

Marketing authorization process and regulation of veterinary medicinal products in the CIS countries

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List of Abbreviations

| | |
|---------|---|
| API | Active Pharmaceutical Ingredient |
| BP | British Pharmacopoeia |
| CCP | Certificate of Pharmaceutical Product |
| CIS | Commonwealth of Independent States |
| CTD | Common Technical Document |
| CU | Customs Union |
| CVP | Commission of Veterinary Products |
| DAB | German Pharmacopoeia |
| EAEC | Eurasian Economic Community |
| EAEU | Eurasian Economic Union |
| EEA | European Economic Area |
| EEC | Eurasian Economic Commission |
| EMA | European Medicines Agency |
| EU | European Union |
| GDP | Gross Domestic Product |
| GMP | Good Manufacturing Practice |
| HAB | German Homeopathic Pharmacopoeia |
| HMP | Human Medicinal Product |
| ICH | International Council on Harmonisation |
| ISO | International Organization for Standardization |
| MAH | Marketing Authorisation Holder |
| MP | Medicinal Product |
| MRL | Maximum Residue Limit |
| NTA | Notice to Applicants |
| NTD | Normative and Technical Documentation |
| Ph. Eur | European Pharmacopoeia |
| Ph. Int | International Pharmacopoeia |
| PPP | Purchasing Power Parity |
| PSUR | Periodic Safety Update Report |
| RCVD | Department of Veterinary Medicine Quality Control |
| SCDMTE | Scientific Center of Drug and Medical Technology Expertise |
| SICVC | State Institution Committee of Veterinary Control |
| SPC | Summary of Product Characteristics |
| SSCIBSM | State Scientific and Control Institute of Biotechnology and Strains of Microorganisms |
| SVC | State Veterinary Center |
| TSE/BSE | Transmissible Spongiform Encephalopathy/ Bovine spongiform encephalopathy |
| USP | United States Pharmacopeia |
| VICH | Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products |
| VMP | Veterinary Medicinal Product |
| VPFSD | Veterinary Pharmaceutical and Feed Supervisory Department |
| WHO | World Health Organization |
| WTO | World Trade Organisation |

1. Introduction

Like humans, animals are vulnerable for a wide range of diseases. However, only about one-fortieth of the amount spent worldwide on human medicines is invested in animal medicines. This investment is used to cover animal health innovations for livestock and pets, ensuring a steady stream of new innovative products and thereby an improvement of the health condition and well-being of animals. In light of vector-borne disease being on the rise and an increasing demand for animal protein to feed a growing human population, it can be said that also the human well-being depends on the effectivity, quality and geographical availability of animal medicines [1].

Animal medicines are divided into three primary categories:

- pharmaceuticals which cover a variety of medicines such as pain medications, anesthetics, antibiotics and chemotherapy drugs
- biologics (vaccines, antibodies, etc.)
- veterinary biocidal products and antiparasitics

As the result of scientific research, today's medicines dramatically improve veterinarians' ability to prevent pet illnesses and diagnose and treat diseases. Veterinary medicinal products prevent various kinds of diseases like flea and tick infestation, Lyme disease, rabies, diabetes, feline leukemia and many others in pets. Using diagnostic tests and medical equipment specifically designed for animals are used leads to better treatments and more options for pet owners and veterinarians [1].

In addition, research shows that healthy animals are also an important factor in providing safer food. Therefore, animal medicines are a critical link in the food safety chain. Like human medicines, animal medicines undergo extensive trials and testing before getting the marketing authorization from the federal government [1].

The pharmaceutical industry for humans and animals is one of the most important components of the strategy of national and political security of any state. Moreover, it is also one of the most profitable and rapidly developing segments. Accordingly, the pharmaceutical markets of both developed and developing countries are regulated by a significant number of laws, regulations, guidelines and orders, guaranteeing the national public quality, efficiency and safety of medicinal products.

Registration is a key process in the system of finished pharmaceutical products circulation. In all countries of the world, the registration allows to allocate a medicinal product on the respective pharmaceutical market. The main target of medicines registration in any country is the provision of its population with high-quality, safe and efficacious medicines. Therefore, the registration is complex and time-consuming [2].

One of the most dynamically developing regions in the world for pharmaceutical products is the Commonwealth of Independent States (CIS). CIS was formed during the breakdown of the Soviet Union and includes most of the former Soviet Republics. The member states of CIS are Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Uzbekistan and former member Georgia, which has withdrawn its membership in 2008. Two associate member states are Turkmenistan and Ukraine, which did not ratify the CIS charter, yet. These eleven CIS countries together have a population of 280 million people which is the reason why the interest of pharmaceutical companies in expanding their business and product footprint across the CIS region

Introduction

has been constantly growing [3]. To achieve this goal, the knowledge of the respective veterinary medicinal product regulations is indispensable.

The main objective of this master thesis is therefore a comprehensive overview of the most relevant aspects, the similarities and differences of the national registration process for veterinary medicinal products in each of the CIS countries.

In the second chapter of this thesis, the underlying methodology used to elaborate the contents is introduced and explained. In chapter 3, a short introduction of the geo-political and economic background will be provided for the member states. Chapters 4 and 5 provide an overview of the most relevant livestock and companion animals in the CIS region, pointing out the potential as well as the specifics of the CIS markets. In chapter 6 the competent authorities and the most relevant regulatory aspects of the CIS countries are presented per member state. Chapter 7 focuses on the marketing authorization process per CIS-country. In chapter 8, the aspects of similarities and differences of the marketing authorization process and regulation of veterinary medicinal products in the CIS countries and the EU are discussed. Chapters 9 and 10 present a conclusion based on the work done as well as an outlook and a short summary of the contents.

2. Methodology

As mentioned in the previous chapter, the main objective of this thesis is to provide a structured overview of the marketing authorization processes of each of the CIS countries. As the CIS consists of eleven independent states with own languages, legal requirements, structures and regulations, the authorization process of each of the states is quite heterogeneous when it comes to a detailed analysis. Apart from the process itself, the information available is very heterogeneous as well. To address this complexity and transform the heterogeneous information pool into a structured overview, the methodology presented in this chapter has been designed and applied in the scope of this work (see Figure 1).

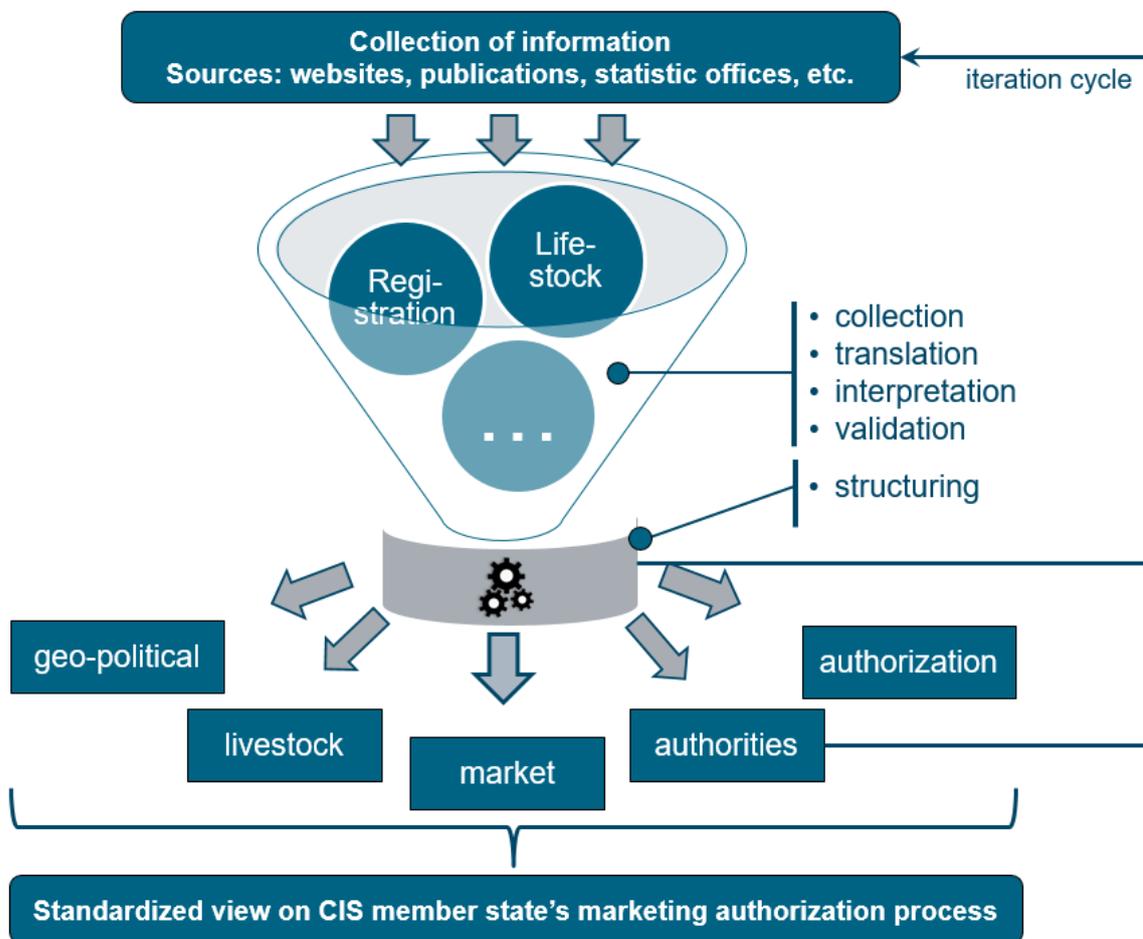


Figure 1: The methodology process

One of the most important parts of this thesis and the first step defined by the methodology is the information gathering. Due to the reasons mentioned above this part is very resource-intensive, but at the same time, important as it builds the foundation for the next steps. Due to the limited public access to information and its highly deferring formats (different languages, different structures, different sources, etc.), the process of information collection needs to be executed iteratively until a certain expected level of quality is reached. The iterations basically consist of the collection of information, the translation from the native language of the CIS member state (only in few cases the information is available in English), interpretation, validation by other references and structuring. Each reference potentially refers to further sources of information, which is basically the reason for the mentioned iterative approach.

Methodology

The process of structuring the information consists of its assignment to the following categories per CIS member state:

1. Political background and economy (geo-political)
2. Livestock and companion animals (livestock)
3. Pharmaceutical market for veterinary medicinal products (market)
4. Competent veterinary authorities and most relevant regulatory aspects (authorities)
5. Marketing authorization process (authorization)

The information assigned to category 4 “competent veterinary authorities” itself builds a source directory for information on the authorization process, which is the reason why figure 1 shows an information flow from this category back to the step of information collection.

The categories shown above build therefore the main structure of this thesis and provide a holistic view on the CIS member states with the focus on the marketing registration process, its similarities and differences.

3. The Commonwealth of Independent States: Member States, Political Background and Economy

The CIS was established in Minsk on December 8, 1991 on the basis of the agreement signed by the heads of the Russian Federation, the Belarus and the Ukraine. Later the Commonwealth included eight more member-states: Azerbaijan, Armenia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Turkmenistan and Uzbekistan. In 1993, Georgia joined. Thus, out of the 15 former Soviet republics, all but the three Baltic republics (Lithuania, Latvia and Estonia) became members of the CIS (see Figure 2). In 2008, Georgia withdrew the membership and ceased being a CIS member officially in 2009 [4].



Figure 2: Map of CIS countries [5]

In September 1993, an agreement on the creation of an Economic Union was adopted to form a common economic space and cooperation in the field of plant quarantine, veterinary medicine, the provision of sanitary and epidemiological welfare of the population, the implementation of an agreed policy in the field of standardization, metrology and certification [4].

In 1995, Belarus, Kazakhstan and Russian Federation signed an Agreement on the Customs Union (CU), later joined by Kyrgyzstan, Tajikistan and Uzbekistan. In 2000, the heads of these states formed the Eurasian Economic Community (EAEC) as an international organization, the statutory goal of which was the formation of the CU and the Eurasian Economic Space. In 2007, within the framework of the EAEC, the heads of state of Belarus, Kazakhstan and Russia signed the treaty on the creation of a single customs territory and the formation of the CU. On May 29, 2014, the heads of the states of Belarus, Kazakhstan and Russia signed the Agreement on Eurasian Economic Union (EAEU), which entered into force on January 1, 2015 [4], [6].

In accordance to the treaty on the establishment of the Economic Union (1993), the main economic goal of the CIS is the creation of a common market for goods, services, capital and labor. To achieve

this goal, a gradual and consistent formation of a free trade zone, a customs-, a payment- and, in the long term, a currency-union is considered [6].

In practice, the achievement of these goals has faced great obstacles. On the one hand, the countries were neither politically nor economically ready for integration on a new market basis. On the other hand, the CIS members have followed different development paths since the early 1990s, which complicates this economic step [7], [8].

A short overview of most relevant indications of the of the CIS countries' economic state / development is presented in Table 1 and the subsequent sections of this chapter.

| Country | Population | GDP - per capita (PPP) | Exports - partners | Imports - partners | Total area (sg km) | Capital city |
|------------|-------------|------------------------|---|--|--------------------|--------------|
| Armenia | 3,051,250 | \$8,900 | Russia 15.2%, China 11.1%, Germany 9.8%, Iraq 8.8%, Georgia 7.8%, Canada 7.6%, Bulgaria 5.3%, Iran 5.3% | Russia 29.1%, China 9.7%, Germany 6.2%, Iran 6.1%, Italy 4.6%, Turkey 4.2% | 29,743 | Yerevan |
| Azerbaijan | 9,872,765 | \$17,700 | Italy 19.7%, Germany 10.7%, France 7.5%, Israel 7%, Czech Republic 4.8%, Indonesia 4.2% (2015) | Russia 15.6%, Turkey 12.7%, US 9.2%, Germany 7.5%, Italy 6.4%, Japan 6.1%, UK 6%, China 5.6% | 86,6 | Baku |
| Belarus | 9,570,376 | \$17,500 | Russia 39.1%, UK 11.1%, Ukraine 9.5%, Netherlands 4.3%, Germany 4.1% | Russia 56.6%, China 7.9%, Germany 4.6% | 207,6 | Minsk |
| Kazakhstan | 18,360,353 | \$25,700 | China 15.1%, Russia 12.3%, France 9.3%, Germany 7.9%, Italy 6.7%, Greece 4.1% | Russia 32.9%, China 25.9%, Germany 4.2% | 2,724,9 | Astana |
| Kyrgyzstan | 5,727,553 | \$3,500 | Switzerland 26.1%, Uzbekistan 22.6%, Kazakhstan 20.8%, UAE 4.9%, Turkey 4.5%, Afghanistan 4.5%, Russia 4.2% | China 56.6%, Russia 17.2%, Kazakhstan 10% | 199,951 | Bishkek |
| Moldova | 3,510,485 | \$5,200 | Romania 23%, Italy 10.2%, Turkey 9.4%, Russia 8%, Germany 6.6%, Belarus 6.4% (2015) | Russia 22.8%, Romania 18.1%, Ukraine 11.5%, Germany 7%, Italy 4.8%, Turkey 4.4% | 33,851 | Kishinev |
| Russia | 142,355,415 | \$26,100 | Netherlands 11.9%, China 8.3%, Germany 7.4%, Italy 6.5%, Turkey 5.6%, Belarus 4.4%, Japan 4.2% | China 19.2%, Germany 11.2%, US 6.4%, Belarus 4.8%, Italy 4.6% | 17,098,242 | Moscow |
| Tajikistan | 8,330,946 | \$3,000 | Turkey 19.8%, Kazakhstan 17.6%, Switzerland 13.7%, Iran 8.7%, Afghanistan 7.5%, Russia 5.1%, China 4.9%, Italy 4.8% | China 42.3%, Russia 18%, Kazakhstan 13.1%, Iran 4.7% | 144,1 | Dushanbe |

| Country | Population | GDP - per capita (PPP) | Exports - partners | Imports - partners | Total area (sq km) | Capital city |
|--------------------|------------|------------------------|---|--|--------------------|--------------|
| Ukraine | 44,209,733 | \$8,200 | Russia 12.7%, Turkey 7.3%, China 6.3%, Egypt 5.5%, Italy 5.2%, Poland 5.2% (2015) | Russia 20%, Germany 10.4%, China 10.1%, Belarus 6.5%, Poland 6.2%, Hungary 4.2% (2015) | 603,55 | Kiev |
| Uzbekistan: | 29,473,614 | \$6,500 | Switzerland 25.9%, China 17.6%, Kazakhstan 14.2%, Turkey 9.9%, Russia 8.4%, Bangladesh 6.9% | China 20.8%, Russia 20.8%, South Korea 11.9%, Kazakhstan 10.8%, Turkey 4.6%, Germany 4.4% (2015) | 447,4 | Tashkent |

Table 1: Short overview of some economic indicators of the CIS countries [8], [9]

3.1 Armenia

Armenia is a sovereign state in the South Caucasus region of Eurasia. Armenia is an industrial and agrarian country. The priority of the economy of Armenia consists of small-scale agricultural production. Apart from this, the country has significant reserves of copper-molybdenum and polymetallic ores, bauxites, building stone, mineral waters, etc. [7], [8].

Despite the continuous economic growth during the last years, more than 30% of the population are still living below the poverty line. There are several reasons for this: Armenian's geographic isolation, the conflict with Azerbaijan, a low export base and monopolies in important business sectors.

Armenia is particularly dependent on Russia's commercial and governmental support, as most of the key Armenian infrastructure is Russian-owned and/or managed. Remittances from Armenians working in Russia are equivalent to approx. 7-8% of GDP [7], [8].

In 2015, Armenia joined the EAEU. At the same time, the country has also expressed its interest in expanding the economic ties with the EU as well. As a result, in March 2017 an EU-Armenia Comprehensive and Enhanced Partnership Agreement was initiated [7], [8].

3.2 Azerbaijan

Azerbaijan is located in the eastern part of Transcaucasia on the coast of the Caspian Sea. Azerbaijan is an industrial and agrarian country with highly developed industry and diversified agriculture. The most relevant economic sector of Azerbaijan is the oil and gas industry followed by non-ferrous metallurgy, various food (canning, wine etc.) and light industries (cotton, silk, wool and carpet-weaving). The main agricultural crops are cotton, tobacco and tea [7], [8].

Azerbaijan is leading among the CIS countries in terms of economic growth in the recent years. Between 2003 and 2008, Azerbaijan's GDP grew by 2.6 times. The economic growth continues uninterrupted since 1996. For ten years, the economy of Azerbaijan, on average, added 13.6% annually (compared with 1995, the GDP increased by 8.4 times) [7], [8].

The oil-rich Azerbaijan is a major player on the regional energy market. In parallel to the trade with Russia and the other former Soviet republics, Azerbaijan has expanded the trade relationship with Turkey and Europe and is seeking new markets for non-oil/gas exports, mainly from the agricultural sector [7], [8].

3.3 Belarus

Belarus is the largest European state without an access to the sea. After its independence in 1991, Belarus has retained closer political and economic ties to Russia than any of the other former Soviet republics [7], [8].

The economy of Belarus is built on the principles of a socially-oriented market model. The structure of the economy is characterized by the dominance of state ownership in production, energy, transport, mining, construction, agriculture and banking. Only a small share of the private sector exists. The government regulates prices for socially important groups of goods. Belarus does not have any open sources of hydrocarbons, that is why a significant part of oil and gas has to be imported.

The important economic sectors are agriculture and dairy farming. Agriculture is historically an important part of the local economy, giving more than 7% of the national GDP and providing employment for more than 9% of the population [7], [8].

Since 2012, Belarus's economy has suffered stagnation, which has led to devaluation, decreasing of productivity and income gaps between Belarus and the other CIS countries.

3.4 Kazakhstan

Kazakhstan is geographically the largest of the former Soviet republics (excluding the Russian Federation). Kazakhstan possesses substantial fossil fuel reserves and other minerals and metals (iron ore, copper ore, lead-zinc ores, uranium ore, nickel ores, bauxites and others). Kazakhstan is about to increase oil production to become one of the ten largest oil-producing countries in the world [7], [8].

The main source of the country's budget revenues is the export of oil and oil products. Kazakhstan also has a large agricultural sector featuring livestock and grain. Livestock is represented by the sheep breeding, dairy and cattle breeding, camels and horses breeding [7], [8].

Despite some positive institutional and legislative changes in the last several years, there are still factors influencing the economic development and investments negatively: corruption, bureaucracy and arbitrary law enforcement at the regional and municipal levels [7].

3.5 Kyrgyzstan

Kyrgyzstan is a landlocked, mountainous (more than three quarters of the territory of Kyrgyzstan are mountains), lower-middle income country with an economy dominated by minerals extraction and agriculture (48% of the Kyrgyz workers are engaged in agriculture and livestock). A big part of the country's population relies on remittances from citizens working abroad (predominantly in Russia and Kazakhstan). The remittances from Kyrgyz migrant workers are equivalent to over 1/4 of Kyrgyzstan's GDP [7].

The economic recession after the collapse of the Soviet Union led to a weak development of industry, lack of own technological base, poor condition of transport routes and widespread corruption. In addition, the state borders and the economic dependencies with Kazakhstan and Uzbekistan that emerged after the collapse of the Soviet Union, created great difficulties for the republic [7], [8].

To date, the Kyrgyz government remains dependent on foreign donor support to finance its annual budget deficit of approximately 4-5% of GDP [7], [8].

3.6 Moldova

Moldova is one of the poorest countries in Europe. The country has no deposits of mineral resources, with the exception of deposits of nonmetallic minerals - cauldron and raw materials for the production of cement. All energy resources are imported predominantly from Russia and Ukraine [7], [8].

With a moderate climate (with warm summers and mild winters) and productive rich-soil farmland, Moldova's economy relies heavily on its agriculture sector, featuring fruits, vegetables, wine, and tobacco. The country has a well-established wine industry (vineyard area of 147,000 hectares). Moldova is a major supplier of agricultural products in southeastern Europe. Due to an increase of the agricultural production, the economic growth of the country in 2014 was higher than expected [7], [8].

Moldova also depends on annual remittances from the roughly one million Moldovans working in Europe, Russia and other former Soviet Union countries.

Moldova signed an Association Agreement and a Deep and Comprehensive Free Trade Agreement with the EU in the fall of 2014, connecting Moldovan products to the world's largest markets. Moldova's growth has been hampered by endemic corruption and a Russian import ban on Moldova's agricultural products [7], [8].

3.7 Russian Federation

The Russian Federation is the largest country in the world by surface area, the sixth - in terms of GDP and the ninth most populous [10]. Russia is one of the world's leading producers of oil and natural gas, and is also a top exporter of metals such as steel and primary aluminum [7].

Russia has experienced significant changes since the collapse of the Soviet Union, moving from a globally-isolated, centrally-planned economy towards a more market-based and globally-integrated economy. Despite economic reforms, Russia's manufacturing sector is generally uncompetitive on the world market at this point of time [11], [12].

10% of the arable land in the world belong to Russia. Main crops are: cereals, sugar beet, sunflower, potatoes and flax. In addition, meat and dairy and meat-wool animal husbandry are developed in Russia. Between 2000 and 2008, there was a constant increase in the annual volume of meat production [7], [8].

After 16 years of negotiations, Russia finally became a member of the World Trade Organization (WTO) in 2011. In 2013, Russia also received the label of a high-income economy according to the World Bank [7], [8].

As Russia is still dependent on its natural resources for much of its GDP, the economy slowed down to a growth rate of just 1.3 percent (for comparison: 7% growth during 1998-2008) in 2013 because of the rapid oil prices reduction [7], [8].

To date, due to low oil prices, international sanctions and structural limitations Russia undergoes a deep recession, with the falling of GDP in 2015 and 2016 [11].

3.8 Tajikistan

Tajikistan is one of the poorest countries in the world. The most of the large industrial enterprises, the industrial and social infrastructure facilities as well as financial and banking institutions belong to the government [7], [8].

Today, Tajikistan has one of the lowest per capita GDPs among the 15 former Soviet republics. The basis of the economy is agriculture and primarily irrigated agriculture. Less than 7% of the land area is arable, and cotton is the most important crop. Tajikistan imports approx. 70% of its food [7].

Because of the lack of employment opportunities in Tajikistan, more than one million Tajik citizens work abroad - roughly 90% of them in Russia – supporting their families back home through remittances. In 2014, the sum of the remittances was equivalent to nearly 50% of the GDP, but fell significantly in 2015 due to the economic crisis in Russia. The value of the narcotic drugs transiting Tajikistan every year is equivalent to 30-50% of the GDP [7].

Tajikistan became a member of the WTO in March 2013. However, its economy continues to face many problems, including dependence on remittances from Tajiks working in Russia, corruption and the illegal drug trade [7], [8].

3.9 Turkmenistan

Turkmenistan is a state located in Central Asia. It is ranked fourth in the world in terms of natural gas reserves and has the second largest gas field in the world. In Turkmenistan, the industry, agriculture, energy, transport and communication sectors continue to be mainly controlled and mostly owned by the state. As a result, many public services remain free of charge (electricity, water use and gas consumption) and depend on subsidies [7], [8].

The main industries are extraction and processing of natural gas and oil, electric power, textile and construction. Turkmenistan is largely a desert country with intensive agriculture in irrigated oases. The two largest crops are cotton, most of which is produced for export, and wheat, which is domestically consumed. Although agriculture accounts for roughly 9% of GDP, it continues to employ nearly half of the country's workforce. Hydrocarbon exports (mainly natural gas) make up 25% of Turkmenistan's GDP, the bulk of which is natural gas going to China [7], [8].

The Turkmen economy is determined by several factors. First, Turkmenistan possesses large reserves of natural resources. Secondly, the country has a closed type of economy. Thirdly, Turkmenistan is a geographically closed space: it has no access to the sea and is surrounded by states whose political situation makes it difficult to promote a transport of Turkmen Hydrocarbon to the world markets [7], [8].

The development of industry is slowing down due to the reduction of sales markets in the CIS countries and the reduction of the world prices for raw materials. Currency depreciation, corruption, isolationist policies, and limited spending on public services have resulted in a stagnating economy [7], [8].

3.10 Ukraine

After Russia, the Ukrainian republic was the most important economic component of the former Soviet Union. With the dissolution of the Soviet system, the country moved from a planned economy to a market economy.

The majority of Ukrainian exports (transportation vehicles, spacecraft, KrAZ trucks, etc.) are marketed and sold to the EU and CIS. The country imports most of its energy supplies, especially oil and natural gas and to a large extent depends on Russia as its main energy supplier.

Ukraine is an industrial-agrarian country. Its fertile black soil (third place in the world) generated more than one-fourth of Soviet agricultural output, and its farms provided substantial quantities of meat, milk, grain, and vegetables to other republics.

After the collapse of the Soviet Union, a systemic crisis ensued in agriculture, which had a negative impact on the industry's performance indicators. By the middle of the 2000s, the indicators of crop production by main types of products reached the level of 1990 or even surpassed it. At the same time, the livestock industry has not been able to restore the previous volumes.

Russia's occupation of Crimea in March 2014 and on-going military dispute in eastern Ukraine had a negative effect on the economic growth during the last years [7], [8].

3.11 Uzbekistan

Uzbekistan is a state located in the central part of Central Asia. Uzbekistan is a doubly landlocked country in which 51% of the population lives in urban settlements. The country takes the fourth place in the world in terms of the gold reserve. The main energy resource in Uzbekistan is natural gas.

The most important agricultural products of Uzbekistan are cotton, fruits, vegetables and grains (wheat, rice and corn). Despite ongoing efforts to diversify crops, Uzbek agriculture remains largely centered on cotton: Uzbekistan is the world's fifth-largest cotton exporter and seventh-largest producer.

Since its independence in September 1991, the government has largely maintained its Soviet-style command economy with subsidies and tight controls on production, prices, and access to foreign currency.

In summary, despite sharing a common political and economic past, the CIS countries are quite different in their success of implementing market reforms and embracing a global competitive environment. The keys to future growth for all these countries include progress in fighting corruption, improving administrative transparency and attracting foreign aid and investment [7], [8].

4. Livestock and Companion Animals in the Region of the CIS Countries

CIS countries occupy a territory of approximately 22.25 million square kilometers, which exceeds the territory of Europe, North and Latin America, Australia and Oceania. On this territory with a population of more than 280 million, the livestock plays an important role in the agricultural economy as a major contributor to total food production [8], [13].

The data on the livestock and domestic pets in the CIS countries provided in this chapter gives an opportunity to get an impression about the livestock / pet situation in the CIS region.

In Armenia, the agricultural industry sector has been developing dynamically over the last ten years. Due to a mountainous surface of the country, the animal husbandry branches as cattle, sheep and goats are developed. The production of livestock products as well as the volume of exports of dairy products and meat export are increasing [13].

In the Republic of Azerbaijan, the breeding of coarse-wool, fine-fleece sheep and dairy cattle is of great importance [13].

Leading branches of animal husbandry in Belarus are the dairy cattle, beef and pig meat production. The dairy industry is the basis of domestic agricultural exports [13].

In Russia, there are several branches of livestock breeding of cattle, sheep, pig, horse, goat, camel, anchovy, maral, reindeer, beekeeping, as well as fur farming, pond fishery and poultry farming. Cattle breeding is the largest branch of animal husbandry in the country (it gives more than 60% of gross output per year) [13].

Leading branches of animal husbandry in the Republic of Moldova are cattle breeding, pig production and sheep breeding. Sheep breeding is the most developed field in the southern steppe regions of the republic [13].

Kazakhstan is mostly a flat country and is one of the largest livestock regions of the CIS. Important branches of livestock breeding are cattle, horse and camel breeding. The main branch of animal husbandry is sheep breeding [13].

The territory of Kyrgyzstan and Tajikistan is mostly occupied by mountains. Specialization of mountain areas is the cattle breeding (sheep, horses and dairy cattle). In the Republic of Tajikistan, karakul and Hissar sheep, yaks and others are bred [13].

In contrast to Kyrgyzstan and Tajikistan, the majority (90%) of Turkmenistan is occupied by deserts. The main branch of livestock breeding of desert pastures is karakul sheep breeding, silkworm breeding and dairy cattle breeding. Camel breeding and horse breeding are also developed [13].

The specialization of livestock breeding in the desert regions of Uzbekistan is the breeding of the karakul and fine-fleece steppe. Uzbekistan also specializes in silkworm breeding and breeding of dairy cattle [13].

The branches of the specialization of animal husbandry in Ukraine are the breeding of dairy cattle, pigs, fine-fleeced and semi-fine sheep and poultry farming [13].

The CIS statistical online [14] published comparable statistical material based on official data of the national statistical services of the CIS and other countries. The data in percentage reflects the situation on the world market of milk, livestock and poultry production. One can see that the CIS countries took a strong position in the world market competing with the USA, EC and China in the production of livestock/poultry and milk (see Figure 3).

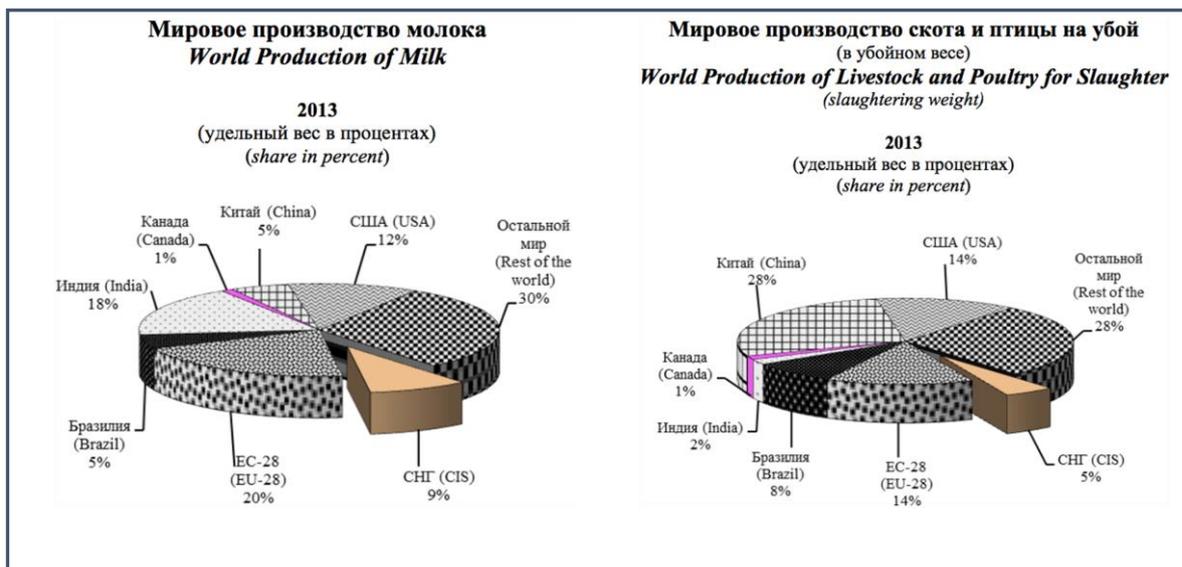


Figure 3: World production of milk, livestock and poultry [14]

Table 2 provides a herd size of different livestock species for the seven countries in the period from 2014 to 2015 [15]. According to the data presented, Russia is a leader in the cattle, pigs, sheep and goats, horses, poultry and beehives population out of seven CIS countries.

| Country | Cattle | Pigs | Sheep & goats | Horses | Poultry | Beehives |
|---------------|---------------|---------------|---------------|--------------|----------------|--------------|
| Armenia | 678 | 140 | 718 | 12 | 4,101 | n.a |
| Azerbaijan | 2,698 | 6 | 8,645 | 75 | 28,852 | 243 |
| Belarus | 4,321 | 3,267 | 131 | 82 | 45,700 | 217 |
| Kazakhstan | 6,033 | 885 | 17,915 | 1,938 | 35,020 | 114 |
| Moldova | 189 | 420 | 849 | 45 | n.a | 116 |
| Russia | 19,264 | 19,546 | 24,683 | 1,373 | 527,326 | 3,474 |
| Ukraine | 3,884 | 7,351 | 1,371 | 317 | 213,336 | 2,700 |

Table 2: Herd size in thousands of animals for the year 2014 [15]

The dynamic of the production of the key kinds of animal products for each CIS country from the year 2010 to 2015 is presented in Figure 4. The positive dynamics can be traced for such countries as Armenia, Belarus, Uzbekistan and others, while the decline in production in milk, eggs, wool, livestock and poultry is observed for Moldova and Ukraine, which certainly correlates with the current instable economic situation in the countries [14].

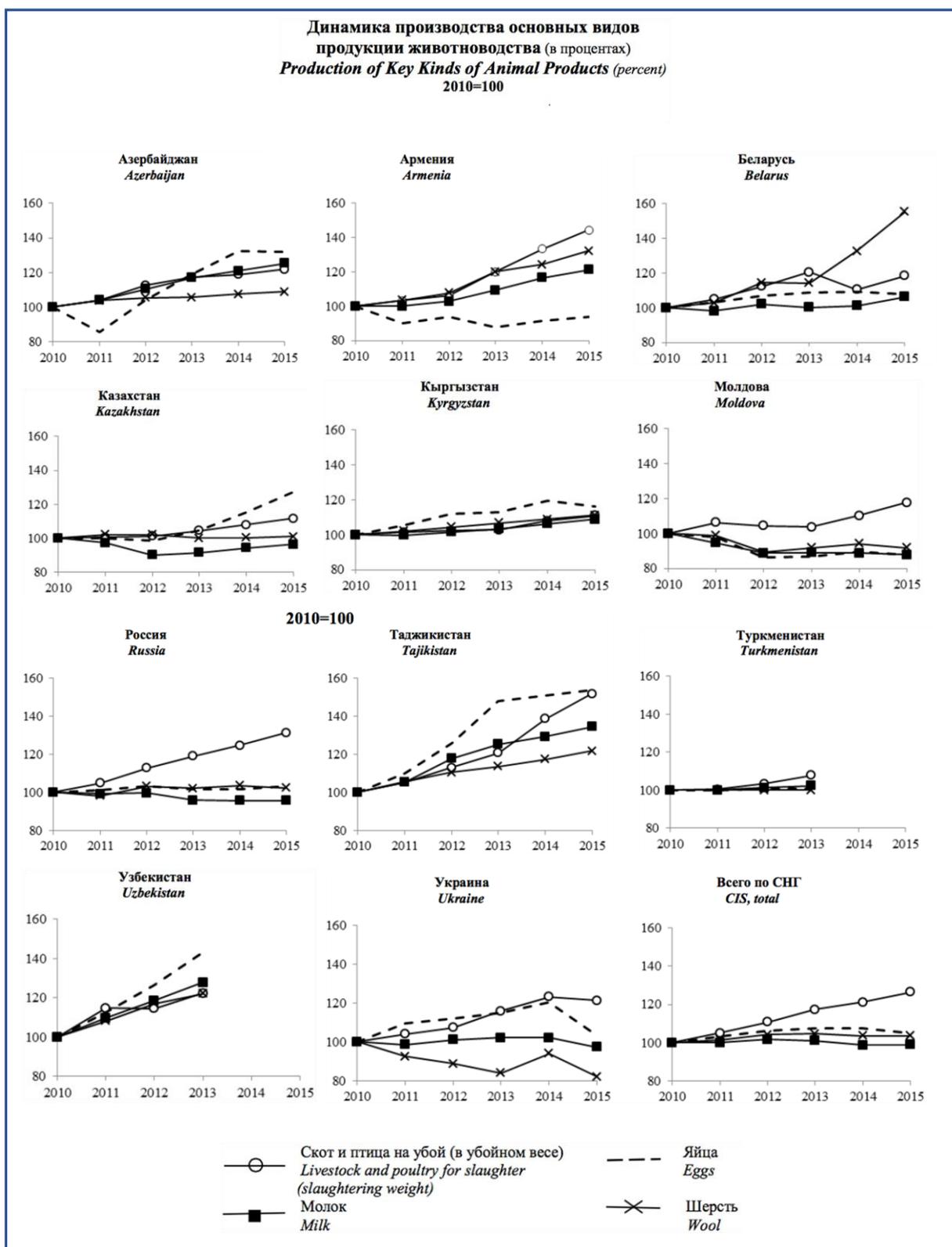


Figure 4: Production of key kinds of animal products 2010-2015 [14]

The CIS countries are the second largest in the world in terms of the number of domestic pets [16]. One of the biggest markets out of 11 CIS countries is Russia. Almost half of Russian families have pets (47%), including 12.5 million cats and 17.8 million dogs (see Figure 5). Ukraine took the ninth place in the ranking of countries whose residents contain the most domestic cats. The number of these pets in the country is 7.5 million, according to the website worldatlas.com. Russia also takes the ninth place in a top 20 of bird and fish populations [17], [18].

Livestock and Companion Animals in the Region of the CIS Countries

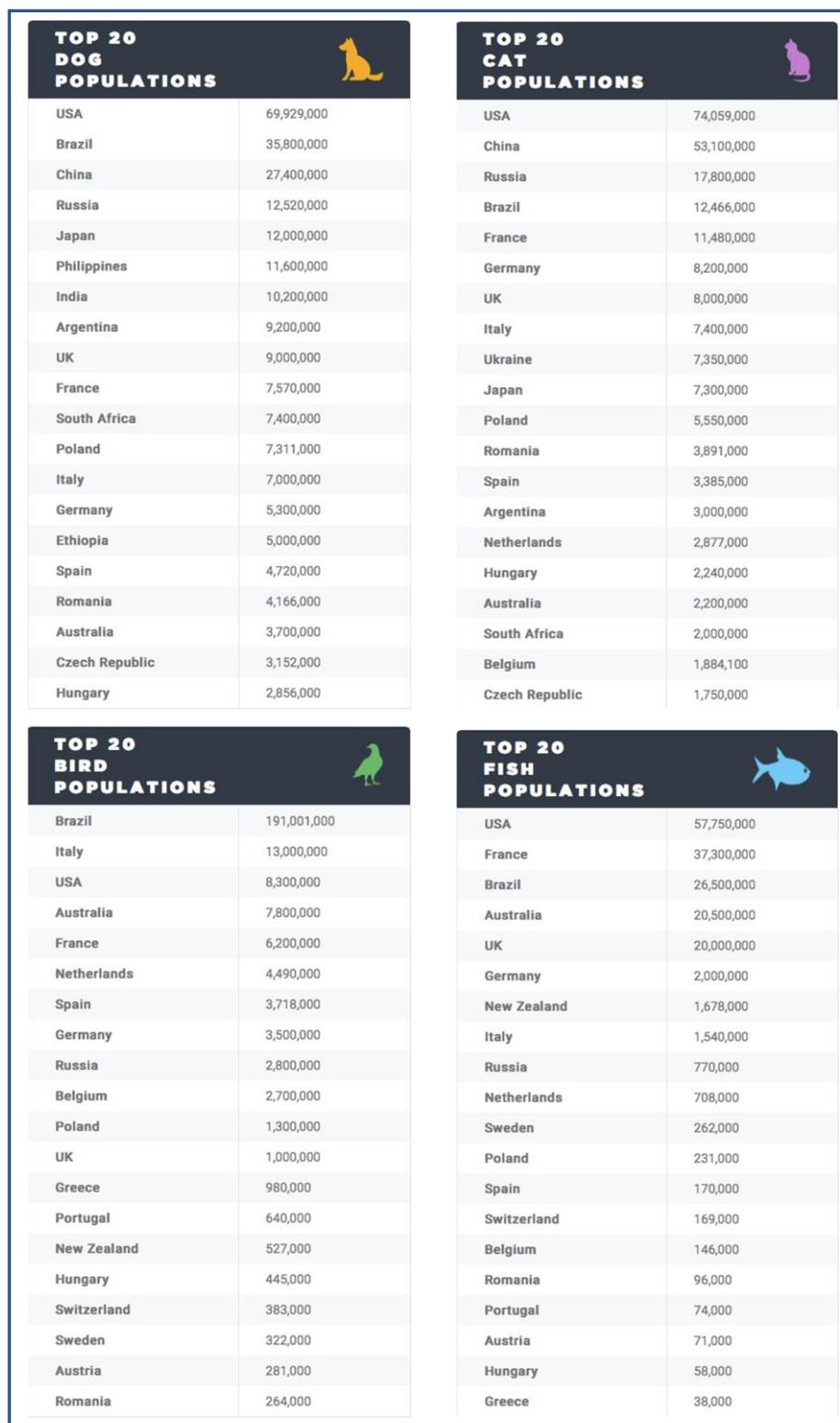


Figure 5: World's largest populations of dogs, cats, birds and fish [17]

Apart from Russia and Ukraine, no information is publicly available for the other CIS countries. Nevertheless, the trend will also apply for those countries as well. This implies a high relevance of the CIS region as a potential market for veterinary medicinal products.

5. Pharmaceutical Market for Veterinary Medicinal Products in the CIS Countries

Animal healthcare has become globally a focus area for many pharmaceutical companies in the past decade. The particular market has become even more important because of greater instances of animal disease outbreaks coupled with large-scale factory farming that requires high quality veterinary medicinal products, animal feed additives, vaccines as well as hygiene management products [19].

Currently, the market of veterinary drugs for agricultural animals in CIS countries is growing dynamically from year to year.

The most highly saturated CIS countries in terms of pharmaceutical distribution are Russia, Kazakhstan, Belarus, Azerbaijan and Ukraine (see Figure 6). Approximately 92% of the veterinary drugs applied in the CIS countries are applied in these four countries [9].

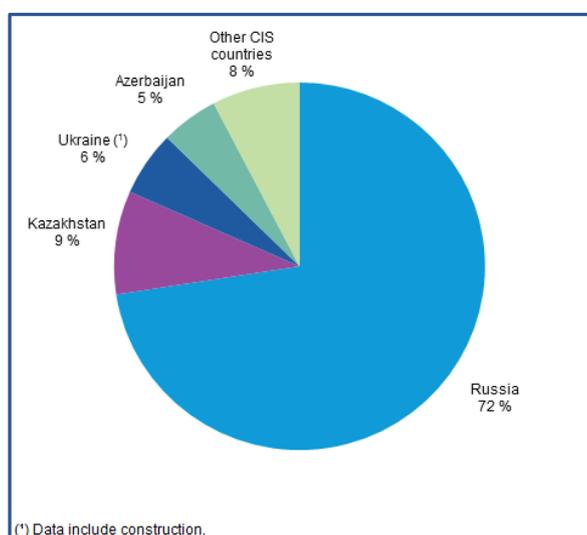


Figure 6: Share of total CIS industry gross value added by country 2012 [9]

The major part of pharmacological and biological medicines registered in the CIS countries are imported. In the Russian Federation, the veterinary pharmaceutical market consists to date to 65% of imported drugs and just 35% of domestic ones. Thus, 90% of anti-mastitis gels, 80% of oral anti-inflammatory drugs, 75% of antibiotics and antiparasitic drugs in the form of tablets are imported [20].

The structure of the Russian market for drugs by types is similar to that in the EU and the US: 39% are vaccines, 34% - antibiotics, 10% - vitamins and feed additives, 9% - hygiene and disinfectants, 8% - for other drugs [21].

According to a report published in the year 2015, the share of Russian domestic drugs does not exceed 35-37% and continues to decline steadily. Only 10 years ago, the market structure was completely different: 25% - foreign drugs and 75% - Russian. To date the market for veterinary drugs in Russia is about \$ 630 million [21].

The Ukrainian market is also dominated by the import of veterinary drugs. Most of these drugs are imported to Ukraine from Germany, Netherlands, France and Switzerland. A significant part of the imported veterinary drugs is feed supplements. Among the veterinary drugs registered in Ukraine, antimicrobial (34%) drugs predominate, which coincides with the trends of the world market of

these preparations. Vitamin and mineral substances (28%), followed by biological means (18%) and antiparasitic drugs (15%) are on the second place. More than 60% of all animal protection products are preparations for cattle, sheep and goats [22].

A similar trend has been observed on the vaccine market. The most vaccines used for the animals are imported into the CIS countries from abroad. For example, 60% of the total volume of vaccines consumed by Russia falls on imported vaccines. Russia is the main consumer among CIS countries for all types of vaccines. The share of the Russian Federation in total consumption of vaccines for birds, for farm animals and for carnivores are 70%, 43%, 41% respectively. In countries like Turkmenistan, Tadjikistan or Uzbekistan the most vaccines are imported as well. In Uzbekistan, for example, 7% of the total volume of consumption of veterinary vaccines is made by vaccines produced in the territory of Uzbekistan, the rest is fully imported from the countries of the CU and far abroad [23].

In summary, the relevance of imported veterinary medicines highlights the importance of an understanding of the respective regulatory systems and procedures also for international companies.

6. Competent Veterinary Authorities and Most Relevant Regulatory Aspects in the CIS Countries

From a high-level perspective, the process of placing pharmaceutical products on the market of a particular country and / or community of states follows similar structures and rules.

The registration is a key process to place the medicinal product on the market. During the registration, a stringent, scientific and independent review is being carried out by the authorities to ensure that the new medicinal product is safe, of high quality and efficacious. Only after this review, a marketing authorisation may be granted for a product. After the authorization process, the production of veterinary preparations is permitted for legal entities and individuals and the authorized veterinary medicinal product (VMP) can be engaged in the sale and other means of veterinary medicine.

The registration of VMPs is a complex process and requires a certain period of time. The respective laws on veterinary medicine determine the legal, organizational and economic basis of activities in the sphere of veterinary medicine and aims to the provision of veterinary-sanitary safety.

Leaving the high-level perspective and diving more into the details of the registration processes of the CIS countries shows important differences in the process itself as well as in the related regulations and laws.

Every CIS country has its own laws, standards, rules and practices, including the organization of business and product promotion.

The transparency of the processes itself varies dramatically between the CIS member states. In particular, Moldova, Tajikistan and Turkmenistan are examples of CIS member states with nearly no publicly available information on the registration process. In contrast, Armenia and Ukraine do provide a very clear and easy to access information (registration process, legislation, normative documentations etc.).

The goal of this chapter is to provide an overview on the competent veterinary authorities and most relevant regulatory aspects for each of the CIS countries.

In general, three types / patterns of how the control and regulation process is organized need to be differentiated for the VMPs:

1. One law regulates both: human and veterinary medicinal products under supervision of the Ministry of Health (“**one law, one authority**”)
2. One law regulates both human and veterinary medicinal products, but under supervision of two different regulation authorities: Ministry of Health for the Human Medicinal Products (HMPs) and Ministry of Agriculture for the VMPs (“**one law, two authorities**”)
3. Two different laws regulating human and veterinary medicinal products. The HMPs are under control of the Ministry of Health and the VMPs are under supervision of the Ministry of Agriculture (“**two laws, two authorities**”)

In the following section describing the main legislative acts, competent authorities and their responsibilities in the CIS member states, this differentiation will be applied to make the differences more transparent.

6.1 Armenia

In Armenia, the veterinary medicine is part of the registration pattern: “one law, one authority” that regulates human and veterinary medicines under supervision of the national Ministry of Health (excluding vaccines, serums and diagnostics, which are under the control of Ministry of Agriculture). The legislations are available in the national, Russian language as well as in English. The detailed

registration procedure is described in “Requirements to the Registration of Medicinal products in the Republic of Armenia” which is available in the English language [24].

The import, production, storage, distribution, sell and use are only allowed for those veterinary medicinal products, which are registered in Armenia.

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Armenia:

- Ministry of Health of the Republic of Armenia: The Ministry is responsible for the authorization of medicinal products [25].
- Ministry of Agriculture of the Republic of Armenia: The Ministry is responsible for the authorization of veterinary vaccines, serums and diagnostics [26].
- The Scientific Centre of Drug and Medical Technology Expertise: The Centre is responsible for the scientific expertise of safety, efficacy and quality of medicinal products submitted for the state registration [27].

The following pharmaceutical products are subject to registration in the Republic of Armenia:

- new original and generic medicinal products
- additional dosage strengths, pharmaceutical forms and new indications of registered medicinal products
- new combinations of medicinal products [28]

The following table shows the most relevant, current legislation acts for the VMPs in Armenia:

| | |
|--|--|
| Laws of the Republic of Armenia “On drugs” of 13 June 2016, HO-86-N [28] | This law regulates the circulation of medicinal products, medicinal substances, medicinal plant raw materials and researched pharmaceutical products. |
| Law “On veterinary medicine” of July 2014, No HO-137-N [29] | This law regulates the application, production, import, export, trade or marketing of veterinary medicinal products. |
| Law „On veterinary“ of December 1999, No ZR-16 [30] | This law regulates legal relations in the field of veterinary medicine between the authorized body and the institutions, enterprises, organizations, sole entrepreneurs operating in Armenia, as well as the citizens. |

Regulatory aspects and requirements for the VMP registration in Armenia [28], [29]:

| | |
|--------------------------------------|--|
| Validity of VMP registration license | License is valid for 5 years. |
| Dossier requirements | Normative and Technical Documentation (NTD) (the local format of the dossier) or dossier in CTD (Common Technical Document) format submitted in Armenian, Russian or English. |
| Labeling requirements | Labeling is to be written in Armenian, Russian or English language. |
| Maximum Residue Limit (MRL) | Member of Codex Alimentarius. Armenia is also a part of the EAEU MRLs established by the EAEU is applied to Armenia. |
| Quality Standards | European Pharmacopoeia (Ph. Eur), International Pharmacopoeia (Ph. Int), United States Pharmacopoeia (USP), British Pharmacopoeia (BP), German Pharmacopoeia (DAP), German Homeopathic Pharmacopoeia (HAB) and in some cases – temporary Pharmacopoeial monographs of Armenia. |

| | |
|------------------------------------|---|
| | Good Manufacturing Practice (GMP), Certificate of Pharmaceutical Product (CCP), Transmissible Spongiform Encephalopathy (TSE) - certificates are needed for registration. |
| Post-authorization variations | Scientific Center should be informed about any changes of the registered VMP. List of variations is provided by the Ministry of Health [25]. The variation procedure takes 30 days. |
| Renewal | Renewal is completed in a maximum of 23 working days. The validity then is unlimited. A simplified renewal procedure is applicable in case of an accelerated registration [25]. |
| State Register after authorization | Not later than 30 days after issuing the registration certificate the VMP will be added to the state register [24]. |
| Additional information | VMPs which are registered at least in one of the International Council on Harmonisation (ICH) countries undergo a simplified registration procedure (30 days) without registration tests and clinical trials. |

6.2 Azerbaijan

In Azerbaijan, the veterinary medicine follows the registration pattern: “two laws, two authorities” which regulates human and veterinary medicines separately. The legislations are available in the national language only [31].

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Azerbaijan:

- Ministry of Agriculture: The Ministry is a central executive power authority, which executes among others the control and regulates the veterinary sector [32].
- Azerbaijan State Veterinary Inspection Institute under the Ministry of Agriculture: The Institute is responsible for the examination and validation of the registration documents and samples of the veterinary preparation during the registration [32].
- State Veterinary Service: This Service is responsible for monitoring the safety and quality of veterinary preparations and the registration of veterinary medicines [31], [32].

The following medicinal products are subject to registration in the Republic of Azerbaijan:

- original medicinal products
- analogues of medicinal products (generics)
- new combinations of medicinal products (which have been registered)
- medicinal products, the state registration term of which has expired
- active substances used in the manufacture of medicinal products [33]

The following table shows the most relevant, current legislation acts for the VMPs in Azerbaijan:

| | |
|--|--|
| Laws of the Republic of Azerbaijan “On Veterinary” No 922-IIQ of Mai 2005 [33] | This law establishes the legal and organizational basis for veterinary activities in Azerbaijan. |
| “Decree No 66 for approval, control and approbation of technical documents related to veterinary drugs, equipment and feed additives” of April 2007 [34] | This decree sets provisions on the NTD on production and application of veterinary preparations, examination, testing, state registration, production, import, storage, transportation, sale and use of veterinary preparations, equipment and feed additives in Azerbaijan. |

Regulatory aspects and requirements for the VMP registration in Azerbaijan [33], [34]:

| | |
|--------------------------------------|--|
| Validity of VMP registration license | License is valid for 5 years. |
| Dossier requirements | NTD should be submitted in Azerbaijan, Russian or English language. |
| Labeling requirements | Labeling is to be written in Azerbaijan language. |
| MRL | Azerbaijan is a member of Codex Alimentarius. |
| Quality Standards | Valid quality standards are: Russian Pharmacopoeia, BP, Ph. Eur, USP. |
| Post-authorization variation | State Veterinary Inspection Institute should be informed about any changes of the registered VMP. Other details are not specified. |
| Renewal | A renewal is needed after 5 years. The renewal may be rejected if the Marketing Authorisation Holder (MAH) fails to submit changes to the composition, the use procedure or the NTD. |
| State Register after authorization | The registry information is available in the State Register Book [35]. |
| Additional information | Import of VMP from abroad without registration in Azerbaijan is only permitted with the consent of the leadership of the State Veterinary Service. |

6.3 Belarus

In Belarus, the veterinary medicine is part of the registration pattern: “two laws, two authorities” and is regulated by the national Ministry of Agriculture (separately from human medicine). The legislations are available in the national and Russian languages [36]. Some laws are available in the English language as well.

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Belarus:

- Belarussian Ministry of Agriculture and Food: The Ministry is responsible for the implementation of a unified state policy the implementation of state management and regulation among others in the field of veterinary and veterinary medicine [37].
- Department of Veterinary and Food Supervision / Head Department of Veterinary Medicine (Vetbiopharmsovet): The Department is a part of the central office of the Ministry of Agriculture and Food, endowed with state authority and exercising control and supervision in the field of animal health [36].
- Belarussian State Veterinary Center: The Center is responsible for the control, tests and standardization of veterinary preparations and feed additives [38].

The following medicinal products (veterinary drugs, disinfectants, antiseptics and animal feed products) are subject to registration in the Republic of Belarus:

- new (with the original composition) veterinary medicines
- generic medicines - bioequivalent to already registered ones, but produced by another manufacturer or in collaboration with another manufacturer
- veterinary medicines manufactured or registered in other countries and intended to be used on the territory of Belarus [39]

The following table shows the most relevant, current legislation acts for the VMPs in Belarus:

| | |
|--|--|
| Laws of the Republic of Belarus “On Veterinary” of 1995, No 4 [40] | This law provides the legal, organizational and social bases of veterinary activity to protect the health of animals and to prevent illnesses that can be transmitted by animals. |
| “Decree No 44 of the Ministry of Agriculture and Food validating the Regulation on registration of veterinary drugs” of June 2007 [39] | This decree determines the procedure for registration of veterinary medicinal products (pharmacological and biological preparations, disinfectant and antiseptic agents and products for animal feeding used in veterinary medicine) intended for use on the territory of Belarus. |

Regulatory aspects and requirements for the VMP registration in Belarus [39], [40]:

| | |
|--------------------------------------|--|
| Validity of VMP registration license | License is valid for 5 years. |
| Dossier requirements | NTD are submitted in Russian (Belarussian). |
| Labeling requirements | Labeling is to be written in Belarussian (Russian) language. |
| MRL | Belarus is a member of Codex Alimentarius and a part of the EAEU. MRLs established by the CU apply to Belarus. |
| Quality Standards | Valid quality standards are: Belarussian and Russian Pharmacopeia. |
| Post-authorization variations | During the validity period of the registration certificate, the applicant must report any changes that are expected to be made to the registration documents and provide comprehensive information on the reasons for these changes and their effect on the effectiveness, safety and quality of the registered veterinary drug, as well as cases of receiving claims for the drug. Other details are not specified. |
| Renewal | The applicant must apply to the Belarussian State Veterinary Center no later than 5 months before the expiry of the registration period (for temporary registration - no later than 2 months) and submit documents in accordance with paragraphs 9, 10, 12, 13 of the Instruction [39]. |
| State Register after authorization | The registry information is written in the State Register Book [41]. |
| Additional information | Without registration, it is only allowed to use diagnostic kits, veterinary drugs used for treatment and disease prevention for pets, as well as veterinary medicines, which have already been scientifically tested and used for field trials in accordance with research program of a particular medicine, agreed with the Head Department of Veterinary Medicine. |

6.4 Kazakhstan

In Kazakhstan, the veterinary medicine is part of the registration pattern: “two laws, two authorities” and is regulated by the national Ministry of Agriculture (separately from human medicine). The legislations are available in Kazakh, English and Russian languages [42].

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Kazakhstan:

- Department of State Institution Committee of Veterinary Control and Supervision under Ministry of Agriculture of Kazakhstan [43]: The department is responsible for the

Competent Veterinary Authorities and Most Relevant Regulatory Aspects in the CIS Countries

registration and quality certificate for the veterinary drugs, as well their import, sale and use.

- National Veterinary Reference Center: The Center conducts registration tests, approbation of veterinary drugs and fodder additives, studies on quality control of veterinary preparations and examination of NTD of the VMPs [44].

The following products need to be registered in Kazakhstan in accordance with the laws "On veterinary Medicine":

- medicines for the treatment and prevention of infectious/non-infectious diseases in animals
- hyperimmune serum, vaccines, immunomodulators
- diagnostic kits

The following table shows the most relevant, current legislation acts for the VMPs in Kazakhstan:

| | |
|--|---|
| "Law on Veterinary Medicine" of July 2002, No 339 [42] | The law defines the legal, organizational and economic basis for carrying out activities in the field of veterinary medicine. |
| "Rules for the State Registration of Veterinary Preparations and Feed Additives in Kazakhstan" of January 2015, No 7-1/31 [45] | Description of registration rules of veterinary preparations and feed additives in the Kazakhstan. |

Regulatory aspects and requirements for the VMP registration in Kazakhstan:

| | |
|------------------------------------|---|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | NTD in the Kazakh and Russian language (for foreign applicants of NTD with a notarized translation in Kazakh and Russian languages and a copy of the NTD with a copy of the notarized translation). CTD format is also accepted. |
| Labeling requirements | Labeling is to be written in Kazakh or bilingual Russian/Kazakh languages. |
| MRL | Member of Codex Alimentarius. MRL on veterinary drugs corresponds to international standards of World Health Organization (WHO). Kazakhstan is a part of the EAEU. MRLs established by the CU apply to Kazakhstan. |
| Quality standards | National Pharmacopoeia, which is significantly harmonized with the Ph. Eur. |
| Post-authorization variation | MAH has to inform of any changes and / or additions that are planned to be made in the NTD, and provide comprehensive information on the reasons for these changes and their impact on the effectiveness, safety and quality of veterinary drugs. |
| Renewal | 5 years after the registration a renewal is obligatory. The validity of the registration certificate after the successful renewal is unlimited. |
| State Register after authorization | The registry information is available [45]. |

6.5 Kyrgyzstan

In Kyrgyzstan, the veterinary medicine is part of the registration pattern: “one law, two authorities” under control of the national Ministry of Agriculture. The legislations are only available in Russian and the national languages [46].

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Kyrgyzstan:

- Authorized State Body of the Kyrgyz Republic in the Field of Public Health [46]: The State Body arise out the state registration of medicinal products, medical-cosmetic and homeopathic medicinal products, as well as medicines used for the treatment of animals.
- Center for Certification of Veterinary Medicinal Products of the Ministry of Agriculture and Melioration of the Kyrgyz Republic: The Center carries out the certification and laboratory testing of the VMPs during the registration [47].

The following products need to be registered in Kazakhstan in accordance with the laws "About medicines":

- new medicines
- new combinations of previously registered medicines
- medicines registered earlier but produced in other dosage forms, with a new dosage or other formulation of excipients
- generics
- homeopathic medicines
- biologically active food additives
- medical immunobiological preparations
- medical and cosmetic products
- veterinary medicines

The following table shows the most relevant, current legislation acts for the VMPs in Kyrgyzstan:

| | |
|---|--|
| Laws of the Republic of Kyrgyzstan “About medicines” of April, 2003 No 91 [48] | This law determines the production, manufacture, preclinical and clinical research of medicines, the control of their quality, effectiveness, safety, trade in drugs and other activities in the field of medicinal products. |
| Law “About veterinary science” of December 2014, No 175 [49] | This law determines legal, social, organizational, financial and economic basis in the field of veterinary science. |
| Law “On veterinary” of March 1992, No 805-XII [50] | The law determines general legal, economic social and organizational basis of protection of animals' health. |
| Regulation "On the safety of veterinary medicinal products" of August 2013, No 444 [51] | The regulation determines the mandatory requirements for all produced on the territory of the Kyrgyz Republic veterinary medicinal products, the processes of their production, storage, transportation, sale, use and disposal. |

Regulatory aspects and requirements for the VMP registration in Kyrgyzstan [48], [51]:

| | |
|----------------------------------|--|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | NTD in Kyrgyz, Russian and the original language. CTD format is also accepted. |
| Labeling requirements | Labeling is to be written in Kyrgyz and Russian languages. |

| | |
|------------------------------------|---|
| MRL | Kyrgyzstan is member of Codex Alimentarius. MRL on veterinary drugs corresponds to the international standards (WHO). Kyrgyzstan is a part of the EAEU. MRLs established by the CU apply to Kyrgyzstan. |
| Quality standards | Valid quality standards are: Ph. Eur., USP, Russian pharmacopoeia, GMP certificate. |
| Post-authorization variation | MAH is obliged to report any changes that they intend to make to the registration documents and provide exhaustive information on the reasons for these changes and their impact on the effectiveness, safety and quality of the registered medicinal product, including changes in technology and place of production. |
| Renewal | Not specified. |
| State Register after authorization | The state register is available for open access from 2018. |

6.6 Moldova

In Moldova, the veterinary medicine is part of the registration pattern: “one law, two authorities”. The law regulates human and veterinary medicines, but VMPs are under the control of the Ministry of Agriculture and Food. In March 2017, the cabinet of ministers in Moldova approved a draft law on veterinary preparations, in order to protect the public and animals’ health in Moldova. Also, the draft stipulates the requirements concerning the labeling and notice to veterinary preparations and pharmacovigilance. In respect to this fact, the responsibilities of the National Agency for Food Safety and the commission of veterinary preparations are established. The implementation of the draft’s provisions will help to adjust the national legislation to the EU’s one; thus, the technical and legal barriers to the foreign trade will be reduced dramatically [52].

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Moldova:

- The Veterinary Pharmaceutical and Feed Supervisory Department (VPFSD): The Department is responsible for supervising, testing, approval, registration, manufacture, storage, export, marketing and use of veterinary medicaments in Moldova [53].
- Department of Veterinary Medicine Quality Control (RCVD) [53]: The Department is responsible for updating the State Register of Veterinary Pharmaceuticals. Only veterinary medicines presented in this database are allowed for import, production, distribution, marketing and use in Moldova.

The following table shows the most relevant, current legislation acts for the VMPs in Moldova:

| | |
|--|--|
| Law No 221-XVI "Veterinary-Sanitary Activities" of October 2007 [54] | This law defines veterinary and sanitary rules and regulations, including the rights and the duties of the state and of natural and legal persons in the manufacture, processing, storage, transportation and trade of live animals and products of animal origin. |
| Law No 1409-XIII „About drugs“ of December 1997 [55] | The law regulates all fields of the medicines: research, registration, production, implementation in practice, application, import, export, storage, distribution, leave and control. |
| Law “About pharmaceutical activity” of May, No 1456 [56] | The law regulates activities for the development of drugs, their standardization, registration, production, quality control, storage etc. |

Regulatory aspects and requirements for the VMP registration in Moldova [55]:

| | |
|------------------------------------|--|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | NTD or CTD has to be in Romanian, Russian or English language. |
| Labeling requirements | Labeling is to be written in Romanian and Russian languages. |
| MRL | Not specified. Moldova is not a Member of Codex Alimentarius. |
| Quality standards | GMP certificate. |
| Post-authorization variation | Not specified. |
| Renewal | Not specified. |
| State Register after authorization | The registry information is available online [57]. |
| Additional information | Since January 2013 the dossier is to be in the CTD format. VMPs registered in the European Medicines Agency (EMA) or in European Economic Area (EEA), or in Switzerland, USA, Canada, Japan and Australia do not need to be submitted for the quality control procedure carried out by the laboratory of the Medicine Agency. Registration time in this case is not exceeding 60 days. |

6.7 Russian Federation

In the Russian Federation, the veterinary medicine follows the registration pattern: “one law, two authorities” and is regulated by the national Ministry of Agriculture (separately from human medicine). The legislations are available in the Russian language [58].

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in the Russian Federation:

- Federal Service for Veterinary and Phytosanitary Surveillance (Rosselkhoznadzor) [58]: The Service carries out functions on control and supervision in the field of veterinary science.
- Federal State Institution "Russian State Centre of Quality and Standardization of Animal Drugs and Feeds" [59]: The Institution implements the state policy in the field of quality assurance of medicines for animals. It acts as a reference center for scientific and methodological support of the Rosselkhoznadzor.

According to the law N 61-FZ the following registration procedures for VMPs exist:

- registration of original medicinal products
- registration of generics
- registration of new combinations of medicinal products
- registration of previously registered medicinal products but manufactured in other dosage forms

The following table shows the most relevant, current legislation acts for the VMPs in the Russian Federation:

| | |
|--|--|
| Federal Law “On the Circulation of Medicines” of April 2010, No 61-FZ [60] | This law regulates the preclinical research, the clinical research, the expertise, the state registration, the standardization and quality control, the production, the manufacturing, the storage, the transportation, the import, the export, the advertising, the sale, the transfer, the use and the destruction of medicines. |
|--|--|

Competent Veterinary Authorities and Most Relevant Regulatory Aspects in the CIS Countries

| | |
|--|---|
| Rules of “State Registration of Medicinal Products for Animals and Feed Additives” of April 2005, No 48 [61] | The rules establish a unified procedure for the state registration of domestic and foreign medicinal products for animals. |
| Standard relementation (GOST P 54763—2011) [62] | This standard applies to pharmacological, biological and homeopathic medicinal products for veterinary medicine and establishes general requirements for the content, order of development, harmonization and approval of technological production regulations. |
| “Rules of production and quality control of drugs” of June 2013, N 916* [63] | The rules establish the requirements of the organization of production and quality control of medicinal products for human and veterinary use. |
| Law “About veterinary science” of May 1993, No 4979-1 [64] | The law regulates the relationships in the field of veterinary medicine. |

*The rules presented in N 916 are the Russian GMP rules, which are a literal translation of the GMP rules, functioning in the EU.

Regulatory aspects and requirements for the VMP registration in the Russian Federation [60]:

| | |
|------------------------------------|--|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | NTD should be submitted in Russian language or have a certified translation into Russian. |
| Labeling requirements | Labeling is to be written in Russian language. |
| MRL | Russia is a Member of Codex Alimentarius. Russia is a part of the EAEU. MRLs established by the CU apply to Russia. Russia has also a national MRL list, which differs from EU standards. For example, the standards for tetracyclines are even more stringent: less than 0.01 mg / kg in all standardized products compared to those recorded in the Codex Alimentarius (from ≤ 0.1 to ≤ 1.2 mg / kg depending on the product) and the European Union (EU) (from ≤ 0.1 to ≤ 0.6 mg / kg). |
| Quality standards | Valid quality standards are: Russian pharmacopoeia, GMP** and CPP certificates, manufacturing license. |
| Post-authorization variation | MAH is obliged to report any changes that they intend to make to the registration documents and provide exhaustive information on the reasons for these changes and their impact on the effectiveness, safety and quality of the registered medicinal product. Variations are reviewed within 90 working days. |
| Renewal | 6 months before the expiration of the validity, the applicant is entitled to apply for re-registration of the medicinal product. |
| State Register after authorization | The registry information is available online [65]. |
| Additional information | Clinical studies are accepted only in case they have been performed in Russia (this applies also for generics, new indications and line extensions). |

**According to the law “On circulation of medicines” the registration of medicinal products for human or veterinary use produced outside of the Russian Federation are accepted by the Russian NCA only after conducting GMP conformity assessment for all manufacturing sites involved in manufacturing process (including Active Pharmaceutical Ingredients (APIs)). The GMP conformity assessment for the veterinary products is conducted by the Rosselkhoznadzor on the basis of decision of the Russian State Center for Quality Control and Standardization of Veterinary Drugs and Feeds by examination of provided documents and mandatory inspections of all manufacturing sites involved in manufacturing process.

6.8 Tadjikistan

In Tadjikistan, the veterinary medicine follows the registration pattern: “one law, two authorities”. The law regulates human and veterinary medicines, but VMPs are under control of the Ministry of Agriculture [66].

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Tadjikistan:

- The State Veterinary Supervision Office of the Ministry of Agriculture of Tajikistan: The Supervision Office is responsible for the organization of production and purchase of medicines intended for the diagnosis, prevention and treatment of animals, as well as the production of veterinary and veterinary zoo-technical products and veterinary equipment [66].
- State Control of Circulation of Pharmaceuticals: The State controls the clinical trials of drugs, quality, efficiency, production, manufacturing, storage, transportation, import/export to/from the territory of the Republic of Tajikistan, sale, use, application, advertisement and destruction of pharmaceuticals [67].

According to the law „About medicines and pharmaceutical activities” the following registration procedures for VMPs exist:

- registration of new drugs
- registration of new combinations of previously registered drugs
- registration of medicines registered earlier, but produced in others dosage forms or with a different composition of excipients
- registration of generics

The following table shows the most relevant, current legislation acts for the VMPs in Tadjikistan:

| | |
|---|--|
| Law “On veterinary” of January 2007, No 73 [68] | This law establishes general, legal and organizational requirements for veterinary and sanitary safety of foodstuffs of animal origin, ensuring veterinary and epizootic well-being, livestock quarantine and establishes the modalities of carrying out state veterinary control. |
| Law „About medicines and pharmaceutical activities” of August 2001 [69] | This law determines the legal basis in the field of drug circulation of medical goods and pharmaceutical activities (production, preclinical and clinical testing, quality control, efficiency and safety, trade in medicines and other relations arising in this field). |

Regulatory aspects and requirements for the VMP registration in Tadjikistan (according to available information) [69]:

| | |
|----------------------------------|--|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | NTD should be submitted in Tadjik and Russian languages. |
| Labeling requirements | Labeling is approved in Tadjik and Russian languages. |
| MRL | Member of Codex Alimentarius. |

| | |
|------------------------------------|---------------------------|
| Quality Standards | Not specified. |
| Post-authorization variations | Not specified. |
| Renewal | Not specified |
| State Register after authorization | No information available. |

6.9 Turkmenistan

In Turkmenistan, the veterinary medicine follows the registration pattern: “one law, two authorities”. Since 2014, the registration process of veterinary medicines is under supervision of the national Ministry of Agriculture. In 2012, the State Veterinary Service under the Ministry of Agriculture and Water Resources was established to bring its activities in line with world standards for the medicinal products for animals. In 2014, in order to regulate and improve the quality and safety of livestock and poultry products, the Law of Turkmenistan on Veterinary Activities was adopted [70].

As there is not enough publicly available information on the registered VMPs and the authorization process, the key aspects and requirements provided within this section are based on the regulations for HMPs described in the law “About provision of medicines”.

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Turkmenistan:

- State Veterinary Service of Turkmenistan (no more information available)
- Central Veterinary Laboratory (no more information available)

The following table shows the most relevant, current legislation acts for the VMPs in Turkmenistan:

| | |
|---|---|
| Law “About Veterinary Practice” of November 2014, No 143-V [71] | This law determines the legal and organizational basis for veterinary affairs. |
| Law “About provision of medicines” of January 2016, No 319-V [72] | This law establishes the legal and organizational basis for state regulation of relations arising in the field of drug provision. |

The medicinal products can be admitted in Turkmenistan only after their state registration, including [72]:

- therapeutic teas, homeopathic medicines, disinfectants, including other means for the prevention of infectious diseases, medicinal cosmetics, hygiene products, curative mineral water, mud and salts used for medical and preventive purposes
- original medicinal products
- generics
- medicinal products registered earlier, produced in other dosage forms and a new dosage
- medicines manufactured at an additional production site
- medicinal products with the change of ownership of the Certificate

Regulatory aspects and requirements for the VMP registration in Turkmenistan [72]:

| | |
|----------------------------------|---|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | NTD should be submitted in Turkmen language. |
| Labeling requirements | Labelling is approved in Turkmen or Russian language. |
| MRL | Turkmenistan is not a member of Codex Alimentarius. |
| Quality Standards | Not specified. |

| | |
|------------------------------------|---|
| Post-authorization variations | In case of any changes, the applicant has to submit the application and relevant documents to the authorized body within 30 calendar days. |
| Renewal | The application needs to be submitted in a period no later than three months before the expiry of the registration certificate. |
| State Register after authorization | No public information available. |
| Additional information | VMPs are allowed to be imported to Turkmenistan from foreign countries, sale, use and storage on the basis of conducted relevant studies with the permission of the State Veterinary Service. |

6.10 Ukraine

In Ukraine, the medicinal products are a part of the registration pattern: “two laws, two authorities” and are regulated by the national Ministry of Agriculture. The legislations are available in the national language [73].

Registration of veterinary medicinal products, feed additives, premixes and prepared feeds for animals is carried out by the:

- State Committee for Veterinary Medicine: The State Committee is responsible for the regulative acts for the medicinal products for animals [73].
- State Pharmacological Commission for Veterinary Medicine: The Commission is an expert advisory body on registration, regulation of safety and effective using of veterinary medicinal products, feed additives, premixes and pet foods [74].
- State Scientific-Research Control Institute of Veterinary Medicinal Products: The Institute ensures the implementation of the state policy in the field of veterinary medicine, food safety, quarantine and plant protection, protection of plant varieties and state supervision for breeding livestock [75].
- State Scientific and Control Institute of Biotechnology and Strains of Microorganisms (SSCIBSM): The SSCIBSM is a leading facility within the area of development, expertise, registration and re-registration and quality control of veterinary immunobiological preparations [76].

The state registration system of veterinary products is determined by the law of Ukraine “On Veterinary Medicine”. The objects of the state registration are the following:

- veterinary medicines
- veterinary immunobiological products
- substances for veterinary products manufacture
- veterinary diagnostic products
- antiseptics, disinfectants, insect acaricides and deratization agents employed in animal production and veterinary medicine
- feed supplements

The following table shows the most relevant, current legislation acts for the VMPs in Ukraine:

| | |
|---|--|
| Law “On veterinary medicine” of November 2001, No 2775-III [77] | This law determines general legal, organizational and financial grounds of functioning of veterinary medicine. |
| Resolution “On approval of the provisions on the state | This regulation establishes the mechanism of state registration of veterinary medicines. |

| | |
|---|---|
| registration of veterinary medicines, feed additives, premixes and prepared feeds” of November 2007, No 1349 [78] | |
| “Order N 133” of June 2008 [79] | On approval of application forms, list of materials of the registration dossier and the order of its formation. |

Regulatory aspects and requirements for the VMP registration in Ukraine:

| | |
|------------------------------------|---|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | The registration dossier must be in English, Russian or Ukrainian languages. In case the dossier is presented in English, a translation into Russian or Ukrainian language is mandatory. |
| Labeling requirements | Labeling is to be written in Ukrainian and Russian languages. |
| MRL | Ukraine is a member of Codex Alimentarius. MRL on veterinary drugs corresponds to international standards. |
| Quality Standards | Valid quality standards are: Ph.Eur, USP, Ukraine Pharmacopoeia, etc. |
| Post-authorization variations | MAH has to report any changes that they intend to make to the registration documents and provide exhaustive information on the reasons for these changes. |
| Renewal | Simplified registration procedure within 60 business days. After confirmation of registration, it is unlimited. Documents for re-registration of the drug are filed no later than three months before the expiration of the registration certificate. |
| State Register after authorization | The registry information is available online [80]. |

6.11 Uzbekistan

In Uzbekistan, two different laws about medicines regulate human and veterinary medicinal products (“two laws, two authorities”). The animal MPs are under the supervision of the Ministry of Agriculture and Water Resources [81]. The legislations are available in the Uzbek and Russian languages.

The following competent authorities do control the regulatory activities for veterinary pharmaceuticals in Uzbekistan:

- Main State Veterinary Administration under the Ministry of Agriculture and Water Resources of Uzbekistan: The administration is responsible for the registration of VMPs for domestic and imported veterinary medicinal products [81].
- State Scientific Center for Quality Control of Veterinary Medicines and Feed Additives: The Center is responsible for the scientific expertise of safety, efficacy and quality of medicinal products submitted for the state registration (no public information is available).
- In 2016 the Main State Veterinary Administration under the Ministry of Agriculture and Water Resources has established the State Veterinary Committee: The committee has the following tasks: ensuring the implementation of regulatory and legal regulation in the field of veterinary medicine, coordinating the interaction of state, economic management bodies etc. (no public information available).

The following table shows the most relevant, current legislation acts for the VMPs in Uzbekistan:

Competent Veterinary Authorities and Most Relevant Regulatory Aspects in the CIS Countries

| | |
|---|--|
| Law "On veterinary" of 4 December 2015 [82] | The law regulates the state veterinary service, preventive, diagnostic and therapeutic measures, veterinary inspection and other activities. |
| Regulation "On the procedure for registration and registration certificate for domestic and imported veterinary medicinal products and feed additives" of March 2017, No 139 [83] | Both regulations determine the procedure for registration of domestic and imported veterinary medicinal products and issuance of a registration certificate for veterinary medicines and feed additives. |
| Regulation "On licensing procedures in the field of entrepreneurial activity" of December 2012, No 3PY -341 [84] | |

Regulatory aspects and requirements for the VMP registration in Uzbekistan [82]:

| | |
|------------------------------------|--|
| Validity of registration license | License is valid for 5 years. |
| Dossier requirements | NTD in Uzbek, Russian or English languages. In case the dossier is presented in English, translation into Russian or Uzbek is mandatory. |
| Labeling requirements | Labeling is to be written in Uzbek and Russian languages. |
| MRL | Uzbekistan is a Member of Codex Alimentarius. |
| Quality Standards | Valid quality standards are: Ph, Eur., Uzbek Pharmacopoeia, GMP, CPP, BSE/TSE. |
| Post-authorization variations | Variations are considered within 90 working days. |
| Renewal | Not specified. |
| State Register after authorization | Not available. |

7. An Overview of the Marketing Authorization Process in the CIS Countries

Registration of medicinal products in each CIS country is based on the results of the scientifically justified criteria and expertise of safety, efficacy and quality of medicinal products.

In general, a competent authority of each CIS country is responsible for:

- validation and evaluation of the registration documents
- evaluation of the results received during the registration (registration tests)
- final decision about registration or refusal of a veterinary drug

During the validation process, a competent authority checks the compliance of the submitted documents with the requirements established by laws and other legislative acts. The validation includes an expertise of pharmacological, toxicological, clinical and pre-clinical studies, technological procedures, specifications and methods of analyses, methods of manufacturing, and quality control.

The evaluation of a sample(s) of a new medicinal product is carried out by the certificated laboratories or scientific centers/institutes indicated above (for each CIS country). An audit of the production place is also conducted by the representatives of a competent authority.

The competent authority collects and analyzes the results obtained and, if they comply with all prescribed requirements, decides on the possibility of issuing a certificate and provides the applicant with information on the results of certification.

In 2015, five CIS countries: Belarus, Armenia, Kazakhstan, Kyrgyzstan and Russia became members of an international organization for regional economic called EAEU (Eurasian Economic Union) with an integrated single market of 183 million people and a gross domestic product of over 4 trillion U.S. dollars (PPP) [85].

The member states of the EAEU agreed upon a common registration of the medicines, which are intended for the circulation on a common market of the union according to the uniform rules of registration and examination of medicines approved by the decision of EAEU. The common requirements for labelling of medicines and to instructions on use of medicines were also agreed in all EAEU countries. On May 6, 2017, after ratification by the EAEU countries of the regulatory framework for medicines circulation in the Union, a set of twenty-six documents prepared by the Commission in cooperation with the Member States enters into effect, including twenty-one decisions of the Eurasian Economic Commission (EEC) Council, four decisions and one recommendation of the EEC Board. Thereby, the manufacturers of medicinal products of the EUEA are able to apply for registration of medicines and their release under common procedures and reduce administrative costs [86].

A transitional period ensuring a smooth transition from national to common regulation is planned to be complete till December 31, 2020. The medicinal products registered under national regulations till December 31, 2020 should pass re-registration under the regulations of the common market before December 31, 2025. If the drug was registered before December 31, 2020 by national rules in no less than in three member-countries and applied for more than 5 years, then when bringing this drug to the requirements of Union rules, an unlimited registration certificate is issued. When filing a Drug Application for registration before December 31, 2018, the manufacturer may provide national documents issued by the Union Member States that confirm compliance of manufacture of medicines with the requirements of national GMP instead of a GMP certificate of the EAEU.

Registration can be carried out either consistently in several countries (mutual recognition procedure) or simultaneously in several countries (decentralized procedure). The applicant independently chooses the reference state and the registration procedure [87].

In this chapter, the authorization process is presented for each CIS country in a scheme form. A list of documents needed for the registration process is provided.

7.1 Armenia

As shown in Figure 7, the registration process in Armenia consists of 5 major stages. In the first stage, the applicant submits the dossier together with the samples and reference standards to the Scientific Center of Drug and Medical Technology Expertise (SCDMTE).

The SCDMTE validates the submitted documents in the second stage of the process within ten days. The total period for the standard registration procedure including laboratory testing is 180 days. In case the product has already been registered in the EU, USA or in Japan, the accelerated procedure can be applied and takes up to maximum 30 days by bypassing the fourth registration phase, as no laboratory testing and clinical trials are needed.

In the final (for both the standard and accelerated procedures), the fifth stage the Ministry of Health provides its decision on the registration of the product to the applicant which takes up to 10 days [28].

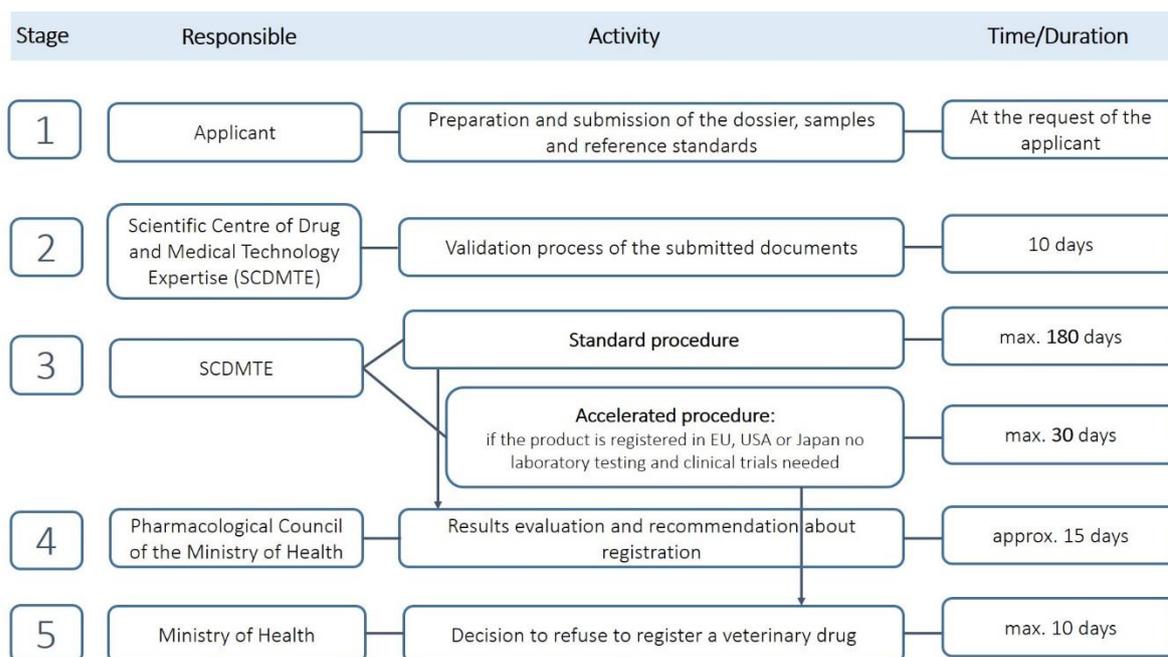


Figure 7: VMP(s) registration process in Armenia

The following documents are required for the registration in Armenia [28]:

- application form
- CPP certificate
- GMP issued by the authorized body of the country of origin (for all participants of the manufacturing process including packaging)
- manufacturing license for all participants of the manufacturing process (including packaging)
- registration status in other countries
- Summary of Product Characteristics (SPC) and instruction for use for specialists and patients
- labeling, packaging and mock-up

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- certificate (verified copy) or verified extract from appropriate register about legal protection of trademark or patent issued by the Intellectual Property Agency of the Ministry of Economy of the Republic of Armenia
- pharmacopoeia monograph(s) and/or control method(s), specification(s) of the finished medicinal product and its ingredients (2 copies)
- quality certificates of APIs and excipients
- packaging specification(s)
- TSE-Certificate
- data on stability study (if necessary, including stability data after opening)
- brief description of the technological process, chemical, technological and equipment schemes of the production, including controls of critical steps

For generics

- if available: data on pharmacokinetic and/or bio-equivalence and/or limited clinical trials of the medicinal product, otherwise: data on acute toxicity study
- information on pharmacological, toxicological and clinical trials (literature references or own data)

For new medicines

- reports on the pre-clinical studies of the safety (acute, sub-chronic and chronic toxicity, genotoxicity, carcinogenicity, reproductive and developmental toxicity, local tolerance, antigenicity, Immuno-toxicity and other toxicity studies)
- reports on the clinical trials on the specific activity, pharmacodynamic, pharmacokinetic and adverse reactions of the medicinal product
- information on maximum residue limits in the foodstuff (meat, milk, egg, etc.)
- the time limitation of foodstuff use¹

List of documents for the accelerated procedure (30 days registration) [28]:

- certified true copy of the registration certificate of the medicinal product in one of the member countries of the EU or in the USA, or in Japan, or CPP in format approved by the WHO issued in the last 2 years
- SPC approved by the authorized body of the country that has registered the medicinal product
- data on the qualitative and quantitative composition of the medicinal product (including excipients)
- pharmacopoeia monographs or control methods, specifications of the medicinal product
- label of the medicinal product, packages, their colored mock-ups, patient information leaflet or the instruction for medical use for specialists and patients, as well as their electronic versions for all output forms indicated in the application in English or in Armenian
- Periodic Safety Update Report (PSUR)

7.2 Azerbaijan

As illustrated in Figure 8, the registration process in Azerbaijan is divided into 6 stages. In the first stage, the applicant submits the dossier together with the samples and reference standards to the Azerbaijan State Veterinary Inspection Institute. The Institute validates the submitted documents within 15 days. Then, the Scientific Council of the Veterinary Inspection Institute makes a decision about the registration test period for the VMP. The Laboratory at Azerbaijan State Veterinary Inspection Institute is responsible for the registration tests of the drug. After registration tests, the

¹ Official information states „limitation of foodstuff“ instead of „withholding period“, which would fit better into the context.

Scientific and Technical Council of the State Veterinary Service evaluates the data and makes the final decision about the registration of the drug within one month [31], [33], [34].

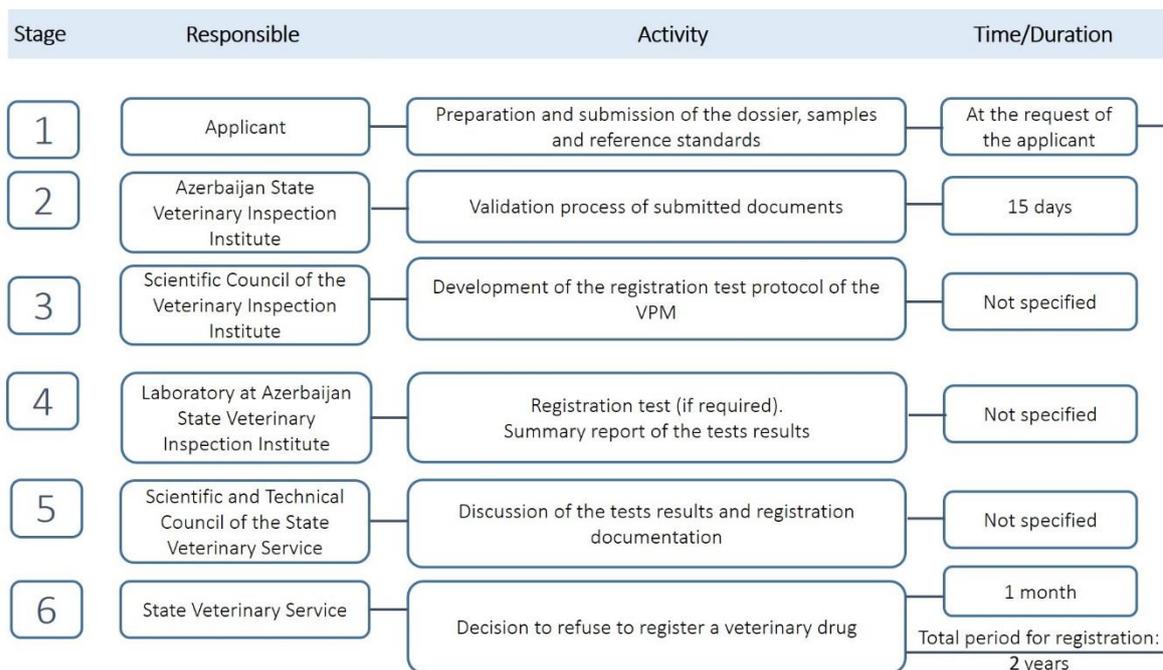


Figure 8: VMP(s) registration process in Azerbaijan

The following documents are required for the registration procedure in Azerbaijan [31]:

- application form
- detailed description of the research methods for the experimental study of the drug, research results and other related documents and materials (in 2 copies)
- materials of the experimental study of the drug by providing information on literature and similar preparations
- description of all components included in the preparation indicating their purpose
- description or scheme of the preparation
- data on each particular animal and all actual material has to be reflected in the report by showing the summarized average figures and statistical results
- results of 2-3 experimental laboratory samples of the preparation
- instruction, temporary instruction or draft of the drug
- technical specifications
- method of quality control
- report on the stability of the drug
- samples and standard specimens (if necessary reagents) in the manufacturer's packaging of 3 parts of the preparation
- first and second packaging labels (if necessary)
- decision of the Scientific Council of the Institute (scientific-research institution laboratory) on the feasibility of the application (excerpt from the protocol)

7.3 Belarus

In the first stage of the registration procedure in Belarus, the applicant submits the dossier together with the samples and reference standards to the State Veterinary Center (SVC) (see Figure 9). The SVC validates the submitted documents within 10 days and sends the decision report to the Commission of Veterinary Products (CVP). The CVP validates the submission document within 15 days and sends then the validation report again to the SVC. Based on the decision of the CVP and expert commission of Vetbiopharmsovet, the SVC competent laboratories conduct the registration

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tests. Based on the results of the registration tests and expert opinion, the Head Department of Vetbiopharmsovet makes a decision to refuse or to register a veterinary drug. The following figure shows the process explained above [39], [40].

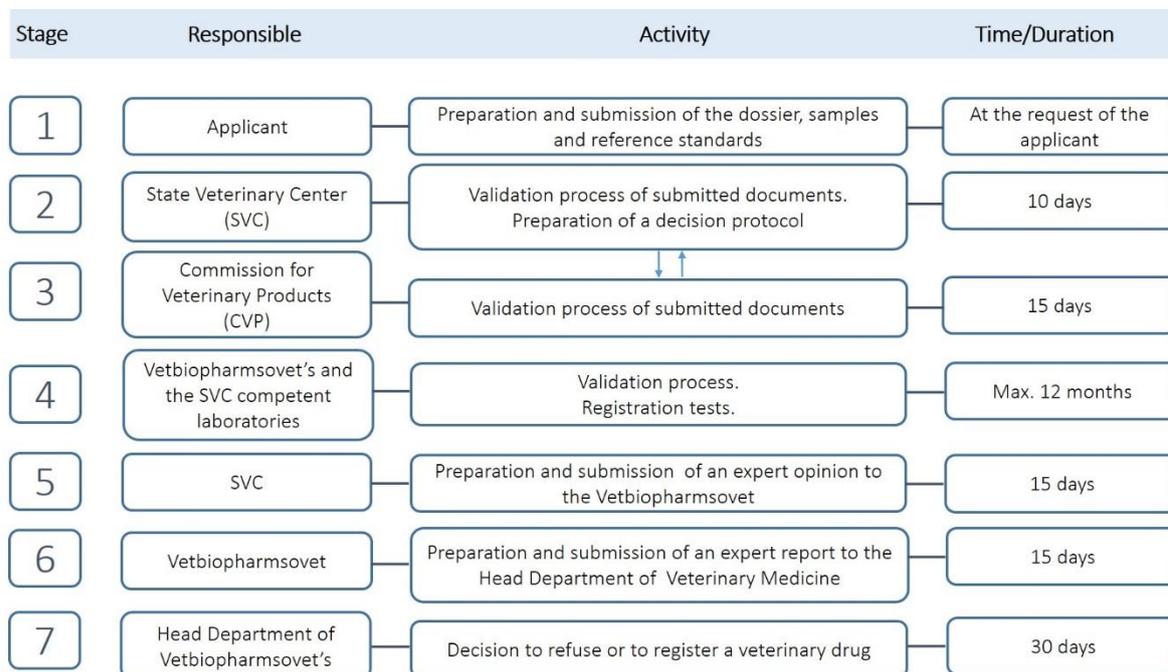


Figure 9: VMP(s) registration process in Belarus

In Belarus, the veterinary medicinal products are divided into 9 groups, depending on the volume of the necessary studies [39]:

1. Original, new drugs that have not previously been used in veterinary. Multiple studies must be carried out for such drugs. These include the toxicity studies in two species of farm and laboratory animals, the specific activity, pharmacodynamics and pharmacokinetics *in vitro* and *in vivo* experiments, storage stability as well as the duration of pre-slaughter holding after using the product.
2. Products, which are used in human medicine and are recommended for use in veterinary medicine. Studies need to be conducted the same way as in the first group, except for toxicity studies in laboratory animals and specific toxicity.
3. New drugs, containing active substances and excipients, approved for use in veterinary. In testing of these drugs on laboratory animals, chronic toxicity has to be revealed. Also, the pharmacokinetics, maximum tolerated dose, pharmacodynamics, therapeutic efficacy must be determined.
4. Veterinary drugs, already known, with a new recommended route of administration.
5. Veterinary drugs already known to be recommended for other animal species. These drugs are subject to studies similar to the ones of the third group except the study of chronic and acute toxicity in laboratory animals.
6. Already known drugs, recommended for use with new timing and dosage.
7. Already known drugs, recommended for the new indications.
8. Already known drugs with a new excipient, allowed for use in veterinary medicine. In this case, studies on the specific activity, acute toxicity in laboratory animals need to be carried out.
9. Medicines, similar to generics produced in Belarus, if their composition is not protected by the relevant patent.

The following documents are required for the registration procedure in Belarus [39]:

- application form
- information on analogues
- report on the experimental pharmacological study of the drug: toxicity (acute, subacute or chronic, specific), pharmacokinetics, pharmacodynamics, specific activity, withdrawal period (period after the use of livestock products after the treatment)
- the report on the study of biological veterinary drug should contain the information about the properties of used strains of microorganisms (fungi, bacteria, viruses), culture techniques, immunological potencies, safety, methods and timing of application, therapeutic efficacy, possible side effects, timing of use of the animal products after application. The report on the study of veterinary chemotherapeutic drugs should contain information on the toxicity, the specific activity, pharmacodynamics and pharmacokinetics, timing of use of the animal products after application
- stability data
- scientific reports, articles, application reports, reviews, expert reports can be submitted as information when registering foreign veterinary drug which was already registered in the country of origin
- shelf-life of the VMP
- composition of the veterinary drug with indication of the active substances and excipients
- instruction for use, technical normative legal act, in which the quality indicators of veterinary preparations should be established and methods of their control
- at registration of a foreign veterinary drug - the document establishing requirements to quality of a registered preparation and monitoring methods
- methods for detecting the residual quantities of the active substance in biological tissues (blood, urine) and products obtained from animals (milk, meat, eggs, etc.), which, according to the instruction, are allowed to use the preparation
- samples of a veterinary drug (one commercial batch)
- a manufacturer's document confirming the quality of the veterinary drug
- standard samples of active substances (when applied in control methods)
- document confirming the registration in the country of production
- GMP Certificate (if available)
- whole sales license
- labeling in Russian
- all documents need to be submitted in duplicate in Russian (Belarusian) language and certified by the applicant (manufacturer)

7.4 Kazakhstan

The registration process in Kazakhstan can be divided into five stages as shown in Figure 10. First, the applicant submits the dossier, samples and reference standards to the State Institution Committee of Veterinary Control (SICVC). Secondly, the SICVC prepares the decision protocol after the validation process, which takes max. 5 days. In the third stage, the National Reference Center tests within max. two years the submitted drug samples in accordance to the methods of control specified in the dossier specification and prepares an examination certificate. Then the State Institution Committee of Veterinary Control evaluates the test results, which are then considered by the Commission and approved by the Inspector of State Veterinary and Sanitary of Kazakhstan. In the final stage, the State Institution Committee of Veterinary Control makes a decision based on an act of the dossier examination and registration tests to refuse or to register a veterinary drug within max. seven days [42], [45].

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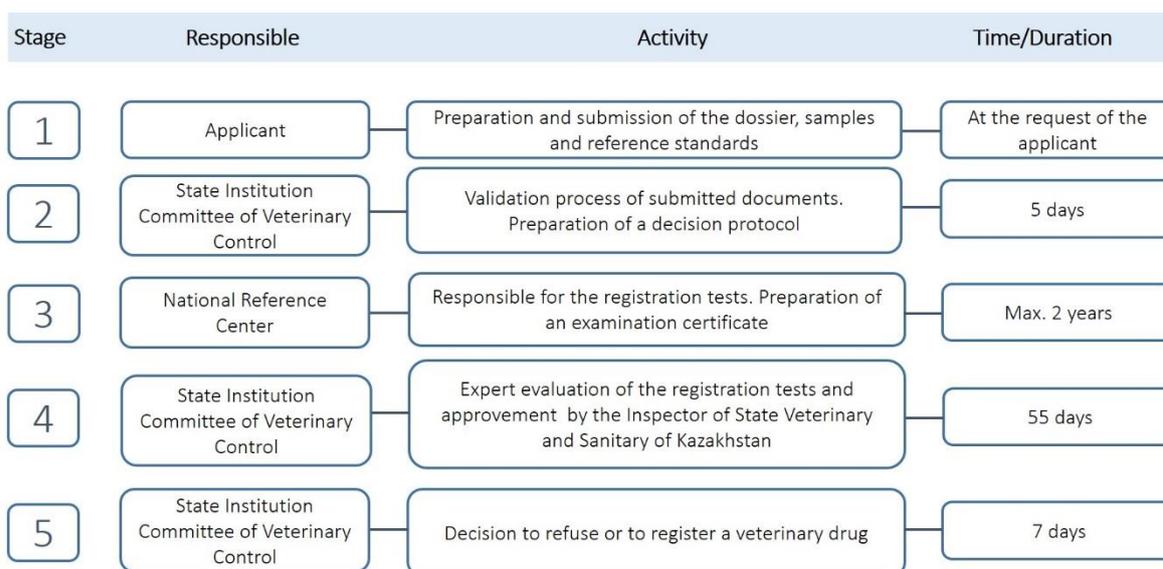


Figure 10: VMP(s) registration process in Kazakhstan

The following documents are required for the registration procedure in Kazakhstan [42], [45]:

- application form
- NTD or CTD format
- instructions for the manufacture and control
- instruction for the use
- a passport for production and control strains of microorganisms and for transplantable cell culture lines (for veterinary preparations)
- a document confirming the registration of a veterinary drug and a notarized copy of the agreement between the manufacturer and the patent holder of the components of the veterinary drug
- a report on the scientific research work, on the development, modification, improvement of the veterinary drug, including the protocol (acts) of laboratory and production testing
- GMP certificate

7.5 Kyrgyzstan

As shown in the Figure 11, the registration process in Kyrgyzstan consists of four stages. In the first stage, the applicant submits the dossier, samples and reference standards to the Center for Certification of VMPs at the Ministry of Agriculture and Melioration. In the second stage, the experts from the Certification Center validate the documents and submit them to the laboratory for further registration tests. Afterwards, a final decision about the registration is made by the Ministry of Agriculture and Melioration of Kyrgyzstan based on the reports and the results of the registration tests. The total time of the registration process is four months [48], [51].

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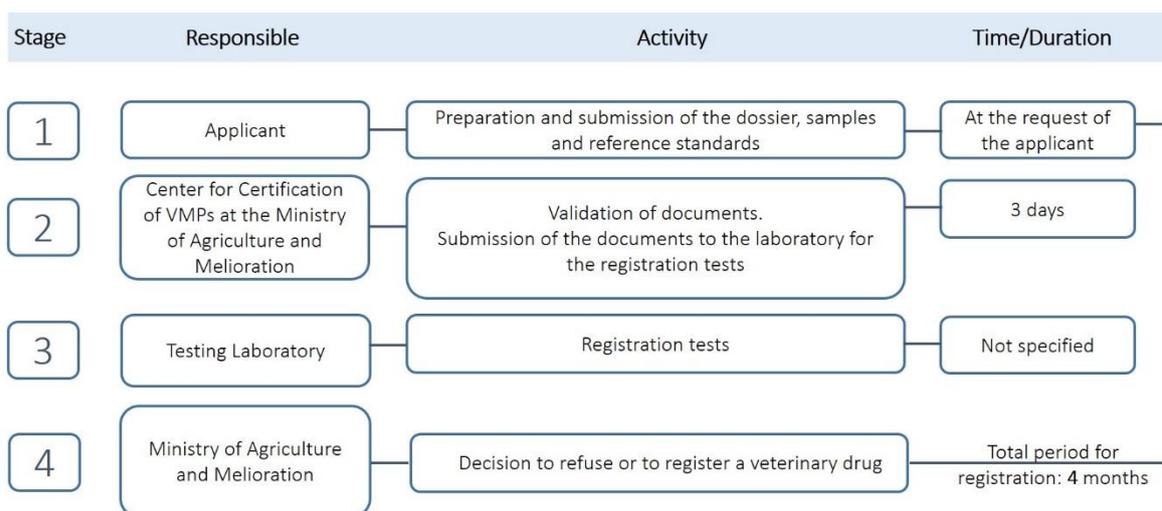


Figure 11: VMP(s) registration process in Kyrgyzstan

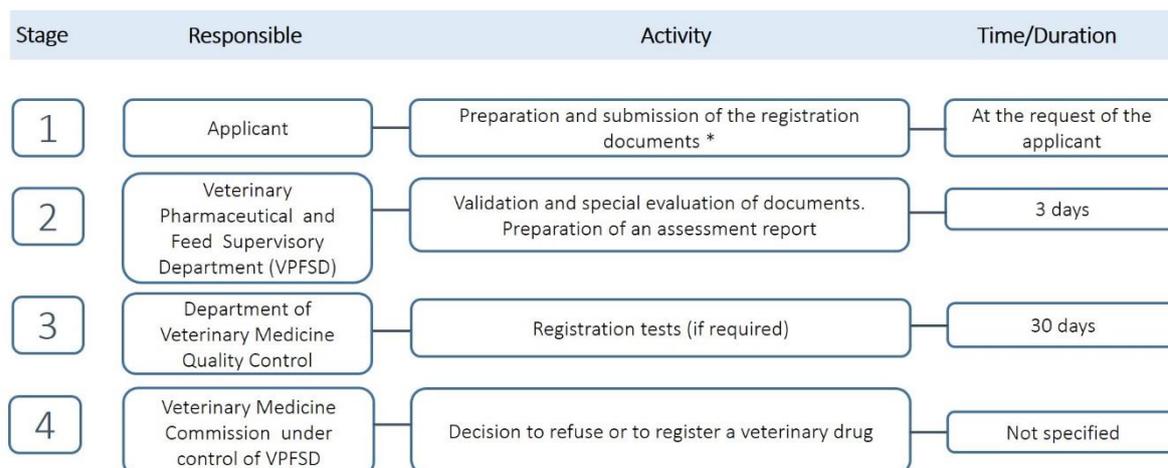
The following documents are required for the registration procedure in Kyrgyzstan [51]:

- application form
- certificate of registration of a VMP in the country of origin and in other country(s) (notarized copy)
- certificate of conformity for a medicinal product, APIs and excipients
- GMP certificate or other certificates on the quality management system (if it is available from the manufacturer)
- normative document used for quality control
- analytical documents on the study of drug stability
- pilot-industrial or technological regulations (for domestic producers)
- sample of standard package, labelling
- in the presence of patent protection for a preparation and / or trademark, a copy of the patent
- copy of the document certifying the registration of the trademark
- instructions for use, with the following information: information about the manufacturer; the name of the medicinal product; composition; pharmacotherapeutic group; indications and contraindications; side effects; mode of application; storage conditions; information, indicating the period between the last administration of the drug before the deadline for slaughter
- experimental data on the efficacy and safety of use in veterinary practice
- samples for 3-fold analysis with a certificate of conformity
- reference standards, standard samples of veterinary medicinal products and impurities with a certificate of conformity
- specific reagents (if necessary)
- list of documents submitted depends on the type and quality of the veterinary drug
- registration documents are submitted in triplicate

7.6 Moldova

In the first stage of the registration process, the applicant submits the dossier together with the samples and reference standards to the Veterinary Pharmaceutical and Feed Supervisory Department (VPFSD). The VPFSD validates the submitted documents in the second stage of the process within three days and prepares an assessment report. The Department of Veterinary Medicine Quality Control is responsible for the registration tests, which have to be done within 30 days. In the final stage, the Veterinary Medicine Commission under control of VPFSD provides its decision on the registration of the product to the applicant. VMPs registered by the EMA or in the EEA, or in Switzerland, USA, Canada, Japan and Australia do not need to be submitted for the quality

controlling by the Quality Control Laboratory. In this case the registration time does not exceed 60 days [55]. The registration process is illustrated in Figure 12.



*Samples for registration are only needed for the products imported from India.

Figure 12: VMP(s) registration process in Moldova

The following documents are required for the registration procedure in Moldova (according to the information available) [55]:

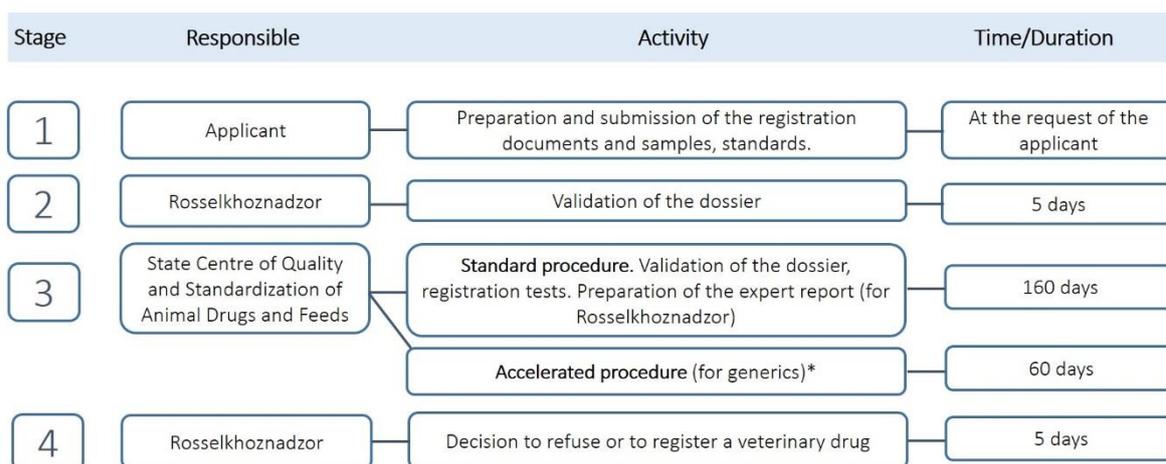
- application form
- samples of the drug (five original packages), models of active substances and quality certificates
- the application and documentation in CTD format in two copies, samples of drugs and active substances
- SPC, package, labeling and instruction
- reports of the experts on chemical-pharmaceutical and biological documentation, on toxico-pharmacological (preclinical) documentation, on clinical documentation
- chemical-pharmaceutical and biological documentation
- pharmaco-toxicological documentation
- clinical documentation
- CPP

7.7 Russian Federation

The registration process in Russian Federation can be divided into four stages as shown in Figure 13. First, the applicant submits the dossier, samples and reference standards to the Rosselkhoznadzor. The Rosselkhoznadzor validates the submitted documents in the second stage of the process within 5 days. The total period for the standard registration procedure including registration testing is 160 days. In case an accelerated procedure the registration procedure takes up to maximum 60 days.

In the final (for both the standard and the accelerated procedure) stage the Rosselkhoznadzor provides its decision on the registration of the product to the applicant which takes up to 5 days [61], [60]:

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Exceptions: biologics, insulin preparations and drugs registered for the first time in Russian Federation.

Figure 13: VMP(s) registration process in Russian Federation

The following documents are required for the registration procedure in Russian Federation [61], [60]:

- application form
- the legal address of the organization that produces the medicinal product; names of the medicinal product, including international non-proprietary name scientific name in Latin, main synonyms; the original name of the medicinal product, if registered
- documents confirming the registration of a medicinal product, if it is registered outside the Russian Federation
- list of components, their quantity and quality
- instructions for the use
- certificate of quality of the drug or supplements
- data on the production of a medicinal product
- methods of quality control of a drug or supplement
- stability data
- results of preclinical studies of the drug or supplement
- results of pharmacological and toxicological studies of the drug (toxicity, teratogenicity, mutagenicity, carcinogenicity, immunotoxicity, allergenicity, pharmacokinetics, MRL, literary review is possible)
- results of veterinary clinical trials
- mock-up, labeling, instruction for use
- samples from three batches (necessary to conduct three complete analyzes of the quality of the preparation in accordance with the requirements of the draft specifications), standard samples
- proposals for the price for a drug

7.8 Tajikistan

According to the little information publicly available for the registration of a VMP in Tajikistan an applicant submits the dossier together with the samples and reference standards to the State Veterinary Supervision Office of the Ministry of Agriculture. In total, the registration process takes up to 6 months. The State Veterinary Supervision Office makes then the final decision to refuse or to register a veterinary drug. The following Figure 14 shows an illustration of the process.

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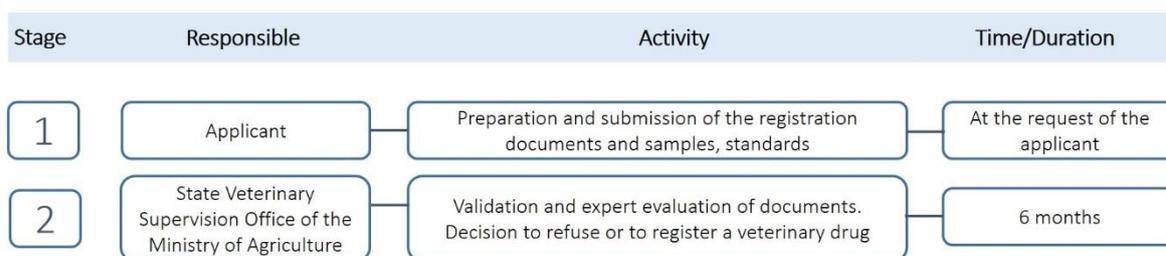


Figure 14: VMP(s) registration process in Tajikistan

The following documents are required for the registration procedure in Tajikistan [88]:

- application form
- SPC and leaflet
- manufacturing license
- registration in other countries
- GMP certificate
- NTD (qualitative & quantitative composition of the product, finished products specification and method of analysis, specifications and pharmacopoeia articles)
- certificate of analysis
- labelling and mock-up
- pharmacological and toxicological reports
- stability data
- short description of manufacturing process
- data on efficiency and safety of a product
- samples of a product (5 packs) and working standards

7.9 Turkmenistan

According to the little information publicly available, an applicant seeking for the registration has to submit the dossier together with the samples and reference standards to the State Veterinary Service under the Ministry of Agriculture. In total, the registration process takes up to 180 days including the registration tests. The State Veterinary Service makes the final decision to refuse or to register a veterinary drug (see Figure 15).

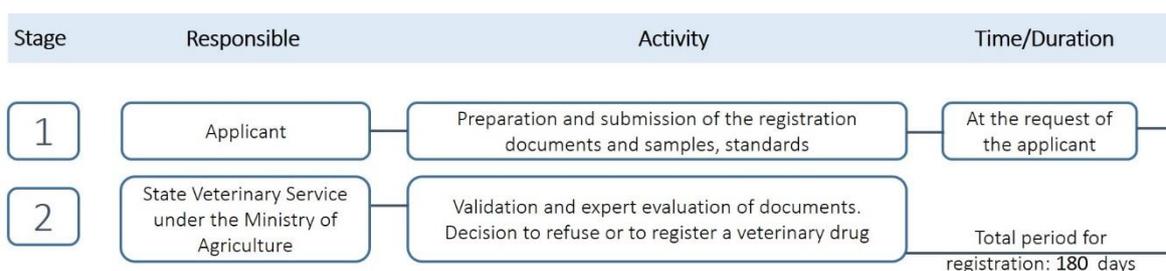


Figure 15: VMP(s) registration process in Turkmenistan

The following documents are required for the registration procedure [71], [72]:

- summary certificate of the preparation, containing brief summarizing information on each of the points listed below
- instructions for medical use (or clinical study)
- certificate of registration of a medicinal product in the producing country and in other countries (original or notarized copy)
- GMP certificate (original or notarized copy)
- normative documentation used for quality control of the drug

An Overview of the Marketing Authorization Process in the CIS Countries

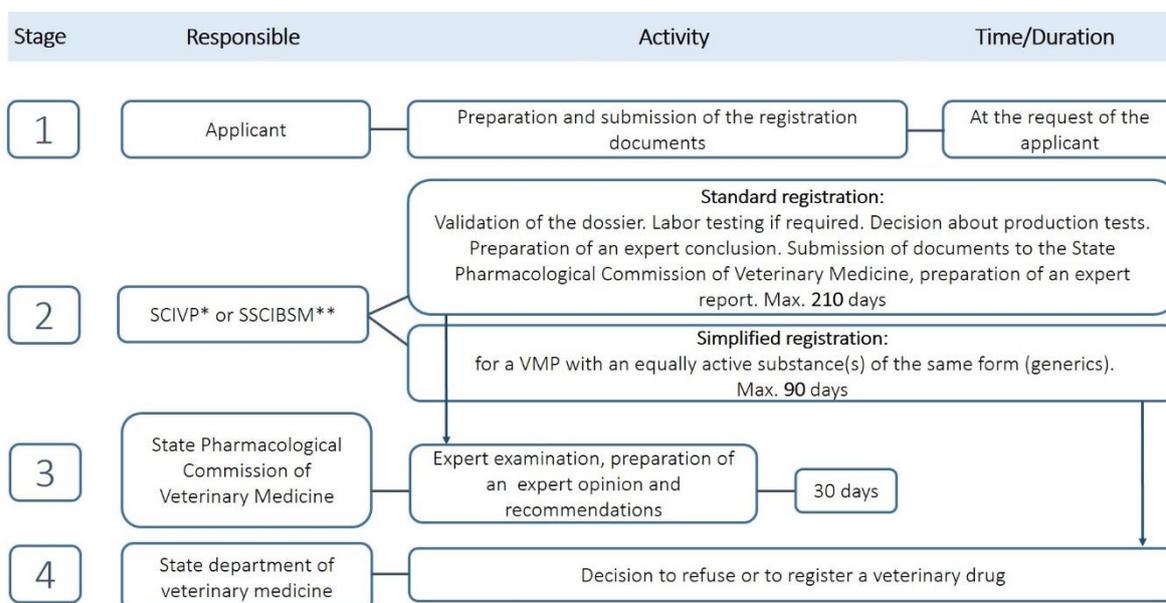
- report on the study of pharmacological (specific) activity, justifying all indications for use, specified in the instruction
- report on the study of toxicity (acute, subacute, subchronic and chronic toxicity)
- report on the study of specific types of action (carcinogenic, mutagenic, teratogenic, embryotoxic, allergic and locally irritating properties, etc.)
- clinical trials reports
- available data on pharmacokinetic studies of the drug in the experiment and clinic
- data on the use of the drug in the clinic and after its registration (copies of publications). It is necessary to provide only copies of publications about the preparation produced by the company
- generalized data on the side effects of the drug, including in comparison with other drugs used for the same indications
- samples of the preparation in the proposed package
- working standards in the amount necessary to conduct a 3-fold analysis

7.10 Ukraine

The registration process in Ukraine consists of 4 stages as shown in Figure 16. In the first stage, the applicant submits the dossier together with the samples and reference standards to the State Scientific-Research Control Institute of Veterinary Medicinal Products or in case of biological medicinal products to the State Scientific and Control Institute of Biotechnology and Strains of Microorganisms.

In case of a registration of generics, the simplified procedure can be applied which takes up to 90 days by bypassing the third registration phase. For this type of registration, the results of the corresponding studies (bioavailability, bioequivalence and therapeutic effect) confirming an identity of a generic drug with a reference drug need to be provided.

In the final (for both the standard and the simplified procedure), the fourth stage the State Department of Veterinary Medicine provides its decision on the registration of the product to the applicant.



*State Scientific-Research Control Institute of Veterinary Medicinal Products

**State Scientific and Control Institute of Biotechnology and Strains of Microorganisms

Figure 16: VMP(s) registration process in Ukraine

The following documents are required for the registration procedure in Ukraine [79]:

- production authorization (copy of license, registration permit, International Organization for Standardization (ISO) certificate, GMP certificate)
- guidelines for use or draft instructions (for domestic drugs)
- labeling, mock-up
- countries of registration of the drug
- chemical, pharmaceutical and biological documentation
- composition (qualitative and quantitative characteristics of components)
- technology of manufacturing veterinary drugs, the description of production
- control of APIs, excipients
- control of the final product (methods of control, certificates of analysis of produced 3 - 5 batches of the drug)
- stability
- pharmacological studies
- toxicological studies
- ecotoxicity
- preclinical documentation (pharmacology, tolerance of animals, resistance
- clinical documentation

7.11 Uzbekistan

As shown in the Figure 17, the registration process in Uzbekistan consists of four stages. In the first stage, the applicant submits the dossier together with the samples and reference standards to the Main State Veterinary Administration. The Main State Veterinary Administration validates the submitted documents in the second stage of the process within three days and forwards them to the Quality Control Laboratory and Scientific-Technical Council. The Scientific-Technical Council validates the documents and develops a protocol for the registration tests (if required). The Quality Control Laboratory performs in the next step the tests and prepares the evaluation report. In the final phase of the registration process, the Main State Veterinary Administration makes the decision about the registration.

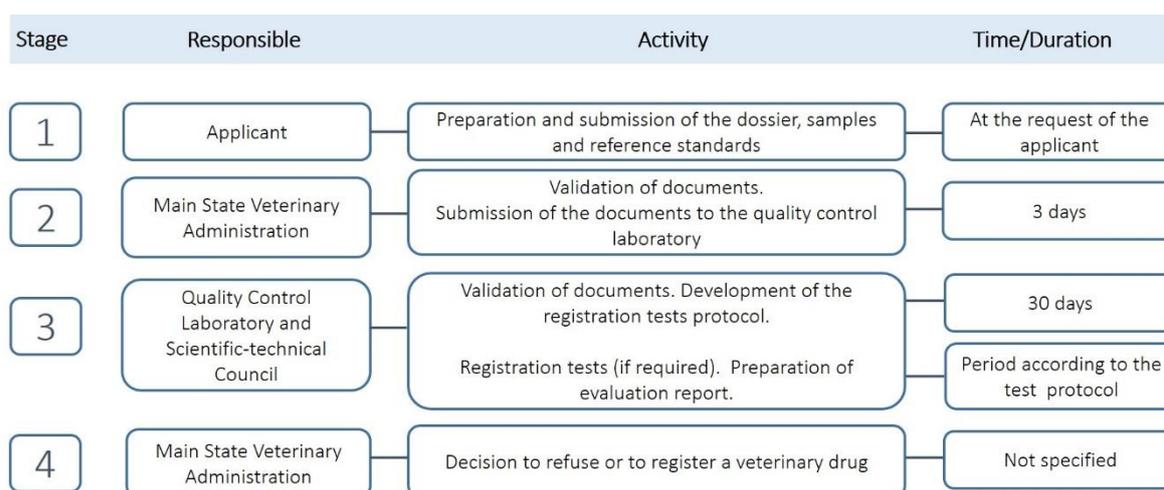


Figure 17: VMP(s) registration process in Uzbekistan

The following documents are required for the registration procedure in Uzbekistan [82], [83]:

- application form
- samples and standards
- composition of veterinary drugs (active substance(s), additives etc.)

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- two certified copies of normative documents in the field of technical regulation for veterinary medicinal products of domestic producers certified according to the established procedure and the locally valid standards TSh, TS, DSt, KSt, TSt and GOST described by the Uzbek Standard Agency [89]
- certified copies of normative documents in the field of technical regulation for VMPs of foreign producers, including CIS countries certified in the established order
- quality requirements and methods for the control of veterinary medicinal products, texts of relevant international or national pharmacopoeial articles
- draft instructions (manuals) on the use of veterinary medicinal products certificates of quality or certificates of conformity of veterinary medicinal products
- production related data of the veterinary medicinal products (technological instruction or regulations, production block diagram)
- results of tests on the efficacy, safety and stability of veterinary drugs
- reasonable information on the effectiveness, immunogenicity, virulence of veterinary biological preparations and strains of microorganisms used in their production (viruses, bacteria, fungi, etc.)
- samples of veterinary medicinal products in volumes sufficient for their technical testing specified in the documentation and their active substances, test systems and diagnostic kits
- documents confirming the state registration of imported veterinary medicinal products

8. Discussion

The registration of medicinal products is an important part of the regulation of medicinal products as it is prerequisite for legal distribution and sales in the marketplace. Despite some similarities in the registration of veterinary and human medicines, the veterinary medicine sector has major differences from the human medicine sector in different regards including multispecies (human medicine sector deals with only one species whereas the veterinary sector with multiple species), MRL studies and others. The veterinary pharmaceutical market is a tiny fraction (about 2%) of the size of the human one [90].

According to WHO data, only 20% (about 35-40 countries) out of 193-member states of the organization have a sufficiently effective control and certification system for medicinal products. 35% of the organization's members (about 55-60 countries) have practically no opportunities to establish such a system, and in the remaining 45% (about 90-100 countries) the existing mechanisms for regulating medicines are not effective enough [91]. As described in the previous chapters, the CIS countries differ massively in their geo-political characteristics, which implies that the member states fall into different of these groups. This explains in part why the amount of available information on the registration process varies from country to country.

Despite the differences among the CIS countries in the development of veterinary products and their registration procedures, the requirements concerning the registration dossier, registration tests procedure and labeling are quite similar. This can be explained by their common history as former states in the Soviet Union. As described earlier in this work, five out of eleven CIS countries have built an economical union (EUEU) and established a common registration procedure which came into force this year (2017).

The system of common registrations in the EUEA is therefore quite recent and was expected to be fully implemented in May 2017, but there are still many issues in operationalization and transition that need to be resolved in the next two to three years; for example, the quality control of medicines which is still not in accordance with the Pharmacopoeia of the Union.

This common procedure is similar to the registration system of the EU in many aspects. Both, the EU and the EUEA, offer several registration procedures for obtaining marketing authorization for veterinary medicinal products in all or at least several countries at once: the centralized, decentralized or mutual recognition procedures in the EU countries and the decentralized and mutual recognition procedures in the EUEA countries.

Taking the EU system as a reference for a well working registration system in a heterogeneous market consisting of many member states, the most relevant topics which need to be addressed by the CIS countries in the next years, mostly relate to the major differences between the systems nowadays. The essential differences in the registration system and post-authorization activities between EU and CIS countries are presented below and will close the discussion section of this work.

Submission system

In the EU, for the decentralized, centralized and mutual recognition procedure (by EMA) the electronic submission via the EMA e-Submission Gateway is applied and obligatory since the 1st January 2017. The submission of the registration dossier to the NCA of an EU country is possible via CESP, Eudralink or on CD/DVD.

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Compared to this, the NCAs of the CIS countries accept the registration dossier in paper form and on CD only. There is no electronic submission system.

Registration documents

In general, the local NTD is accepted for the registration in all CIS countries. In some CIS countries, a dossier in CTD format is also accepted. Compared to the CTD, the NTD has no formally defined structure. However, it usually consists of the following parts: administrative part (instructions for use, power of attorney, GMP certificates, etc.), quality information and information on safety and efficacy (clinical and preclinical studies).

In the EU, the registration dossier for veterinary medicines has to be in the NTA format, which is very clear structured and consists of four parts: Part 1: Administrative information and summary of the dossier; Part 2: Quality documentation; Part 3: Safety documentation (for food-producing animal products this comprises also the residue documentation); Part 4: Efficacy documentation.

Process of the registration

The key difference between the EU and CIS countries is the use of quality control in CIS countries instead of quality assurance applied in EU countries. In general, EU countries examine the quality, safety and efficacy of a medicinal product on the basis of the information submitted in the dossier. No quality tests by the certified laboratories belonging to the competent authority(s) are needed. Whereas, the registration process of a new medicinal products in the CIS countries includes registration tests in certified laboratories, as well as production tests and audits of the production place.

Legislation for the registration

There is a difference in the transparency of the legislation and authorization process within the CIS countries as well as between CIS and EU countries. As described in chapter 6, in Armenia, Kyrgyzstan, Moldova, the Russian Federation, Tadjikistan and Turkmenistan the veterinary medicinal products are controlled by the same law as human medicines. Whereas in Azerbaijan, Belarus, Kazakhstan, Ukraine and Uzbekistan, the medicines for animals are controlled by a law which is valid for the animal medicinal products only. In general, the legislative acts are presented in the local or the Russian language.

In contrast to this, all counties of the EU follow the same legislation pattern: the medicinal products for animals are controlled by a law which is similar but formally mostly separated from the law on human medicines (however, with the new regulation on VMPs, a clearer separation is expected). All European legislative acts presented online in English (and usually all other official languages of the member states) are very well structured and cover various aspects of the registration process from the scientific advice to the post-authorization control.

Duration of the registration process

The registration process in the EU takes about 270 days for the centralized procedure, 210 days for the decentralized procedure and about 210 + 90 days for the mutual procedure (plus stop clocks, if applicable). Compared to the EU procedure, the duration of the registration procedure in the CIS countries varies between member states. For the common submission procedure in the EAEU, the duration for the decentralized procedure is 210 days and 210 days + 90 days for the mutual recognition.

Another difference concerns the registration of generics. While the registration process for generics in the EU is accelerated and an exact timetable is defined, according to the publicly available

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information, an accelerated procedure is available only in some of the CIS countries (Armenia, Russian Federation and Ukraine).

Environmental risk assessment

The environmental risk assessment in accordance to the principles which are set out in Annex II to Directive 2001/18/EC should be applied as a part of NTA dossier in the EU and can constitute a reason for refusal of the marketing authorization. For the CIS countries, no clear regulation for the environmental risk assessment is available.

Quality documentation

In the EU, the GxP rules are harmonized and applied in all EU countries. As to CIS countries, the GxP rules are not implemented and GMP standards are not harmonized with the best global practice and ICH requirements in most of the member states.

The first standards for quality, safety and efficacy of pharmaceutical products in CIS countries were established during the Soviet Union time and were based on Soviet Pharmacopoeia and GOST standards (state standards). After the collapse of the Soviet Union, the countries formed national systems for the quality regulation, as for example a national pharmacopoeia, which is not harmonized neither with Ph. Eur. nor with USP. The Certificate of suitability of monographs of the European Pharmacopoeia (CEP) is also not accepted in the CIS countries.

Although the GMP / GOST Certificates (EU and EAEU) are not based on the same standards, the validity is equally three years.

MRL for veterinary drugs in foods

In the CIS countries there is a deficit of control of the residues of veterinary medicinal products in foods.

For instance, in Russia, two legislation acts, namely TR No. TC 021/2011 "On the safety of food products" and TR TC 033/2013 "On the safety of milk and dairy products", are available. Both define strict MRLs in milk and dairy products, but only for antimicrobial preparations of tetracycline group, chloramphenicol, penicillin and streptomycin. No additional restrictions on residues of other medicinal substances are defined at the moment. Nevertheless, getting more and more restrictive the legislation is now simply interpreted in an implicit way: "No additional restrictions for other medicinal substances" is interpreted as "no MRLs are defined", which again means that all medicinal substances not listed in the legislation have an MRL of zero.

To improve the situation in the CIS countries, the Rosselkhoznadzor appealed to the EEC with an initiative to amend the technical regulations of the CU, which regulate the quality and safety indicators for milk and dairy products, with regard to the inclusion of data on the MRL of drug residues in animal products.

Compared to this, in the EU, the legislation governing the design and implementation of residue monitoring is well organized. There are several legislative acts, namely:

- Directive 96/23/EC - Establishing residue monitoring plans, sampling frequency and range of substances to be tested for
- Decision 97/747/EC - Additional sampling frequencies for milk, eggs, honey, rabbits and game meat
- Decision 98/179/EC - Rules for taking official samples and accreditation requirements for official laboratories

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- Decision 2002/657/EC - Rules for the validation of analytical methods used in the residue monitoring plan

Post-marketing control

Different variation types and no possibility to group variations are good examples of differences between the EU and most of the CIS countries. In the EU, the post-authorization control is very well organized (EC No 1234/2008) and describes three principal types of variation: IA, IB, II. The variation guideline is comprehensive and valid for both veterinary and human medicines.

In general, CIS countries have an insufficient post-marketing control (e.g. no special guidelines for variations etc.). The requirements for the variations are usually presented in a law which states that the applicant must report any changes that are expected to be made to the registration documents and provide comprehensive information on the reasons for these changes and their effect on the effectiveness, safety and quality of the registered veterinary drug. This definition is too general and does not define precisely enough the information to be provided.

The pharmacovigilance requirements for veterinary medicinal products are also less regulated in most CIS countries compared to the EU. In general, no local Qualified Person for Pharmacovigilance is required and no procedure for literature screening is defined by national regulations. However, recently, the Russian Federation started to require PSURs and thus other CIS countries may be expected to follow this example.

Validity and renewal procedure for the registration certificate

There is similarity between CIS and EU countries in validation of the registration license. In both regions, a product license issued by the respective regulatory authority is valid for 5 years and a renewal application has to be submitted to extend its validity. The renewal application in CIS countries and the EU comprises a review of post-approval commitments (if any), variations, pharmacovigilance data and an updated benefit-risk assessment. If the product is found to be performing as expected and the benefit-risk is still fulfilling the requirements, an unlimited license will be granted.

Clinical studies

For clinical trials of veterinary medicinal products, the EU has adopted the Good Clinical Practice (GCP) guideline of the Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH), which provides guidance on the design and conduct of all clinical studies of veterinary medicines in the target species. The guideline is directed at all individuals and organizations involved in the design, conduct, monitoring, recording, auditing, the analysis and reporting of clinical studies in target species. It is intended to make sure that these studies are conducted and documented in accordance with the principles of GCP. The clinical trials done in other countries are accepted if they comply with the GCP / VICH requirements.

Compared to this, a lack of detailed requirements and GCP guidance for clinical trials is common to all member states of CIS. Therefore, in most of the CIS countries only local clinical trials are accepted.

9. Conclusion and Outlook

The structured presentation of the most relevant regulatory aspects and the competent authorities in the CIS member states in this master thesis provides a high-level picture of the multidimensional complexity of the topic when it comes to comparability. The regulatory systems for VMPs in the individual CIS member states and in the EU, have similarities and differences on several levels. An important driver for the complexity and lack of transparency in the laws and regulations of the CIS member states are differences in the level of economics and geo-political stability. Many of the member states are still in the midst of the transition from being a former member of the Soviet Union to an independent state when it comes to standards, regulations and especially the relation between the written law and its interpretation and implementation.

Nevertheless, a steady progress can be observed in the CIS countries. There are member states forming additional unions like the EAEU to bring the standardization to the next level. The overall tendency is clear: the regulation is becoming more transparent and strict leading to the need of a much deeper understanding by international companies intending to place their veterinary medicinal products on the increasingly important CIS markets. Therefore, a continuous monitoring of the developments within the regulations in this region is essential and will become even more relevant due to the increasing velocity of regulatory changes in the CIS region. The current (2017) political situation is an additional factor that is likely to complicate the process of placing medicinal products on the CIS markets for foreign companies in the next years.

Therefore, further and more detailed research on the current and planned changes concerning the marketing authorization process and regulation of veterinary medicinal products in the CIS countries is highly recommended.

10. Summary

The pharmaceutical industry for humans and animals is one of the most important components of the strategy of national and political security of any state, as well as one of the most profitable and rapidly developing segments.

One of the most dynamically developing regions in the world for pharmaceutical products is the CIS. Eleven CIS countries (Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russian Federation, Tajikistan, Uzbekistan, Turkmenistan and Ukraine) together occupy a territory of approximately 22.25 million square kilometers and have a population of 280 million people, which is the reason why the interest of pharmaceutical companies in expanding their business and product footprint across the CIS region has been constantly growing. To achieve this goal, the knowledge of the respective veterinary medicinal product regulations is indispensable.

The CIS countries are not equally successful in implementing market reforms and embracing a global competitive environment. Many of the CIS member states are still in the midst of the transition from being a former member of the Soviet Union to an independent state when it comes to standards, regulations and especially the relation between the written law and its interpretation and implementation.

Every CIS country has its own laws, standards, rules and practices, including the organization of business and product promotion. Despite the differences among the CIS countries in the development of veterinary products and their registration procedures, the requirements concerning the registration dossier, registration tests procedure and labeling are quite similar. This can be explained by their common history as former states in the Soviet Union.

The transparency of the authorization processes itself varies dramatically between the CIS member states. In particular, Moldova, Tajikistan and Turkmenistan are examples of CIS member states with hardly any publicly available information on the registration process. In contrast, Armenia and Ukraine do provide a very clear and easy to access information also in English language (registration process, legislation, normative documentations and others).

Within this master thesis, a comprehensive overview of the most relevant aspects of the marketing authorization processes for each of the CIS countries is provided. A comparative analysis of the registration system of the EAEU and EU, presented as part of the discussion section, shows essential differences in the submission system, duration of the authorization, registration documents, process of registration, legislation, quality assurance, quality documentation and post-authorization control.

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12. Declaration

Hiermit erkläre ich an Eides statt, die Arbeit selbständig verfasst und keine anderen als die angegebenen Hilfsmittel verwendet zu haben.

Hannover, 28.10.2017