developing Economies section below). Also laws and regulations commonly duplicate requirements of the national self-regulatory codes. **The involvement of legal and government regulatory processes therefore remains an option if resolution through Code of Practice procedures is not possible or appropriate.**

Besides the issue of the general welfare of the country, it is important to take into account the interplay of the public authorities and legislation with the self-regulation in regulating the pharmaceutical promotion. The ratio between public regulation and self-regulation is illustrated by the organization of self-regulation and enforcement in the United Kingdom. The British Medicines Act covers the regulation of pharmaceutical advertising, and the Minister of Health is responsible for its implementation. This responsibility is delegated to the Association of British Pharmaceutical Industry (ABPI). This delegating is justified by the high competence of the Association and its desire to conduct this work, as well as the ability of the Department of Health to save costs and working hours.

10.5 Implementation and enforcement of self-regulation in the Kyrgyz Republic through involving associations

One option to introduce the self-regulation of pharmaceutical promotion is to involve associations. This was expressed by several interviewed experts in Kyrgyzstan and is consistent with the practice in many countries, where, in addition to public regulation of the pharmaceutical promotion, the business participation is well developed.

The effective operation of codes requires significant investments of financial and human resources by the national associations. This usually involves the use of staff for administration and implementation of the code. An important pre-condition of successful code implementation through associations is the presence of internal policies and adherence on the part of member companies.

When considering the above-mentioned conditions, it became clear that the **landscape of associations in the pharmaceutical sector in Kyrgyzstan are rather fragmented, the associations themselves are inactive and do not take functions of regulating the promotion or medicines.**

A small number of associations in the 6 million nation with a tiny market and a huge number of pharmaceutical companies looks an acceptable phenomenon. Overall, it prevents excessive fragmentation and thus creates the conditions for greater solidarity of the business around the regulation of advertising and interactions with government agencies. On the other hand, however, there is fragmentation of the principles on which the associations are formed and joined. Some associations do nothing at all. The agenda in all associations does not include the issues of regulation (or self-regulation) of the promotion of medicines.

In Kyrgyzstan, the most active is the Association of Pharmaceutical Business - Pharmaceutical Union of Kyrgyzstan. This association brings together the businesses and represent their interests in the

interactions with public institutions. Members list some regional associations, wholesalers engaged in imports of medicines. This association is vibrant and has been attempted to attract as much as possible of the pharmaceutical business. However, some pharmaceutical manufacturers refrain from entering into this association. When interviewed, they explained this by that the Charter of the Association 'Pharmaceutical Union of Kyrgyzstan' has provisions pursuing the purely commercial objectives, which is contrary to internal policies of foreign manufacturers not engaged in commercial activities. As an alternative, there is Foreign Pharmaceutical Manufacturers Association in Kyrgyzstan, which consists of several representative offices of foreign pharmaceutical companies. These offices do not conduct commercial activity and are designed to deal with representation and marketing activities. The extent of activity of this association is currently limited due to internal factors. The participation of these associations in self-regulation of the pharmaceutical advertising is not part of their routine agenda.

In addition to these two associations, there are associations of pharmacists, consumer protection, patient rights protection, as well as planned association of local producers. In the study, these associations were not covered in detail.

According to the respondents, a **prerequisite for contracts of the Ministry of Health with the associations to enforce the codes of practice is that the member companies have internal codes and SOPs and strict adherence to these policies.** Some companies with legal status in Kyrgyzstan have practiced SOPs and internal corporate codes of practice and ethics. In addition, many representations of major pharmaceutical companies with multinational operations are parties and are subject to the relevant significant documents such as the UK Anti bribery Code, Code of IFPMA and others. According to the representatives of these companies[22], on certain issues of pharmaceutical promotion these codes take more stringent positions than the legislation of Kyrgyzstan.

In contracts of MoH with such associations, however, there is a risk that they will not include pharmaceutical companies and individual representatives who have no such internal codes, or which are not parties to the international codes. There is also a risk of limited membership in such associations of representation offices without legal status. This can leave them out of the self-regulation through the associations.

Thus, the **main barriers to effectively implement the self-regulation through the pharmaceutical associations are i) the unevenly available and adhered internal codes of business practices, ii) differences in the legal registration of company representatives, and iii) fragmented range of activities and promoted interests of existing associations**.

[22]SOP contents are documents for internal use, so this study did not review them.

In neighboring countries, there is a certain extent of success of engaging businesses in the regulation of promotion of medicines. For example, in Kazakhstan, a few years ago the Code of marketing practices was developed and implemented[23]. There is an association of pharmaceutical companies, bringing together over 130 representation offices of foreign manufacturers. The Chairman of the Association is a member of the council under the Ministry of Health of Kazakhstan. While no assessments of the impact of the organization on cooperation between the Government of Kazakhstan with the pharmaceutical business has been conducted, this experience can be considered as the optimal way to establish mechanisms of interaction between government and the pharmaceutical business, with involvement of a non-governmental organization.

11. Discussion

The study reviewed the situation in pharmaceutical advertising and promotion in Kyrgyzstan and discussed the current state and ways to improve the regulation to protect public health. It highlights the key pathways of the influence of pharmaceutical advertising on public health and health system. As in many other countries, in Kyrgyzstan, the most important influence of pharmaceutical advertising was found to be the increased out-of-pocket spending to pharmaceuticals and gaps in rational prescription of medicines.

Among the numerous **factors** contributing to the listed influences of the pharmaceutical promotion to public health, the following were identified and outlined: violation of the rules of prescribing and dispensing of prescription medicines, poor generic medicine substitution practices, gaps in institutional capacity and communications between the State Agency of Antimonopoly Regulation and offices of Ministry of Health, peculiarities of the legislation on advertisement and administrative codes, and corruption in the pharmaceutical market.

In Kyrgyzstan, the violation of legislation on pharmaceutical advertising has become a regular phenomenon. Corruption, patronage on the part of senior officials, weak sanctions and their enforcement can be attributed to the **mechanisms** by which violations of the law occur. It was found that the behavior of service providers (doctors, pharmacists) in cooperating with pharmaceutical companies is largely determined by such **motives** as the need to increase earnings and receive information about medicines, in which the pharmaceutical companies have succeeded more than government agencies. This is confirmed in interviews with the respondents who noted the positive

[23] http://health-kz.com/arhiv/2_yanvar_2013/kodeks_marketingovoj_praktiki_associacii_mezhdunarodnyh_farmacevticheskih_proizvoditelej_v_respublike_kazahstan/

impact of interaction with the pharmaceutical companies, namely the support for daily expenses for office supplies, additional income in the form of bonuses, participation in conferences and seminars with a high level of service, etc.

The described strategies and enabling environment for unethical marketing are important to discuss solutions to improve the regulation of pharmaceutical advertising, the fight against corruption, and the rule of law in general. Special attention should be paid to the facts of bonus payments to doctors, the evidence of collusion between companies and service providers, the risks of improper advertising in the environment of limited skills of doctors and pharmacists to critically evaluate promotional materials or limited knowledge of the language of medicine presentations. Additional complexity is brought by sophisticated schemes of registration of medical representatives.

The effectiveness of radical measures, such as banning the aggressive forms of advertising and promotion, according to some interviewed prominent experts, can not be complete. There have been examples of alcohol and tobacco supply bans in different countries, when the total ban did not bring the intended outcomes. Instead, there have been opinions on the need in consistent and incremental approach to regulation. Potentially strong point of the government regulation of pharmaceutical advertising is viewed in the review of the advertising materials. In Kyrgyzstan, there is such experience in the regulation of advertising of alcohol and tobacco, where the Ministry of Health and other sectors have demonstrated effectiveness.

The study showed that the regulatory system with participation of businesses and associations that for a long time have existed and well-functioned in many other countries, in fact, have already transcended the jurisdiction of Kyrgyzstan with rather real implications for the pharmaceutical promotion. This occurs through the compliance of the transnational pharmaceutical companies with their internal corporate procedures (Standard operational procedures) and the codes of associations to which the companies are members (such as the IFPMA Code, UK Antibribery Code and others).

On the other hand, however, there is a low awareness of the majority of government officials of the existence of self-regulatory practices and their real impact on the situation in Kyrgyzstan. Such trends as the reduction in recent years of the pharmaceutical advertising on TV and the reduction of certain methods of advertising, such as personal meetings with doctors in their offices, many informants among the officials interpreted as a result of the tightened legislation or the position of the regulator agency. However, the study demonstrated that these changes could also be a result of the impact of internal standards and codes of self-regulation in the pharmaceutical companies.

One of the interesting questions that have arisen in the interviews with an expert was to which extent it is feasible and necessary to involve the associations to regulation of the pharmaceutical promotion by linking the membership in the associations to the permission system. It is well known that obedience

and respect of rules of the associations is the prerequisite for membership. The Ministry of Health could bind' the permits (market authorization, licensing, etc.) to the membership of pharmaceutical companies and individual businessmen in those associations which effectively enforce the provisions of the Codes that protect the public health interests and ethical standards of pharmaceutical advertising.

The Ministry of Health could choose from various options of mechanisms for enforcing ethical standards, ranging from the preferences of issuing permitting documents to members of relevant associations or purchases of certain medicines to the membership in these associations as a prerequisite for obtaining permits. In some Euroasian Economic Union states, such as Kazakhstan, there are already examples of the implementation of ethical standards, which can also be of a model for consideration.

Whichever option of enforcement of ethical standards are selected by the Ministry of Health, the involvement of associations and membership of companies in the associations could bring the following:

1) harmonized contents of codes of individual companies with the provisions of the codes of these associations;
2) delegation of responsibilities of the Ministry of Health to associations to regulate pharmaceutical promotion.

Any serious discussion of such enforcement mechanisms of the industry codes needs the improved capacity of the existing associations and activation of these associations.

12. Recommendations

1) Sanctions for unethical marketing need to be tighten and their enforcement needs improvement.

- Size (amount) of sanctions and space for misinterpretation of their application as provided by the Administrative Code are perceived by many interviewed experts as ineffective and contributing to further spread of corruption in the pharmaceutical sector.

2) Carry out evaluation studies around the content of advertisements on foreign national television broadcasted in Kyrgyzstan for compliance with the national law and regulation.

3) Consider the need in more stringent regulation of legal registration of the missions and representatives of pharmaceutical manufacturers and local distributors.

- In case of registration of company representatives as individual entrepreneurs or travelling employees of foreign companies, the issue of responsibility of these representatives in cases of unethical marketing remains a big question.

4) Align the provisions on pharmaceutical advertisement of prescription medicines in the Advertisement Act and the Technical Regulations.

- Regarding the advertisement of prescription medicines, the Advertisement Act provides for such advertisement only in printed publications intended for healthcare professionals, while the Technical Regulations allow such advertisement not only in the printed publications but also through presentations, seminars, Internet and other information media. This difference leads to various interpretations of the law by the executive bodies and, as a result, the facts of unreasonable charges of pharmaceutical companies for violation of the Legislation.

5) Improve communications between the MoH and the State Agency for Antimonopoly Regulation under the Government in matters of review of promotion materials

- In carrying out monitoring in the healthcare organizations, the State Agency staff often cannot know by the Department of Pharmaceuticals and Medical Devices MoH. The improved routine communications between the MoH and the State Agency on the review status of promotional materials, lists of prescription medicines and other issues would largely reduce the prevalence of unethical marketing. This can be facilitated by the electronic system for procurements planned by the Government.

6) The DPhMD MoH should consider further improvement of the review processes of advertising materials.

- In particular, it is recommended to find a solution to ensure the advertising materials (booklets, posters, etc.) had unique ID following the review by the DPhMD MOH. This can be codes, stamps and the like, which could be applied to replicated copies. Such a step would improve the transparency of pharmaceutical companies.

7) The MoH should consider providing official status to the industry self-regulatory codes as an instrument of regulation. The main pathway to enforce the industry self-regulation can be the involvement of associations of pharmaceutical companies.

- Without proper enforcement mechanisms, this initiative is at risk to remain toothless, similarly to the current Code of Pharmacist. At the same time, codes like the UK Antibribery Code have already had a certain effect on the conduct of some of the pharmaceutical companies in Kyrgyzstan. On the one hand, this is due to the transnational nature of the Code; on the other

hand, the involvement of these companies in the associations such as the IFPMA also imposes certain obligations on companies to the shareholders and to the direct administrative offices, often located abroad.

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