e ISSN 2277 - 3290
Print ISSN 2277 - 3282

Journal of science

Pharmacy

www.journalofscience.net

STUDY ON THE REGULATORY REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE IN COMMON WEALTH OF INDEPENDENT STATES

Praneetha K*, Prakash B, Umasankar K, Alagusundaram M, Jayachandra Reddy P

Krishna Teja Pharmacy College, Chadalawada Nagar, Tirupati - 517506, Andhra Pradesh, India.

ABSTRACT

Dossier is a file document submitted based on the requirement of the drug approval process. It is a comprehensive scientific document used to obtained worldwide licensing approval of a drug by diverse health authorities. There are different requirements in different countries for registration of a product. Regulatory agencies require Pharmaceutical Dossiers to gain approval to market drugs. Dossier is a document file which has technical and administrative information. Pharma companies prepare dossier as per CTD / ASEAN CTD / non-CTD (country specific guideline).CIS countries follow their own country specific dossier format.

Keywords: CTD-Common Technical Document, ASEAN CTD, Non-CTD, CIS countries.

INTRODUCTION

In the recent years there has been a phenomenal growth in the pharmaceutical industry of Commonwealth of Independent States (CIS). In order to tap the vast potential existing in this region, India is chalking out a slew of initiatives to boost its exports to the region. The CIS region which once was part of erstwhile USSR (United Soviet Socialist Republic) had disintegrated in to several independent countries in the year 1991. Since then all the CIS nations have been focusing on building trade relations with various countries and India in particular especially in the field of pharmaceuticals and biotechnology. With the growing salience of India in the field of pharmaceuticals and biotechnology on the global stage, the CIS nations are keenly exploring opportunities for building trade relations with India. The Indian government is also equally interested in building a long-term relation with the CIS nations. "CIS is one region where India has huge potential for growth. At present we are taking part in various forums in CIS countries and conducting exhibitions, networking and touring trade delegations to explore the business opportunities and thereby improving our pharmaceutical and herbal exports to these countries", said Dr. P.V. Appaji, DG, Pharmexcil.

Among the CIS nations, India's pharmaceutical exports have been spread across Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Uzbekistan and Ukraine. Relations between India and the CIS nations have remained close and cordial since the Soviet era. However, bilateral trade and commercial relations have not grown commensurately with these newly formed countries. At present CIS constitutes only 1.2 per cent share in India's total exports. The main reason for this can be attributed to factors like distance, language barrier, inadequate transport facility and lack of information about business opportunities. Among the major trading partners, Russia, Ukraine, Kazakhstan, Uzbekistan, Kyrgyzstan and Belarus constitute more than 90 per cent of India's total bilateral trade with the CIS countries[1-3].

Growth prospects in CIS region

It is estimated that pharmaceutical sector in Russia and other CIS nations will have a double digit growth of around 10 to 11 per cent during the year 2012-2016. At present there is no national drug provision

Corresponding Author:- **Praneetha K** Email:- praneebpharm@gmail.com

insurance system in Russia and CIS countries. This means that 60-70 per cent of all pharmaceutical sales are paid out of the Individual pockets. Large, locally-owned pharmacy chains account for most of the market, but there are still a substantial number of small, independent pharmacies, particularly in the small and medium-sized cities. A national insurance scheme is under development. The hospital drug provision system, meanwhile, is more advanced and will continue to develop in the future.

A key factor for pharmaceutical companies to succeed in CIS region would be to balance their portfolio of branded generics, branded ethical products and over-the-counter (OTC) drugs that can be sold primarily at the retail level. A solid pipeline of innovative products aimed at the developing reimbursement and insurance schemes is also critical. Moving in this direction, the world's leading drug maker Takeda is aiming to capture the CIS markets by enriching their product portfolio with ground-breaking drugs that can compete for state money in the national and regional level hospital tenders. In order to achieve future growth within these markets, India needs to explore its opportunities not only the low cost quality generics portfolio but also move in with innovative drugs.

The growth in health care demands has been reflected due to growing sales of pharmaceutical and medical products in the country. For instance the sales by legacy Nycomed in CIS region for the six months ended March 2012 were ¥30.9 billion—a year-on-year increase of 10.9 per cent. This was driven by strong sales growth in Russia, which accounts for around 70 per cent of the overall regional market. In 2011 Nycomed was the fastest growing foreign company in Ukraine and ranked among top three companies in the industry in Kazakhstan. To capture the greater pie in the CIS region, Indian companies needs to move flexibly in meeting market needs and adapting to the changing regulatory environment by changing their regulatory structure and business model as required and by maintaining a product portfolio tailored to local market needs[4].

Among the emerging markets in CIS region, Georgia is playing a vital role in the production of pharmaceuticals. Already, pharmaceutical exports from Georgia have grown at an average 47 per cent over the past six years, and Georgia's own demand for pharmaceuticals has experienced rapid growth, averaging 16 per cent. Georgia offers a strategic base for production, with easy access to surrounding CIS countries and other major emerging markets such as the Middle East. Georgia is a leader in the CIS and emerging market owing to the congenial business environment it provides. Also making Georgia an attractive strategic base for pharmaceutical production are its low costs of energy and labour (average wages approximately 30 per cent less than in nearby Turkey) and an established pharmaceutical production industry totaling US $ 48 million in 2011.

As the pharmaceutical sector in CIS region is still at a nascent stage the Indian pharma industry can capture the business opportunities in these countries and can form partnerships and collaborations with the local players to build a long- term relationship to boost the future growth of Indian pharma.

Indian focus towards CIS

Though initially India's focus in the CIS markets was limited, today many Indian pharmaceutical companies have developed trade relations and are exporting herbals, formulations and APIs to the CIS markets. Many of the top companies such as Cipla, Orchid, Dr. Reddy's, Ranbaxy, Wockhardt, Panacea Biotech, Lupin, Aurobindo, Pirmal health care, Ankur Drugs and Pharma, Glenmark, Nectar lifesciences, Emcure, Claris Life Sciences, Divi's, Hetero, Arch Pharmalabs and Matrix have gained substantially by their exports to CIS nations.

If India's drugs, pharmaceuticals and fine chemicals exports are analyzed region- wise for the year 2010-2011, North America holds the major chunk of 25 per cent with Rs. 11717 crores of exports while Europe and African markets hold the next position with 19 and 17 per cent respectively. The share of Middle East countries is of Rs. 3693 cores and LAC countries is Rs. 3183 crores which accounts to eight and seven per cent share respectively. The CIS countries accounted for export revenue of Rs. 3017 crores during 2010-2011 which is about six per cent share when compared to the other regions. On the whole, total exports for the year 2010-2011 constituted 58 per cent of formulations, 41 per cent bulk drugs and one per cent herbals. Since most of the CIS nations lack the right kind of technical infrastructure and expertise required to set up and develop quality pharmaceutical products, they rely on India to manufacture a large bulk of products needed by healthcare or pharmaceutical companies.

"We are witnessing a robust growth in Russia and have considerable presence in the country. We are also in the process of tapping the markets in other CIS countries. We are slowly planning to acquire small to mid-sized brands to boost our business there. We are also looking aggressively at in-licensing products from multinationals and other companies, of course, our organic pipeline is also playing out. There is good opportunity in the Russian market and we are doing our best to address the opportunity," said Satish Reddy, MD Dr. Reddy's, while sharing his view on their business plans in Russia and CIS region.

Kazakhstan has steadily increased their imports of formulations from India from Rs. 110.79 crores in 2007-08 to Rs. 169.85 crores in 2008-08 and Rs. 223.40 crores in the year 2009-10. Similarly is the case with Uzbekistan, the import figures from India have increased

from Rs. 88.79 crores in 2007-08 to Rs. 109.00 crores in 2008-09 to Rs. 141.00 crores in the year 2009-10.

The bulk drug and herbal markets have been at low with slightly dwindling figure. The other two countries Kyrgyzstan and Ukraine have accounted a slight slowdown in the import of formulations from India.

Russia have shown an increase of $85.35 million from $333.11 in 2008-09 to $ 418.5 million in 2010-11, of all the pharmaceutical components, formulations are the major exports to Russia accounting for $ 402 million during the year 2010-11. Apart from Russia, other nations are also slowly catching up in all the three segments of bulk drugs, formulations and herbals.

Trade boosters between India and Russia

In order to give a push to the pharmaceutical trade between Indian and Russia, during the year 2010, two countries had agreed to exchange of technical know-how for production of pharma products including bulk drugs, serums, biosimilars, vaccines etc and have agreed to participate in setting up of enterprises for scientific and production capacity. According to official sources, the visiting Russian delegation led by Russian minister for Industry and Trade, Victor B Khristenko and the senior officials of the Department of Pharmaceuticals led by secretary, Mukul Joshi have also agreed on a draft MoU to encourage collaborations in the areas of trade, industry, joint ventures and R&D in the pharma and bio-pharma sectors. They have also agreed to exchange of information on the issues of regulation in the export/import of pharmaceuticals products including Active Pharmaceuticals Ingredients etc[5,6].

In 2010, an agreement on Russia-India Biotech Network (RIBN) was also signed in Andhra Pradesh in the presence of Chief Minister K Rosaria. RIBN is a dedicated on-line platform to effectively facilitate collaboration between the Russian and Indian biotech communities.

Challenges faced by Indian firms

Though the Indian pharmaceutical industry is catering to the demands of the CIS nations by understanding their requirements and accordingly developing drugs under contractual manufacturing, in the recent times the Indian firms are increasingly facing challenges and hurdles at the CIS countries. It is high time for the Indian firms and the government to change policies accordingly and adapt to the international standards and explore all possibilities to tap the highly potential CIS markets.

The main challenge for Indian firms is going to be the recent drug policy which the Russian government had brought in intends to bar all the pharma and biotechnological imports from India. They want to reach the target of at least 70 per cent of self sustainability by the end of 2016. But in current scenario this may not be a possible to bar the imports from India or any other country, As Russian government is supporting the local manufacturing of Pharmaceutical products than importing, the Indian companies may have to change their strategy from exporting to setting up a world class manufacturing facilities in Russia/Georgia. The recent changes in the Russian policy are discouraging the Indian exports to that country. Russian regulatory agency is keep updating their regulatory standards at very fast pace which makes it difficult to Indian manufacturers to catch up due to the language barriers.

In Azerbaijan, due to political reasons, the government has stopped giving permission for approvals to the Indian companies. Kazakhstan is also becoming rigid and it is expecting USFDA level documentations for approvals. Countries like Ukraine have so far depended on Indian companies but it is also very rapidly moving towards regulated markets and is also part of PIC/S.

Registration Procedure in Russia

State registration of medicines

As earlier, the state registration of medicines with the special register is prerequisite to their circulation on the market (production, wholesale and retail selling, application, etc.). Roszdravnadzor, an executive body responsible for control and supervision of health care and social development, is in charge of medicines' registration and maintenance of the register. Registration with the register must be preceded by the following stages:

1. Preclinical trial of a medicine
2. Applying for state registration of a medicine
3. Document expertise for obtainment of permission to carry out clinical trial
4. Ethic expertise
5. Clinical trial
6. Medicine's quality expertise and expertise of medicine's benefit/risk ratio.

If the creator of a medicine properly fulfills its obligation on each stage and achieves positive results in trials, Roszdravnadzor registers the medicine. The New Law obliges all state authorities and medical organizations to carry out the whole procedure for the time period no more than 210 days (from submitting an application to registration of medicines). It is necessary to outline the most important features of each stage.

Preclinical trial of a medicine

Preclinical trial may be organized in scientific research organizations, educational institutions possessing necessary equipment and skilled staff. While conducting preclinical trial the testing organization shall apply scientific estimation methods to obtain evidence of security, quality and efficiency of the medicine. Preclinical testing must be organized in accordance with the Good Clinical Practice, internationally recognized rules for clinical trials.

Similar to other countries they were extended throughout Russia by the respective resolution of internal executive body which is charge of health care (the Russian Ministry of Health Care).

Submitting an application for state registration of a medicine

All proceedings following preclinical trial take place after submitting an application by the creator of the medicine for its state registration coupled with supplements as required by New Law. After consideration of documents provided Roszdravnadzor within 5 days issues requests addressed to the expert organizations whereby asks them to conduct the following expertises:

1. Document expertise for obtainment of permission to carry out clinical trial;
2. Quality expertise.

If the applicant submits the document improperly, Roszdravnadzor refuses to issue expertise request.

Document expertise for obtainment of permission to carry out clinical trial

This expertise is one of 3 expertise carried out with respect to the medicine (along with quality expertise and expertise of medicine's benefit/risk ratio). It is shall be carried out by the authorized state budget institution. From the documents expertise are exempted those medicines which have been allowed to be applied in Russian more than 20 years ago and with respect of which it is impossible to organize bioequivalence research and those which have been checked in multi-central clinical trials (including trials in Russia).

Ethic expertise

Ethic expertise, i.e. expertise of possibility to organize clinical testing is carried out to issue a conclusion concerning ethic reasonableness to organize clinical testing of the medicine. It must be conducted by the ethic council to be established at Roszdravnadzor. Currently another institution - the ethic committee – functions at Roszdravnadzor. It established in accordance with Law No. 86 and performs duties similar to those to be performed by the ethic council as stipulated by New Law. Once New Law comes into force, it will become clear whether a new body will be formed or the ethic councils' duties will be delegated to the ethic committee.

Clinical trial of the medicine

Then the applicant shall submit the results of document expertise and ethic expertise to Roszdravnadzor. The latter considers them and decides on possibility or impossibility to issue permission for clinical trial. It must notify the applicant on the decision made. Clinical trial may be organized only on those conditions that Roszdravnadzor positively decided the issue and the applicant filed with it the respective request.

As earlier, clinical trials shall be carried out only in those medical organizations, which are accredited by the Ministry of Health Care pursuant to the Good Clinical Practice. At the same time, New Law regulates the entire procedure in more details in comparison with Law No. 86, stipulates rights and obligations of patients and medical staff involved in clinical trials. In particular, there are special measures to guarantee and protect the rights of patients participating in clinical trial such as voluntariness of participation in clinical trial, keeping patients informed on the medicine's characteristics, confidentiality of information related to participation in clinical trial, prohibition to carry out clinical trial with participation of certain categories of individuals. All conditions of clinical trial shall be stipulated in the agreement between the producer of the medicine which obtained permission to carry out clinical trials and the medical organization conducting them[7].

Medicine's quality expertise and expertise of medicine's benefit/risk ratio

After clinical trials the new medicines shall go through the following expertises:

1. Medicine's quality expertise, i.e. expertise of quality control methods recommended by the medicine's producer and expertise of medicine's samples provided by the producer with use the above methods;
2. Expertise of medicine's benefit/risk ratio. Both expertises shall be carried out by the authorized state budget organizations grounding on the results of clinical trial.

The overall period for conducting both expertises shall not exceed 110 days after the expert organization received requests for them. Roszdravnadzor examines the results of the expertise’s and check compliance with requests. Then it decides on registration or refuse to register the new medicine. The reasons for refusal may be conclusion of Roszdravnadzor on one of the following:

- Results of prior tests and trials do not confirm effectiveness of the medicine
- Risk of damage to health exceeds effectiveness from use.

Roszdravnadzor's refusal may be challenged in court. Repeated filing for registration of the medicine earlier not completed or obtained refusal in registration is treated as registration of a new medicine and shall go through the entire procedure from the beginning. It is obligatory regardless changes in characteristics, name, etc.

This is how the new framework for registration of medicines according to new Federal Law "On Circulation of Medicines" looks like. Experts in pharmaceutical industry, lawyers, state officials and others expect that a number of sub legislative acts will follow[7], and they will allow better understanding new

regulations as a whole and working in the new framework accordingly.

1. Submission the dossier to MOH
2. Within 5 working days MOH considers our dossier and gives the decision regarding carrying out of expertise
3. Applicant submit the POA to FGBU with request to calculate of samples quantity
4. Laboratory calculates the samples during 2 weeks (as maximum) and we can see the calculation in regmed.ru
5. Within 15 working days after receiving the letter for assignment to pharmaceutical examination on hands (!) applicant submit the samples, reference standards and columns to the laboratory.
6. Pharmaceutical examination should be finished after 110 working days from the moment of samples submission. After that MOH give conclusion about registration of product or rejection.
7. Since January 2013 we don't receive the queries from MOH during registration process. We can receive the queries together with registration of product. It means that we have to submit the answers on MOH queries (as variations) within 30 days after receiving the approved documents (MD, LPD, MA) on hands.

Fees Structure

1) For examination of documents for obtaining authorizations to conduct clinical trials of the drug for medical use, and ethical expertise in applying for state registration of the drug - 75 000 rubles.

2) For examination of drug quality and expertise of the expected benefit to the possible risks of the drug for medical use in its state registration - 225,000 rubles.

3) For examination of drug quality and expertise expected benefit ratio for possible risk of drug use that is allowed for medical use in the Russian Federation for more than twenty years, the state registration of the drug - 30 000 rubles.

4) For changes in the instructions for use of the drug for medical use - 50 000 rubles.

5) For changes in the composition of the drug for medical use - 100 000 rubles.

Regulatory Challenges in Russia

- Powerful lobby in favor of local manufacturer
- Unclear regulatory guidelines pertaining to new regulation
- Pre-Clinical and Clinical data requirements for Generics
- Delay in CT protocol approval & CT study performance
- Overall slow MA process/ Increased registration timeline
- Russian Government has approved the concept to Develop Russian Pharmaceutical Industry by 2020. It means, more stringent regulations for imported products
- Preference to domestic generic products
- Local manufacturing in Russia has increased due to discriminatory policy between Locally manufactured and imported pharmaceuticals
- Compliance with approved ND
- Post registration amendment –submission and approval pathway unclear

Pharmaceutical and Health care report for 2013

Russia

Russia's pharmaceutical market continues to be one of the most attractive in the Emerging Europe region, primarily due to its sheer market size, growing economy and increasing government investment in healthcare. The main transformation in the market over the last decade has been the growth of the state 's role , both in establishing an industrial policy and investing in production for the first time since the end of the Soviet Union. Key drivers of growth for pharmaceuticals include programmes to fund medicines for specific segments and disease groups, as well as a pledged universal medicines insurance system due to be put into place later in the decade. Russia's recent World Trade Organization accession should drive improvements in the country's intellectual property (IP) environment, and enforcement in particular, which has been conspicuously lacking[8].

Headline Expenditure Projections

Pharmaceuticals: RUB 756.97bn (US$24.81bn) in 2013 to RUR842.81bn (US$25.73bn) in 2014; +11.2% in local currency terms and 10.4% in US dollar terms.

Healthcare: RUB 2,907.89bn (US$89.47bn) in 2013 to RUB3, 195.48n (US$97.57bn) in 2014; +9.9% in local currency terms and +9.1% in US dollar terms.

Risk/Reward Ratings

Russia's Pharmaceutical Risk/Reward Rating (RRR) score for Q213 is unchanged from the previous quarter. This is the case for all other countries in BMI's proprietary system, which ranks pharmaceutical markets according to their attractiveness to multinational drug makers. A minor re-weighting of one of the RRR components is being implemented to improve the tool, and the adjusted scores for all markets will be published in the Q3 2012 updates of the Pharmaceuticals & Healthcare reports. Russia has a RRR score of 58.0 out of 100.0, making it the second-most attractive pharmaceutical market in Emerging Europe.

Key Trends and Developments

Statements by senior officials in the first quarter of 2013 indicate that the government will seek to shift more of the burden of healthcare funding from the central budget to the contribution and insurance-based system.

From 2014, higher earning Russians, who contribute part of their salary to the compulsory health insurance programme (OMS), will be forced to pay more into the fund. Russians earning more than RUB 512,000 (US$16,670) annually will be forced to pay an additional 5.1% on any income above the threshold. According the Ministry of Healthcare, this will raise an additional RUB102bn (US$3.32bn) in 2014, and RUB113bn (US$3.68bn) in 2015.

At the same time, the president made effective regulations that have increased contributions from the state to the State Insurance Fund. In 2013, the fund could have revenues of RUB1.06trn (US$31.8bn) and in 2015, the fund is expected to have total revenues of RUB1.44trn (US$43.2bn). Essentially, the move will reduce the amount of funding directed through the Ministry of Healthcare. While the move is logical in terms of setting up a theoretically more means tested and ring fenced funding mechanism for costly medical programmes. People fears that past Corruption problems in the healthcare insurance system could reoccur.

In a boost for over-the-counter (OTC) drug makers and pharmacy retailers, the government said in March 2013 that it would not support proposed legislation to ban the advertisement of medicines, Remedium reported. As a result, the amendments to Russia's advertising law have been withdrawn. In a statement, the government said the proposed limits would make it difficult for consumers to find out about medicines, even in pharmacies. The withdrawal of the legislation appears to have put an end to two years of efforts to ban all medicines advertising. In other good news for OTC producers, Russia's Minister of Industry and Trade said that a compromise 'will be found' in talks with the Ministry of Healthcare and other parties to create a list of medicines that can be sold for the first time in supermarkets and other non-pharmacy retailers.

Russian newspaper Vedomosti reported in March 2013 that two of Russia's largest pharmaceutical retail chains, Pharmacy Chain 36.6 and A5 have taken steps toward a possible merger. According to the report, two of the founding shareholders of 36.6 intend to buy back a stake in their company originally disposed of during the financial crisis to service debts owed to a wholesaler, SIA International. These were later sold to a fund, Hi Capital. A merger with A5, which was spun off by X-5 Retail, the country's largest food retail chain, would create by far the largest retail chain in the country. 36.6 pioneered the development of national chain pharmacies in Russia from the late 1990s and, with production subsidiary Veropharm, became the first domestically listed pharmaceuticals group in 2004. Both A5 and 36.6 face a tight competitive environment with the rapid development of Rigla, now reportedly the largest national chain by turnover and backed by Protek.

Registration Procedure for Ukraine

Ukraine Regulatory Process

- State registration of medical products is carried out on basis of application and respective document package submitted to the State Drug Inspectorate by the applicant liable for manufacturing, safety and efficacy of medical products.
- The list of document to be attached to the application is specified by the Procedure for state registration of medical equipment and medical products as approved by the Resolution of the CMU dd. 09.11.2004 # 1497. The State Drug Inspectorate shall examine submitted documents within max. 90 days.
- In order to conduct necessary expert examinations and testing of medical products the State Drug Inspectorate shall engage expert institutions and give the applicant respective referrals.
- The applicant shall choose expert institutions taking into account profile of the expert institution and the list comprised and approved by the State Drug Inspectorate. Results of the expert examination conducted by the expert institution shall be stated in a protocol (report, conclusion) which shall be sent to the State Drug Inspectorate or handed over directly to the applicant.
- Based on motivated conclusion of expert institutions the State Drug Inspectorate shall accept testing of the medical product. It shall be noted that time of such testing shall not be included to the term of expert examination conduction.
- Based on consideration of expert examination (testing) report and recommendation of the advisory body in the sphere of state registration the State Drug Inspectorate shall make a decision on registration of or refusal in registration, if conclusion on safety, quality and efficacy of the product is not confirmed. Within 10 days the State Drug Inspectorate shall inform the applicant in writing.
- Based on decision on state registration medical products shall be included to the State Register of Medical Equipment and Medical Products kept by the State Drug Inspectorate, and the applicant shall receive a certificate on state registration of a medical product. The certificate can be accompanied annexes with information on modification of medical products and component products.
- The certificate is valid for up to 5 years, after expiration of its term import to Ukraine, sale and use of medicinal products is possible only after its re-registration.

Re-Registration

Medicinal products can be used in Ukraine for five years following state registration unless the MOH (if previously unknown hazards are revealed) takes the decision to completely or temporarily ban their use. The

application for re-registration of a medicinal product must be submitted to the SE Centre no earlier than one year but not later than 90 calendar days before the expiry of the registration certificate.

The legislation stipulates that re-registration of medical products is carried out in accordance with the procedure stipulated for state registration.

Variation

The variation of medical products shall be carried out in case of:

- Change of name and location of the owner (manufacturer, developer) medical Products presentation.
- Transfer of rights for manufacturing of medical products to other manufacturer.
- Changes in manuals for medical products.
- Changes in requirements of normative documentation as to medical products.
- Revealing of contra indications and restrictions in use of medical products.
- Use of new materials contacting with human body during manufacturing of medical Products.

Key stages and timing

Materials that are submitted for state registration for a medicinal product are examined under the following stages:

- Primary examination.
- Preliminary examination.
- Specialized examination.

The period of examination must not exceed 210 calendar days following the official date of receipt of a full and independent application for medicinal product registration. The period of examination must not exceed 90 calendar days from the official date of receipt of the application for other types of, such as, for example, application on similar biological medicinal product, active substances.

The period of examination does not include the time taken by applicants to update materials or the time taken for additional examinations (tests).

Fees

The fee for state (re-)registration of a medicinal product (except radioactive medicinal products, diagnostic agents, simple or complex (galenical) preparations from herbal raw materials) is:

- EUR100 per pharmaceutical form.
- EUR10 for each subsequent dose.
- EUR10 for each subsequent package of the medicinal product.

The fee for state (re-)registration of radioactive medicinal products, diagnostic agents, simple or complex (galenical) preparations from herbal raw materials, preparations with donor blood or plasma is:

- EUR25 for one item.
- EUR5 for each subsequent dose.
- EUR5 for each subsequent package of the medicinal product.

Applicants must also pay the cost of an expert evaluation under the agreement on conducting examination, entered into between the SE Centre and applicants. The cost depends on the type of application and is the same for all entities (residents and non-residents).

Post-marketing commitments and pharmacovigilance obligations

A manufacturer/applicant must submit information to the SE Centre about the medicinal product's adverse effects under MOH Order on the Approval of the Procedure for Monitoring of Side Effects of Medicinal Products Permitted for Medical Use No. 898, 27 December 2006.A manufacturer/applicant must also submit regular updated safety reports to the SE Centre.

Regulatory Challenges

- Compliance with EU Norms (BE and other data)
- CTD documents
- GMP inspection
- Labeling in Ukrainian /Russian
- Each batch has to pass at laboratory

Check List for Product Registration in Ukraine

Module 1: Administrative documentation[9]

1.1 Table of contents.

1.2. Application with micro dossier. Micro dossier consists from following parts:

- Document that confirms rights of the person to represent Application (Power of Attorney, Letter of Authorization etc.)
- Copy of manufacturing license
- GMP certificate
- Certificate of the Pharmaceutical Product (CPP)
- Copy of registration certificate from manufacturer's country (can be replaced with CPP) and list of countries where the product is registered
- Written consent of the Marketing Authorization Holder (if different from Applicant) of the registration certificate from manufacturer's country (or from CPP) to register product's on behalf of Applicant
- CV of the person responsible for pharmacovigilance in Ukraine
- CV of the person responsible for quality of medicinal product (batch recall purposes etc.) in Ukraine
- Brief scheme of manufacturing process with mentioned manufacturing sites

- Copies of conclusions/reports of the Authority that performed inspection of the manufacturing site
- Copies of trademark protection certificate, registered brand name, patent
- Guarantee letter that intellectual rights of the third party are not infringed
- Guarantee letter that pharmacological vigilance system in Ukraine will be established and maintained.

1.3. Summary of product characteristics (SmPC), labelling and instructions for medical use:
1.4. Information about the independent experts:
1.5 Specific requirements for different types of applications.
Annex to Module 1. Environmental risk assessment

Module 2: CTD summary (As per EU CTD)
Module 3: Quality (As per EU CTD)
3.2.S. Active substance(s):
3.2.P. Finished medicinal product:
Module 4: Preclinical studies reports (As per EU CTD)
Module 5: Clinical studies reports (As per EU CTD)

Pharmaceutical and Health care report for 2013
Ukraine

Ukraine's legislative environment is continuing to hamper access to market for foreign drugmakers and cause tensions between authorities and the industry. Despite being postponed by three months, to the start of March 2013, the import licensing law No 5038-VI will undoubtedly create severe drug shortages and the withdrawal of drug companies from Ukraine, as it stipulates that all pharmaceutical importers must obtain a special new license. Given factors such as the lack of resources to implement the issuing of new licenses, we believe it will also exacerbate social unrest and add fuel to the already tense political situation. We expect the law to eventually be watered down, given that key trading partners will certainly lodge complaints to the World Trade Organization (WTO), while domestic drug makers that rely on imported active pharmaceutical ingredients will apply pressure at home.

Headline Expenditure Projections
Pharmaceuticals: UAH29.51bn (US$3.65bn) in 2012 to UAH32.93bn (US$3.58bn) in 2013; +11.6% in local currency terms and -0.2% in US dollar terms.
Healthcare: UAH104.89bn (US$12.98bn) in 2012 to UAH114.01bn (US$12.39bn) in 2013; +8.7% in local currency terms and -4.5% in US dollar terms.

Risk/Reward Ratings

Ukraine's Pharmaceutical Risk/Reward Rating (RRR) score for Q213 is unchanged from the previous quarter. This is also the case for all other countries in BMI's proprietary system that ranks pharmaceutical markets according to attractiveness to multinational drug makers. A minor re-weighting of one of the RRR components is being implemented to improve the tool, and the adjusted scores for all markets will be published in the Q313 updates of the Pharmaceuticals & Healthcare reports. Ukraine has an RRR score of 49.4 out of 100, making it the 12th most attractive pharmaceutical market in the Central and Eastern Europe (CEE) region, which covers 20 key countries.

Key Trends & Developments

In February 2013, the Ukraine Ministry of Health announced plans to draft regulations for enabling the Cabinet to authorize compulsory licensing. This law would enable the Ukrainian government to force patent-holders to license out their products to domestic drug makers in the event of a national health emergency or if there is a pressing medical need. Similarly, domestic drug makers can appeal to the state and request a rate reduction for licensing patented drugs. This would effectively give the government the power to set a royalty rate for patented drugs in the event of a dispute between domestic drug makers and foreign multinationals. We believe the potential for abuse of this provision is high, especially if initiated by politically connected domestic drug companies.

Ukraine's pharmaceutical market has been significantly affected by the amendments to the list of prohibited narcotic drugs, psychotropic substances and precursors, which came into force on December 12 2012, after being approved from the Cabinet of Ministers. As the new list includes substances that are extensively used in the manufacturing of various pharmaceuticals, the health ministry and the State Committee for Drug Control have been urged to revoke the new changes and provide additional explanation on the sale of drugs containing prohibited substances across the country.

Registration Procedure for Kazakhstan

The procedures of export of pharmaceutical products to the Republic of Kazakhstan include obligatory registration of the products at Ministry of Health (Committee of Pharmaceutical Control).
The procedures to get the state registration are following:

1. Submission of the Application on registration of pharmaceutical products with enclosed confirmation of payment of state registration fee to the Committee of Pharmaceutical Control. The Application initialed by the head of the Department of the Committee of Pharmaceutical Control transfers to the department of experts' work of National Center of Expertise of the Ministry of Health of RK (NCE).
2. The Applicant concludes the contract with NCE for carrying out expert examination.

3. The specialist of expert department accepts the Application for state registration, checks the availability of contract for expert examination, than issue the referral for payment. The referral for payment initials by specialist and head of department and goes to the account department. The account department prepare invoice within 5 working days.
4. After check the registration dossier, samples and standards of pharmaceutical products validity of samples, standards and storage mode all these goes to small achieve. The certificates of analyze is require for the given standards and samples. (In case of failure to submit the all necessary document within 30 day the company must inform in written form about the term to NCE, otherwise the given pharmaceutical product will get a refusal in state registration.
5. Primary expertise of documents and materials carry out within 20 days for registration of pharmaceutical product and 10 days in case of re-registration from the day of money in payment to the account of NCE. In case of positive finding of primary expertise the product sends for analytic expertise.
6. Analytic expertise conducts out within 50 days, immune biological products - 70 days.
7. Special pharmaceutical expertise conducts by Pharmacopoeia Center (including expertise of technological normative document on control of quality and security, 40 days) within 90 days.
8. Special pharmacological expertise conducts by Pharmacological Center within 90 days after getting the positive decision of pharmaceutical expertise.
9. After passing of complete cycle of expert's work the conclusion on safety, efficiency and quality of pharmaceutical product prepares within 20 days if registration, 10 days if re-registration On the bases of the order of Chairman of Committee of Pharmaceutical Control the registration card issues.
10. The applicant receives following:

- Registration card with term within the given pharmaceutical product is allowed for medical usage on the territory of the Republic of Kazakhstan.
- Confirmed technical limitation document on control of quality and safety of the product.
- Confirmed guidance for medical usage of pharmaceutical product in Russian and Kazakh languages.
- Confirmed package and labels design
- Second exemplar of registration dossier

Fees

4966.5 USD/strength for single component, 3410.30 USD for additional strength, USD 108.82 for additional pack, 7514.20 USD/strength for double component for additional strength.

Timelines: 12 Months

Dossier Requirements

- Dossier in CTD format (as per EU CTD)
- Labeling in Russian/English
- Annex 1 for application form and Annex 4 stating list of documents
- Notarized COPP
- Related Substance data from 3 batches
- Product Development report
- Quality overall summary (QOS)
- Clinical and Non Clinical summaries and overview
- Full shelf life stability data
- Specification compliance with EP or State Pharmacopoeia

Regulatory Challenges

- Lengthy Drug Registration
- Weak IP laws
- GMP Compliance
- Specification compliance with State Pharmacopoeia (prepared based on EP)

Pharmaceutical and Health care report for 2013 Kazakhstan

Kazakhstan remains the most attractive pharmaceutical market in Central Asia, in terms of the overall regulatory environment and ease of doing business compared to neighbouring countries. The domestic market is constrained by the relatively small size of the population and daunting infrastructure challenges. Pending World Trade Organisation (WTO) accession, expected as soon as this year, as well as Kazakhstan ' s membership in the Customs Union (CU) with Russia and Belarus should drive continued improvements in regulation and harmonisation, assuming the contradictions of membership in the two groups (such as common external tariffs) can be ironed out. Meanwhile, foreign investors have acquired controlling stake in the three largest pharmaceutical manufacturers - Chimpharm, Nobel and Global Pharm - and have committed to expanding manufacturing capacity and creating Good Manufacturing Practice (GMP)-complaint facilities. The government announced in February 2012 that it would review options for new pricingregulations to address high prices, a process that both domestic and foreign players will be watching closely.

Headline Expenditure Projections

Pharmaceuticals: KZT245.63bn (US$1.65bn) in 2013 to KZT273.2bn (US$1.86bn) in 2014; up 12.5% in local currency terms and 12.9% in US dollar terms.

Healthcare: KZT1331.5 (US$8.96bn) in 2013 to KZT1, 498.9 (US$10.23bn) in 2014; up 14.2% in local currency terms and 14.6% in US dollar terms.

Risk / Reward Rating:

Kazakhstan's Pharmaceutical Risk/Reward Rating (RRR) score for Q213 is unchanged from the previous quarter. This is also the case for all other

countries in BMI's proprietary system that ranks pharmaceutical markets according to attractiveness to multinational drugmakers. A minor re-weighting of one of the RRR components is being implemented to improve the tool, and the adjusted scores for all markets will be published in the Q312 updates of the Pharmaceuticals & Healthcare reports. Kazakhstan has a RRR score of 47.1 out of 100, making it the 14th most attractive pharmaceutical market in Emerging Europe [9].

Key Trends and Developments

In February, Ministry of Health and competition officials gave the strongest signals yet that they would contemplate "regulation of prices" of medicines , with the head of the Kazakhstan Agency for Protection of Competition saying an analysis of the market found several areas of concern that were driving higher prices. The timeline for the enaction of future pricing regulations is unclear, although BMI is concerned as to whether the development and eventual enaction of such controls will be done in consultation with the domestic and international pharmaceutical industry. BMI has previously outlined areas of concern, such as the fragmented wholesale sector and a lack of clear rules for doctors pharmacists regarding providing patients with the cheapest generic alternatives. However, rather than setting prices or margin limits, we hope that the Kazakhstani officials look at root causes of high prices and contemplates steps that would foster greater competition and the development of more efficient private-sector delivery, such as modern format chain pharmacies[10,11].

The Kazakhstani authorities have claimed continued sustained falls in maternal and infant mortality rates in the country, along with death from circulatory system ailments and tuberculosis, which if correct suggest that sustained increases in healthcare spending in recent years, coupled with economic growth, have made significant inroads in the broader epidemiogical situation following a period of decline in the 1990s after the collapse of the Soviet Union that reversed over the past 15 years. The Ministry of Health released statistics in February that showed maternal mortality rate had decreased by 3.7 times and infant mortality by 25% between 2010 and 2012, according to a transcript of a parliamentary speech published on the website of the ministry. Mortality from circulatory diseases fell by 20% over the same period. The ministry cited the success of the Salamatty Kazakhstan (Healthy Kazakhstan) initiatives, the main state-driven strategy for increasing access to healthcare. In addition, healthcare remains a priority of the president's so-called "Kazakhstan 2050" programme, a blueprint for the long-term development of infrastructure and key social services over the coming decades.

Fig. 1. Regulatory process flow chart for Russia

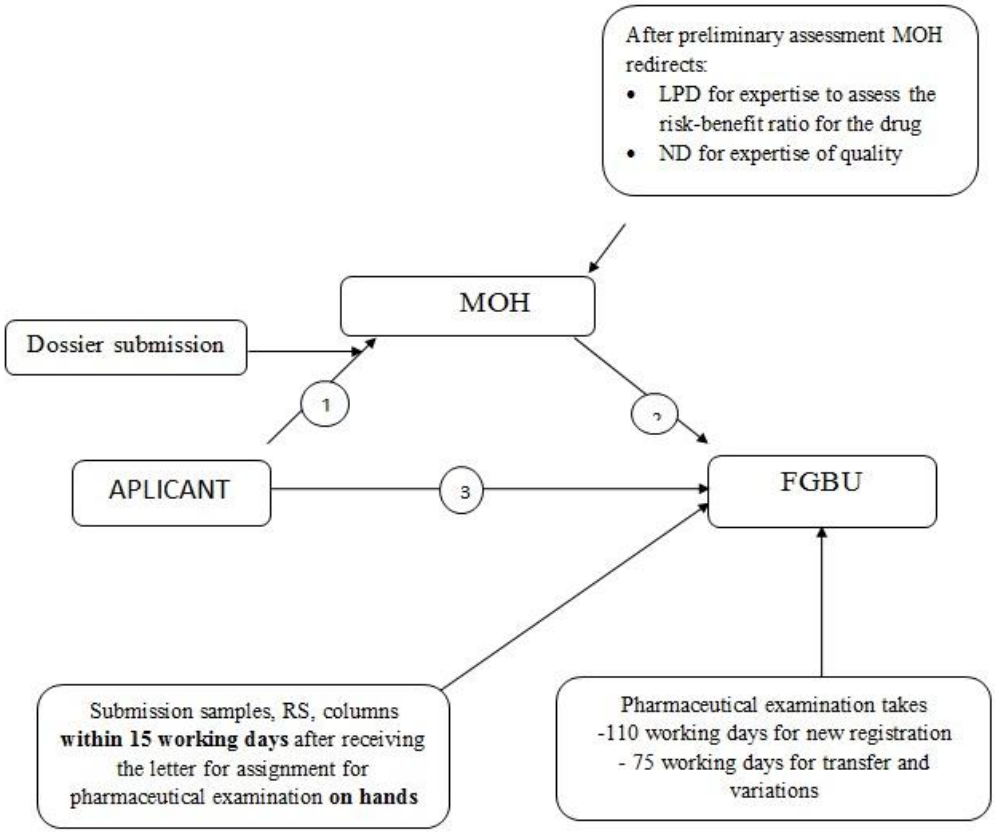

Fig. 2. Regulatory Flow Chat for Ukraine

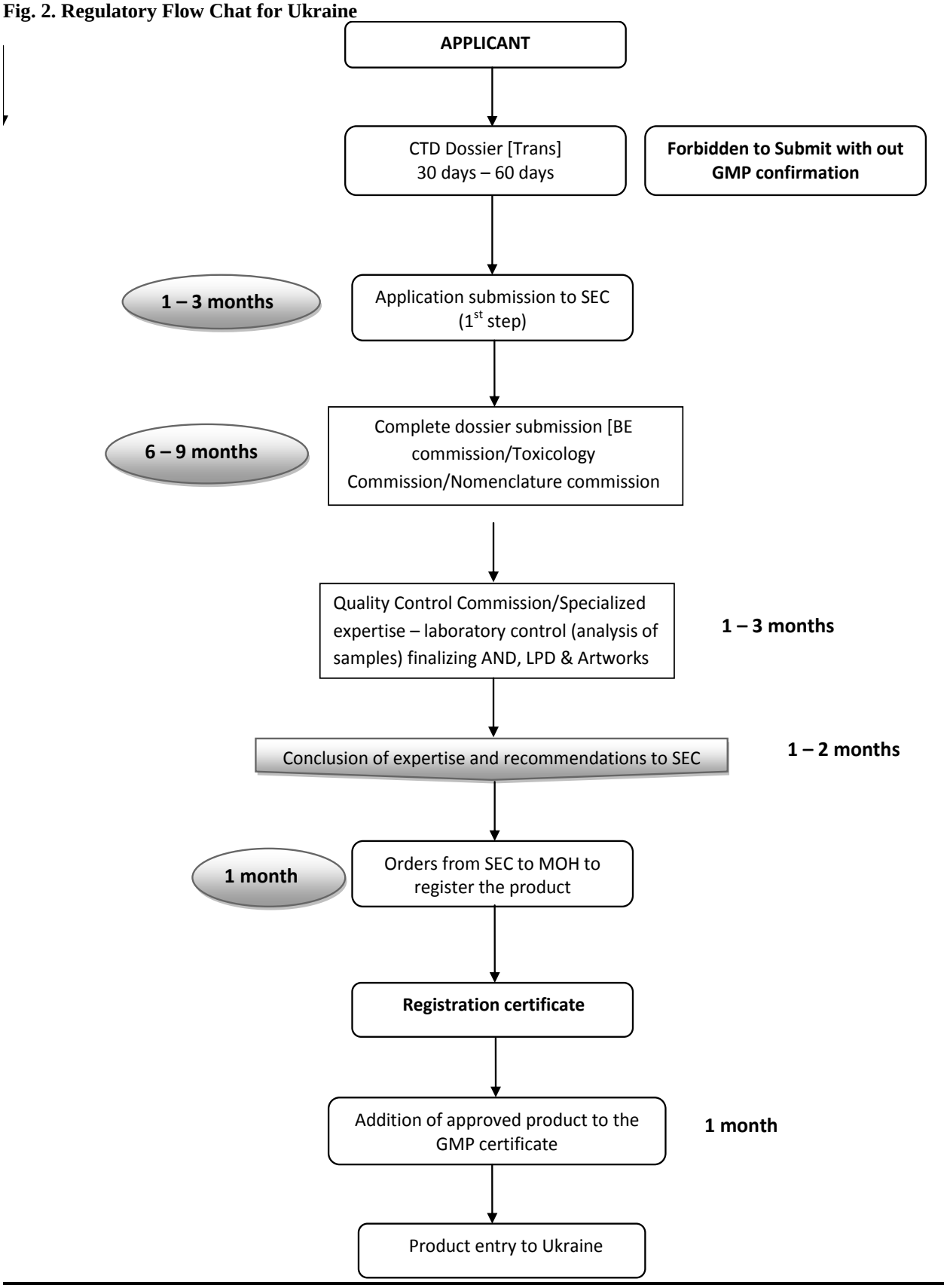

Fig. 3. Regulatory Process Flow Chart for Kazakhstan

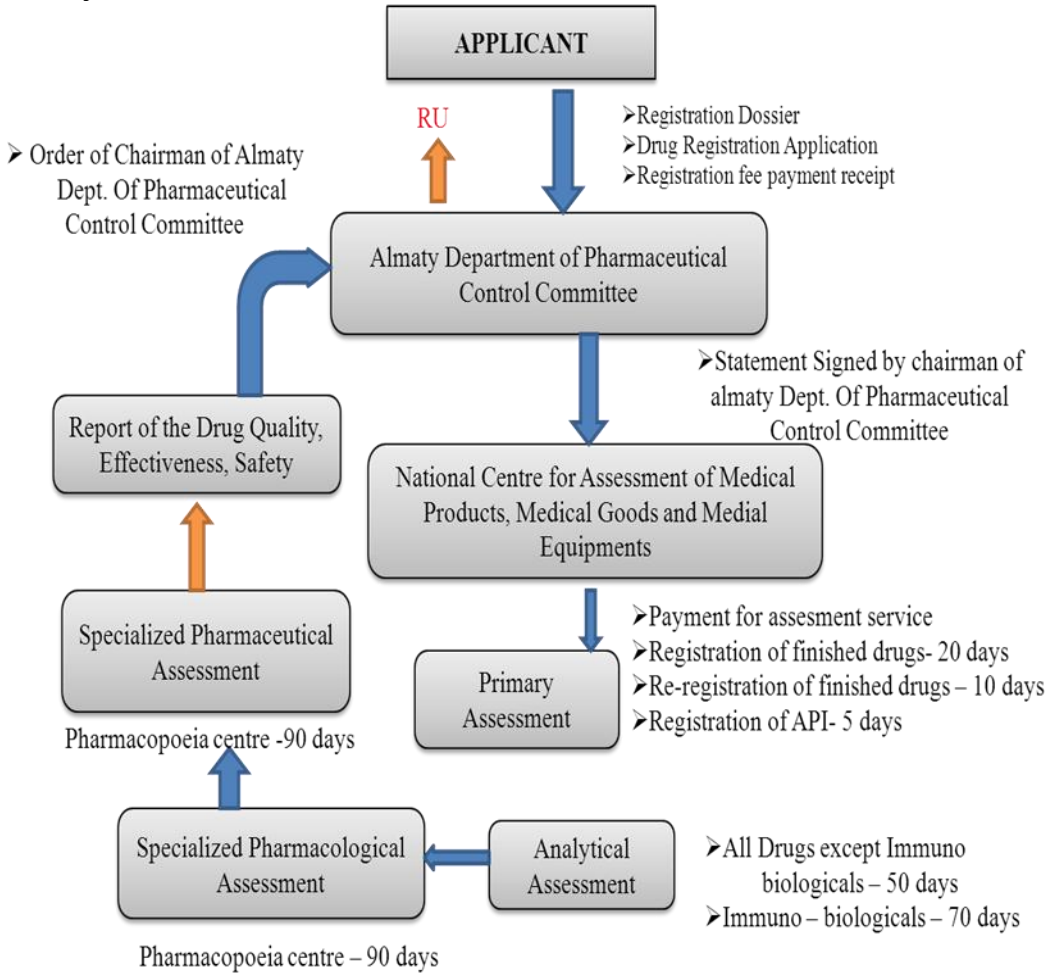

Table 1. Check List for Product Registration in Russia
Ministry of Health and Social Development of the Russian Federation

S.No	Content	Remarks
Module 1: Administrative Documents		
1	Application form	
2	CPP*(Certificate of Pharmaceutical Product)	Legalized by Russian Embassy or Apostilled copy (common CPP is acceptable)
3	Certificate of GMP issued by the authorized body in the country of origin	WHO GMP certificate (notory or Apostilled copy)
4	API-GMP certificate	Legalized by Russian Embassy or Apostilled copy
5	Registration status in other countries	Certificates need to be provided upon request only. Generally not required
6	Instructions for use of specialists and patients	
7	Qualitative and Quantitative composition of the Medicinal product	By listing pharmacopoeial reference for each excipients and API
8	Artworks in Russian Language-5copies	
Module 2: CTD Summary (As per EU CTD)		
Module 3: Quality (As per EU CTD)		
Module 4: Preclinical studies reports (As per EU CTD)		
Module 5: Clinical studies reports(As per EU CTD)		

Note: CPP*: We can submit FSC, Mfg.LIC &GMP certificate instead of CPP

Table 2. Checklist for Kazakhstan
National Drug Expertise Centre, Ministry of Health (NDEC), Kazakhstan

S. No.	Content	Remarks
I	**Module - 1**	
	Administrative information:	
1.1.	**General documentation**	
1.2	Application for state registration in due form (in hard copy and electronic format)	
1.2.1	Certificate for Pharmaceutical Product as recommended by WHO. In the absence of CPP, the following document must be submitted: Certificate (registration certificate) for registration in the country of production (notarized)	Common CPP also accepted and it should be legalized by the Embassy of Kazakhstan or apostilled by the Govt of India.
1.2.2.	GMP certificate (WHO) (indicating the date and results of the last inspection) (notarized)	it should be legalized by the Embassy of Kazakhstan or apostilled by the Govt of India.
1.2.3.	Certificate authorizing free sale (export)	Free Sale Certificate should be on said brand name intended to get registration.
1.2.4.	**Certificate of Origin (for domestic producers)**	This is applicable if the manufacturing plant is located in Kazak.
1.2.5.	License Agreement (Contract) on production right (up to the expiry of the patent for the original product)	it should be legalized by the Embassy of Kazakhstan or apostilled by the Govt of India.
1.2.6.	Information on registration of medicinal products in other countries with number and date of the registration certificate (or copy of certificate or registration certificate)	
1.3.	Summary of product characteristics, labeling and instruction for use	SmPC to be provided in English. Based on SmPC, Our representative should develop LPD in both Russian and Kazak languages.
1.3.1.	Brief description of the medicine approved in producer country	
1.3.2.	Labeling	Should be developed in Kazak and Russian languages (Bi-lingual languages)
1.3.3.	**Instructions for medical use**	LPD should be developed in both Russian and Kazak languages.
1.3.4.	Colored consumer package design (in the absence of commercial package samples – a specimen in the final primary package without final labeling. The final primary and secondary packages must be submitted additionally before the end of expert examination on paper and electronic media in 1:1	Artworks should be developed in both Russian and Kazak languages.
1.4.	Information on experts	
1.4.1.	Information on quality expert	As per EU CTD
1.4.2.	Information about preclinical data expert	As per EU CTD
1.4.3.	Information on clinical data expert	As per EU CTD
1.5.	Specific requirements for different types of applications	As per EU CTD
1.5.1.	Information on bibliographic applications in accordance with Article 4.8 (ii) Directives 65/65/EEC	As per EU CTD
1.5.2.	Information abbreviated application in accordance with Article 4.8 (iii) Directives 65/65/EEC, 1 and 2 paragraph	As per EU CTD
1.6.	Assessment of potential hazard to the environment (Annex to the Module)	As per EU CTD
1.6.1	Medicinal products containing or derived from genetically modified organisms	As per EU CTD
1.7.	Information concerning the applicant's pharmacovigilance in Kazakhstan	Applicable for only for Re-registration products

1.7.1	A detailed description of pharmacovigilance and risk management systems for medical use of the medicinal product offered by the applicant	As per EU CTD
1.7.2	Document proving that the applicant has a qualified person responsible for pharmacovigilance in the Republic of Kazakhstan at its command	Should be from the representative of KZ.
2	**Module 2 Summaries**	As per EU CTD requirements only, In the substance part at least minimum data should be provided.
2.1.	Contents of Modules 2.3.4.5	
2.2.	Introduction to CTD	
2.3.	General quality report	
2.4.	Pre-clinical data review	
2.5.	Clinical data review	
2.6.	Pre-clinical data report	
2.7.	Clinical data report	
	Module 3 Quality	
3.1.	Contents	*The minimum amount of information that must be provided in section 3.2.S. If certain parts of documentation are not included in the materials the applicant must indicate the reason in the appropriate place and under appropriate title. Letter of Access (LOA) is not required as KZ is not a member of EU. Three batches valid COA's required to be provided. Primary and Secondary packing materials – Valid COAs required to be provided.
3.2.	Body of Data	
3.2.S.	Medicinal product (for medicines that contain more than one drug substance information must be supplied in full on each of them)*	
3.2.S.1.	General information*	
3.2.S.1.1.	Name*	
3.2.S.1.2.	Structure*	
3.2.S.1.3.	General properties*	
3.2.S.2.	Production*	
3.2.S.2.1.	Producer*	
3.2.S.2.2.	Description of manufacturing process and its control*	
3.2.S.2.3.	Control of materials	
3.2.S.2.4.	Control of the critical stages and intermediate products	
3.2.S.2.5.	Validation of the process and / or its assessment	
3.2.S.2.6.	Manufacturing Process development	
3.2.S.3.	Characterization *	
3.2.S.3.1.	Proof of structure and other characteristics	
3.2.S.3.2.	Impurities*	
3.2.S.4.	Medicinal product control*	
3.2.S.4.1.	Specification*	
3.2.S.4.2.	Analytical methods*	
3.2.S.4.3.	Validation of analytical methods	
3.2.S.4.4.	Series Analysis *	
3.2.S.4.5.	Justification of specification	
3.2.S.5.	Reference materials or substances	
3.2.S.6.	System Packaging / closure *	
3.2.S.7.	Stability*	
3.2.S.7.1.	Summary regarding stability and conclusions *	
3.2.S.7.2.	Report on post-study of stability and commitment to stability *	
3.2.S.7.3.	Information on stability*	
3.2.P.	Medicinal product	
3.2.P.1.	Description and composition of the medicinal product	
3.2.P.2.	Pharmaceutical Development	
3.2.P.2.1.	Components of the medicinal product	
3.2.P.2.1.1.	Drug Substance	
3.2.P.2.1.2.	Excipients	
3.2.P.2.2.	Medical product	
3.2.P.2.2.1.	Formulation development	

3.2.P.2.2.2.	Excesses	
3.2.P.2.2.3.	Physico-chemical and biological properties	
3.2.P.2.3.	Manufacturing process development	
3.2.P.2.4.	Packaging / closure system	Valid COAs required to be provided.
3.2.P.2.5.	Microbiological characteristics	
3.2.P.2.6.	Compatibility	
3.2.P.3.	Production	
3.2.P.3.1.	Producer (s)	
3.2.P.3.2.	Batch formula	
3.2.P.3.3.	Description of manufacturing process and process control	
3.2.P.3.4.	Control of the critical stages and intermediate products	
3.2.P.3.5.	Validation of the process and / or its assessment	
3.2.P.4.	Excipients Control	
3.2.P.4.1.	Specifications	
3.2.P.4.2.	Analytical methods	
3.2.P.4.3.	Validation of analytical methods	
3.2.P.4.4.	Justification of specifications	
3.2.P.4.5.	Excipients of human and animal origin	
3.2.P.4.6.	New excipients	
3.2.P.5.	Drug regulation	
3.2.P.5.1.	Specification (s)	
3.2.P.5.2.	Analytical methods	
3.2.P.5.3.	Validation of analytical methods	
3.2.P.5.4.	Series analysis	Valid COAs required to be provided
3.2.P.5.5.	Characteristics of impurities	
3.2.P.5.6.	Justification of specification (s)	
3.2.P.6.	Reference samples and substances	
3.2.P.7.	Packaging / closure system	
3.2.P.8.	Stability	
3.2.P.8.1.	Summary and conclusion about stability	
3.2.P.8.2.	Post-registration stability studies and liabilities in relation to stability	
3.2.P.8.3.	Stability information	
3.2.A.	Supplements	
3.2.A.1.	Technical facilities and equipment	
3.2.A.2.	Safety assessment of foreign microorganisms	
3.2.A.3.	New excipients	
3.2.R.	Regional information	
3.3.	Copies of used literature sources	
	Module 4. Pre-clinical (nonclinical) studies reports	
4.1.	Contents	
4.2.	Surveys	
4.2.1.	Pharmacology	
4.2.2.	Pharmacokinetics	
4.2.3.	Toxicology	
4.3.	Copies of used literature sources	
	Module 5. Reports on clinical studies and (or) trials	
5.1.	Contents	As per EU CTD
5.2.	List of all clinical trials in the form of tables	
5.3.	Clinical trials reports	
5.3.1.	Reports on biopharmaceutical studies: bioavailability studies report; bioavailability and bioequivalence comparative studies report; invitro-invivo studies correlation report; report on analytical and bioanalytical methods	

5.3.2.	Research reports on pharmacokinetics in the use of human biomaterials: a report of studies of binding to proteins - binding to proteins studies report; report studies of hepatic metabolism and interactions	
5.3.3.	Reports of pharmacokinetic studies in humans: report on studies of pharmacokinetics in healthy volunteers and initial tolerability study report; pharmacokinetic research internal factors studies report; pharmacokinetic research external factors studies report; report on pharmacokinetics studies in different populations;	
5.3.4.	Reports on pharmacodynamic studies in humans: report on studies of the pharmacodynamics and pharmacokinetics / pharmacodynamics in healthy volunteers; report on studies of the pharmacodynamics and pharmacokinetics / pharmacodynamics in patients;	
5.3.5.	Efficacy and safety studies reports: report on controlled clinical trials based on reported testimonies; uncontrolled clinical studies reports. Data analysis reports based on more than one research, including any formal integrated tests, meta-analyses and cross-analysis, reports on other researches	
5.3.6.	Reports on pre-registration application experience	
5.3.7.	Samples of individual registration forms and individual lists of patients	
5.4.	Copies of literature sources used	

Note:

1. Analytical Method Validation: - Need to give brief info, even if the method is official.
2. Duration for Registration: 9-12 months
3. Registration fees: USD 4200 (single generic) USD 4500 (Multiple generic) , USD 800 for additional strength, USD 1200 for additional dosage.

Table 3. Comparative Studies of Russia, Ukraine, Kazakhstan

S.No	Contents	Russia	Ukraine	Kazakhstan
Module -1	Administrative Documents			
1	Application form	YES	YES	YES
2	CPP (Certificate of Pharmaceutical Product)	YES	YES	YES
3	Certificate of GMP issued by the authorized body in the country of origin	YES,(Notary or Apostilled copy)	YES	YES, common CoPP is accepted
4	API - GMP certificate	YES	YES	YES
5	Registration status in other countries	YES	NO	YES
6	Instructions for medical use of specialists and patients	YES	NO	YES
7	Qualitative and Quantitative composition of the medicinal product	YES	NO	YES
8	Art works 1.Carton 2.Label or Foil 3.Leaflet	YES, 5 copies	NO	YES
9	CV of the person responsible for pharmcovigilance	NO	YES	YES
10	Copies of trademark protection, registered brand names, patents	NO	YES	NO
11	Guarantee letter that intellectual rights of the third party are not infringed	NO	YES	NO

12	Guarantee letter that pharmacological vigilance system established and maintained	NO	YES	YES
13	Guarantee letter in a free form from manufacturer of active substance to inform FP manufacturer	NO	YES	NO
14	Certificate of analysis for three manufacturing batches for finished product	NO	YES	NO
15	Summary of product characteristics, labelling and package leaflets/insert	YES	YES	YES
16	Expert reports on chemical, pharmaceutical, biological, toxicological and clinical documentation	NO	YES	YES
17	Specific requirements for different types of applications	NO	NO	YES
18	Information on bibliographic applications in accordance with Article 4.8 (ii) Directives 65/65/EEC	NO	NO	YES
19	Information abbreviated applications in accordance with Article 4.8 (iii) Directives 65/65/EEC	NO	NO	YES
20	Assessment of potential hazard to the environment	NO	NO	YES
21	Medicinal products containing or derived from genetically modified organisms	NO	NO	YES
22	A detailed description of pharmacovigilance and risk management systems.	NO	YES	YES
23	Manufacturing facility audit	No Plant audit is required.	If plant does not have PIC/S GMP certification, audit by Ukraine MOH is mandatory. Every product should have GMP certification before filing for marketing authorization.	No plant audit required.
24	Module 4 Preclinical (nonclinical study reports)	One manufacturer can supply to one customer	Can be supply to multiple customers	Can be supply to multiple customers
		Conducting bioequivalence study is compulsory	Any bio-study is accepted	Any bio-study is accepted
		For injectables for generic phase 3 clinical trials are required to be done(100 volunteers)	Is accepted against U.S and E.U innovator also	Is accepted against U.S and E.U innovator also

		Antimicrobial test need to be performed either in Russia or India. For oral solid dosage forms Bio study to be performed in Russia only.	PICS approved bio-analytical facility. Suppose if clinical facility does not have any PICS approval then Ukraine MOH will come and audit facility.	PICS approved bio-analytical facility. Suppose if clinical facility does not have any PICS approval then Ukraine MOH will come and audit facility.
25	Registration Fees	8,000 USD for generic and multiple dosage forms.		USD 4200 (Single generic) USD 4500 (Multiple generic), USD 800 for additional strength, USD 1200 for additional dosage.
26	Duration for registration	9-12 months	9-12 months	9-12 months

SUMMARY

Although there is a continuous process of harmonization taking place all around the world, still we see a huge challenge, which is yet to be overcome by the Pharmaceutical industry in case of generic drug development and filing. This is due to the heterogeneity in the regulatory landscape of the various countries. Therefore, to meet these challenges, a lot of strategic planning is required before the development of any generic drug product.

In the emerging markets like C.I.S countries like Russia, Ukraine and Kazakhstan the registration process is different from other countries. In these countries for generic drug application the bio- stability studies are conducted in their own population only.

In the emerging markets the common technical document is compared between the C.I.S countries. The registration process for the generic product is mentioned and compared.

The regulatory process for the C.I.S countries is different from the other countries, different stability studies are conducted for different countries.

CONCLUSION

Maintain a balance between ensuring a product is safe, efficacious and of good quality and not delaying public access to the products by Clearly separate the tracks of registration submission into standard review and priority review and Reduce the timelines for each steps were announced.

The Russian healthcare market is attracting increasing global interest – not least because its value is expected to triple within the next decade. However, market access across this vast region is complex and challenging – and has become even more so following the introduction of the on Fundamentals of Protection of Public Health in the Russian Federation, on January 1st 2012. The Russian market is vast, fast growing and clearly offers massive opportunities for pharmaceutical companies. However, this is a complex market, with huge scale and very different pharma-economies. From the introduction last year of new price registration for Essential and Vital Drugs (EDL), to the move towards greater standardisation in care pathways, changes are occurring at every level of health provision as the government attempts to reduce self-prescribing, and provide greater access and choice to healthcare services for its citizens.

EDL pricing is now based on the lowest prices paid in European reference markets, effectively creating a price freeze; and the EDL will be the basis of the reimbursement schemes being rolled out across regions over the next few years.

It is estimated that pharmaceutical sector in Russia and other CIS nations will have a double digit growth of around 10 to 11 per cent during the year 2012-2016"We are witnessing a robust growth in Russia and have considerable presence in the country. We are also in the process of tapping the markets in other CIS countries.

- Kazakhstan has steadily increased their imports of formulations from India.
- Ukraine has accounted a slight slowdown in the import of formulations from India.
- Russian regulatory agency is keep updating their regulatory standards at very fast.
- Kazakhstan is also becoming rigid and it is expecting USFDA level documentations for approvals.

Countries like Ukraine have so far depended on Indian companies but it is also very rapidly moving towards regulated markets and is also part of PIC/S.

REFERENCES

1. http://www.pharmabiz.com/article/detnews.asp?articleid=22502&sectionid=50

2. http://cispharma.blogspot.in/2011/06/ukraine-import-of-drugs-to-ukraine.html
3. http://www.business-standard.com/article/companies/pharmexcil-plans-business-delegation-to-cis-nations-in-jan-114010301236_1.html
4. http://www.ibef.org/exports/pharmaceutical-exports-from-india.aspx
5. http://pharmabiz.com/ArticleDetails.aspx?aid=73006&sid=21
6. http://www.indiacis.in/russia.html
7. http://www.indiacis.in/russia.html
8. http://hosted.comm100.com/knowledgebase/PHARMEXCIL-(Pharmaceuticals-Export-Promotion-Council)_A131.aspx?id=131&siteid=95439
9. http://www.ipapharma.org/pt/sep2011/15-20.pdf
10. http://www.ich.org/cache/compo/276-254-1.html
11. http://www.ich.org