e-ISSN: 2249-7625
Print ISSN: 2249-7633

International Journal of
Pharmacy Practice & Drug Research
www.ijppdr.com

EVALUATION AND COMPARISION OF REGULATORY PROCESS AND COMMUNICATION RECEIVED FROM VARIOUS REGULATORY AUTHORITIES DURING PRE AND POST REGISTRATION OF MONTELUKAST CHEWABLE TABLETS

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ABSTRACT

The pharmaceutical research and development process of bringing a new drug to the market takes many years,In today's competitive environment the reduction of the time taken to reach the market is critical to a product's and hence the company's success. The proper conduct of its Regulatory Affairs activities is therefore of considerable economic importance for the company.The drug regulatory affairs (DRA) professional plays an important role in every phase of this process, from developing regulatory strategies following the discovery of a new chemical entity to planning post-marketing activities Regulatory Affairs (RA), also called Government Affairs, is a profession within regulated industries, such as pharmaceuticals, medical devices, energy, and banking.Worldwide regulatory agencies such as USFDA1 (United States Food and Drug Administration) and European Union of Drug Regulatory Affairs (EUDRA). A number of organizations such as the Regulatory Affairs Professional Society (RAPS), the Drug Information Association (DIA), the Food and Drug Law Institute (FDLI) and international organizations such as the European Society of Regulatory Affairs play a vital role in providing relevant information. The main objective of the work is to evaluate pre and post registration of "MONTELUKAST CHEWABLE TABLETS" filled in various countries so as to reduce the risk of regulatory delays and to reduce the registration lead time.Based on the experience gained from this product registration countries regulatory filing strategy has been developed to improve the quality of the submission file which helps to reduce the number of deficiencies received from each regulatory authority. It also helps to reduce the product registration lead time which allows commercial team to launch the product at the earliest.

Keywords: Regulatory, DRA, USFDA, EUDRA, RAPS, DIA, Registration, Communications.

INTRODUCTION

The regulation of medical products has been expanding since early 20th century. Regulatory agencies are being established in an ever increasing number of countries across the globe. Those that have established are reorganizing their systems and attempting to harmonize with organizations of other countries [1].

The pharmaceutical research and development process of bringing a new drug to the market takes many years, it is therefore essential that the process be managed effectively from beginning to end in order to meet the regulatory requirements and permit a favorable evaluation of efficacy and safety in the shortest possible time. The drug regulatory affairs (DRA) professional plays an important role in every phase of this process, from developing regulatory strategies following the discovery of a new chemical entity to planning post-marketing activities Regulatory Affairs (RA), also called Government Affairs, is a profession within regulated industries, such as pharmaceuticals, medical devices, energy, and banking [2].

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Regulatory Affairs also has a very specific meaning within the healthcare industries (pharmaceuticals, medical devices, Biologics and functional foods). The person indulging in the regulatory affairs must be familiar with all the guidelines, guidance and regulatory documents. He should have thorough understanding of a particular regulatory document which has been drafted. Such people are the primary communication link between the company and worldwide regulatory agencies such as USFDA1 (United States Food and Drug Administration) and European Union of Drug Regulatory Affairs (EUDRA). A number of organizations such as the Regulatory Affairs Professional Society (RAPS), the Drug Information Association (DIA), the Food and Drug Law Institute (FDLI) and international organizations such as the European Society of Regulatory Affairs play a vital role in providing relevant information[3]. Commercial training companies such as Parexel - Barnett and the Pharmaceutical Education and Research Institute (PERI) conduct meetings on the regulatory affairs, which would be helpful to the professionals. Most companies, whether they are major multinational pharmaceutical corporations or small, innovative biotechnology companies, have specialist departments of Regulatory Affairs professionals and those who don't, rely on the expert advice of independent regulatory consultants to meet their obligations. The success of regulatory strategy is less dependent on the regulations than on how they are interpreted, applied, and communicated within companies and to outside constituents. The regulatory affairs professional is the only one who is completely responsible for holding products incompliance and maintaining all the records. One of the vital activities of the regulatory specialist is to ensure that the all the information regarding medicines has been correctly established to the patient covering labeling also. Even a small mistake in any of the activities related to regulatory can make the product to be recall in addition to loss of several millions of the money.

In today's competitive environment the reduction of the time taken to reach the market is critical to a product's and hence the company's success. The proper conduct of its Regulatory Affairs activities is therefore of considerable economic importance for the company. Inadequate reporting of data may prevent a timely positive evaluation of a marketing application. A new drug may have cost many millions of pounds, Euros or dollars to develop and even a three-month delay in bringing it to the market has considerable financial considerations. Even worse, failures to fully report all the available data or the release of product bearing incorrect labeling, may easily result in the need for a product recall. Either occurrence may lead to the loss of several millions of units of sales, not to mention the resulting reduction in confidence of the investors, health professionals and patients.

The Regulatory Affairs professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products. They also advise on the legal and scientific restraints and requirements, and collect, collate, and evaluate the scientific data that their research and development colleagues are generating. They are responsible for the presentation of registration documents to regulatory agencies, and carry out all the subsequent negotiations necessary to obtain and maintain marketing authorization for the products concerned. They give strategic and technical advice at the highest level in their companies, right from the beginning of the development of a product, making an important contribution both commercially and scientifically to the success of a development program and the company.

1. Keep in touch with international legislation, guidelines and customer practices.
2. Keep up to the date with a company's product range.
3. Ensure that a company's products comply with the current regulations.
4. The Regulatory Affairs professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products. They also advise on the legal and scientific restraints and requirements, and collect, collate, and evaluate the scientific data that their research and development colleagues are generating.
5. Formulate regulatory strategy for all appropriate regulatory submissions for domestic, international and/or contract projects.
6. Coordinate, prepare and review all appropriate documents for example dossier and submit them to regulatory authorities within a specified time frame in conjugation with the organization.
7. Prepare and review of SOPs related to RA. Review of BMR, MFR, change control and other relevant documents.
8. Monitor the progress of all registration submission.
9. Maintain approved applications and the record of registration fees paid against submission of DMF's and other documents.
10. Respond to queries as they arise, and ensure that registration/ approval are granted without delay.
11. Impart training to R&D, Pilot plant, ADl and RA. Team members on current regulatory requirements.
12. Advising their companies on the regulatory aspects and climate that would affect proposed activities. i.e. describing the "regulatory climate" around issues such as the promotion of prescription drugs and Sarbanes-Oxley compliance.
13. Manage review audit reports and compliance, regulatory and customer inspections.
14. Regulatory Affairs professionals help the company avoid problems caused by badly kept records, inappropriate scientific thinking or poor presentation of

data. In most product areas where regulatory requirements are imposed, restrictions are also placed upon the claims which can be made for the product on labeling or in advertising.

15. Have a duty to provide physicians and other healthcare professionals with accurate and complete information about the quality, safety and effectiveness of the product [3, 4].

OBJECTIVE OF WORK

The main objective of the work is to evaluate pre and post registration of "MONTELUKAST CHEWABLE TABLETS" filled in various countries so as to reduce the risk of regulatory delays and to reduce the registration lead time.

- Evaluation of regulatory requirements to register human medicine product in identified countries.
- Developing filing strategy for each country.
- Evaluating the communications received from respective regulatory authority.
- Evaluation of variation requirement from respective countries due to the post approval changes. Comparison of communications received from various regulatory authorities.

PLAN OF WORK

- Identify the countries based on the commercial needs
- Understanding the regulatory requirements of each region

For example: Asian, Europe, Africa, Latam……etc.

- Developing the filling strategy country wise/region wise.
- Comparative study of regulatory requirements country wise/region wise
- Preparation of comparison status by analyzing the communications received from regulatory authority.

RESEARCH METHODOLOGY

Literature review was done mainly on collection of the regulatory authorities of product filling countries, concentrating on their registration procedures and communications received during pre and post registration of Montelukast Chewable Tablets. The research carried out the collected data by analyzing the terms of the below parameters:

Methodology

Each and every study has some patterns and follows certain pathways in order to reach the objective, the method to be followed play an important role in determining the output as well as the consequences of study.

Types of study

The study was conducting with an objective to chalk out the regulatory guidelines of product filling countries. The major emphasis has been developed to improve the quality of the submission file which helps to reduce the number of deficiencies received from each regulatory authority.

DISCUSSION

Product Selection

- Product selection is done by product management team, if required business management team involved in selection of country.
- Regulatory has no role in the product Vs country matrix.
- Following are the few parameters which will be consider to identify the selecting the country for any particular molecule.
  - Increase % growth in demand for the molecule year on year
  - Number of companies are already lunched
  - Price comparison with competitors
  - Marketing strategy
- Based upon the above parameters we have selected a drug "MONTELUKAST CHEWABLE TABLETS"

COUNTRY SELECTION

Based on the IMS data and market survey by project management team & business potential survey by business development team identified following countries to register. Montelukast Chewable Tablets. Country and their MOH are listed in Table 1.

AFRICAN REGION

The African pharmaceuticals market has been growing at a fast pace. The continent has a population close to a billion. The pharmaceutical market in Africa is set to grow between $8bn and $10bn a year, with pharmaceutical spending in Africa expected to increase to about $30bn by 2016. Africa's healthcare market is growing at an annual rate of 10.6%. Industry growth is attributed to the extensive surge of middle-class spending on diseases, and rapid urbanization. The industry has been growing fast despite the infrastructural shortcomings in many of the African countries.The filing strategy for identified African region countries are listed in TABLE 2.

KENYA

Overview

Republic of Kenya is a country in Africa. Its capital and largest city is Nairobi. Kenya covers 581,309 km2 (224,445 sq mi), and had a population of approximately 44 million people in July 2012.

Kenya has a warm, humid climate along its Indian Ocean coastline. The Republic of Kenya obtained independence in December 1963. Following a referendum in August 2010 and adoption of a new constitution, Kenya

is now divided into 47 semi-autonomous counties, governed by elected governors.

The capital, Nairobi, is a regional commercial hub. The economy of Kenya is the largest by GDP in Southeast and Central Africa. Agriculture is a major employer; Kenya is a member of the East African Community. Compared to other African countries, Kenya enjoys relatively high political and social stability.

UGANDA

Overview

The Republic of Uganda is a landlocked country in East Africa. It is bordered to the east by Kenya, to the north by South Sudan, to the west by the Democratic Republic of the Congo, to the southwest by Rwanda, and to the south by Tanzania. Uganda is the world's second most populous landlocked country after Ethiopia. The southern part of the country includes a substantial portion of Lake Victoria, shared with Kenya and Tanzania, situating the country in the African Great Lakes region. Uganda also lies within the Nile basin, and has a varied but generally equatorial climate. Uganda takes its name from the Buganda kingdom, which encompasses a large portion of the south of the country including the capital Kampala.

Uganda gained independence from Britain on 9 October 1962.

TANZANIA

Overview

The United Republic of Tanzania is a country in East Africa within the African Great Lakes region. Tanzania's population of 44.9 million is highly diverse, composed of numerous ethnic, linguistic, and religious groups. Tanzania is a presidential constitutional republic, and since 1996, its official capital has been Dodoma. As of 2014, Tanzania's gross domestic product (GDP) was an estimated $36.6 billion, or $86.4 billion on a purchasing power parity (PPP) basis. Tanzania is a poor country, with a per capita GDP of $1,813 (PPP), which was 32 percent below the average of $2,673 for the 45 sub-Saharan African countries and ranked 23rd among those countries. From 2009 through 2013, Tanzania's per capita GDP (based on constant local currency) grew an average of 3.5 percent per year, higher than any other member of the East African Community (EAC) According to the United Nations Development Program, however, recent growth in the national economy has benefited only the "very few", leaving out the majority of the population. Tanzania's 2013 Global Hunger Index was worse than any other country in the EAC except Burundi

CIS REGION

Commonwealth of Independent States (CIS) was created in December 1991.In the adopted Declaration the participants of the Commonwealth declared their interaction on the basis of sovereign equality. At present the CIS unites: Azerbaijan, Armenia, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Uzbekistan and Ukraine [5-7].

In September 1993 the Heads of the CIS States signed an Agreement on the creation of Economic Union to form common economic space grounded on free movement of goods, services, labour force, capital; to elaborate coordinated monetary, tax, price, customs, external economic policy; to bring together methods of regulating economic activity and create favourable conditions for the development of direct production relations. In order to facilitate further integration the Agreement on deepening of integration in economic and humanitarian field of four countries (Belarus, Kazakhstan, Kyrgyzstan, Russia) and Agreement on creation of Commonwealth of Sovereign Republics (Belarus and Russia) were signed in 1995.

In February 1999 by the decision of the Interstate Council of four countries (Belarus, Kazakhstan, Kyrgyzstan, Russia) the Republic of Tajikistan was recognized as participant of the customs union enjoying full rights [8]. The filing strategy for identified Cis region countries is listed in TABLE 3.

KAZAKHSHAN

Overview

Capital city: Astana

Population: 16,197,000 (2010), the population density - 5.95 inhabitants per sq. km. Languages: Kazakh, spoken by over 52% of the population, is the state language. Russian, spoken by two-thirds of the population, is used in everyday business and enjoys on official status under the Constitution.

Nominal GDP (2013): USD 220 billion

Form of government: A unitary state with a presidential form of government

UKRAINE

Overiew

Population (million): 45.4

GDP per capita (USD): 3,945

Exports (USD billion): 65.0

Imports (USD billion): 84.6

Border countries: Belarus, Hungary, Moldova, Poland, Romania, Russia, Slovakia

Capital: Kiev

Area: 603,628 km²

Currency: Ukrainian hryvnia

Official language: Ukrainian

Government: Unitary state, Semi-presidential system, Constitutional republic, Republic

ASIAN REGION

The continent of Asia is the world's largest and most populous continent with over 4 billion people calling

Asia home. Asia also contains the world's most populous country, China, and the world's largest country, Russia. Asia borders Africa and Europe to the west and the Pacific Ocean to the east. Asia is rich in diverse races, cultures, and languages. Many of the world's major religions came out of Asia including Christianity, Judaism, Islam, Hinduism, and Buddhism.

Asia has a major influence on world culture and the world's economy. Countries such as Russia, China, Japan and India produce products and services that are used by every nation in the world. Asia is also abundant in natural resources. Oil in the Middle East is a major supplier of much of the world's energy [9]. The filing strategy for identified Asian region countries are listed in TABLE3

MALAYSIA

Overview

Location: Southeastern Asia, peninsula bordering Thailand and northern one-third of the island of Borneo, bordering Indonesia, Brunei, and the South China Sea, south of Vietnam

Area: total: 329,847 sq km, Land: 328,657 sq km, Water: 1,190 sq km

Industrial production growth rate: 5% (2013 est.)

Population: 29.9 million

Currency: Ringgit (RM) (MYR)

Malaysia's economy expanded almost 5% in 2013 and has a purchasing power parity (PPP) per-capita GDP of more than $17,000. The total healthcare market in Malaysia, a country of 30 million people, was worth about $12 billion in 2013. Malaysia's pharmaceutical market is valued at over $3 billion and has a double-digit annual growth rate. Healthcare in Malaysia is structured into two tiers: a government universal healthcare scheme covering approximately 60% of Malaysians and a private healthcare system. The private system is growing quickly, especially in urban areas. Approximately half of healthcare spending is out-of-pocket. Overall, more than 8% of Malaysian GDP is spent on healthcare, comparable to most European countries The filing strategy for identified Asian region countries are listed in TABLE3

LATAM REGION

Latin America is a region of the Americas, that comprises countries whereRomance languages are spoken; primarily Spanish and Portuguese, but also French. It consists of twenty sovereign states which cover an area that stretches from the southern border of the United States to the southern tip ofSouth America, including the Caribbean. Latin America has an area of approximately 19,197,000 km^2 (7,412,000 sq mi), almost 13% of the earth's land surface area [10-13].

As of 2013, its population was estimated at more than 604 million and in 2014, Latin America has a combined nominal GDP of 5,573,397 million USD and a GDP PPP of 7,531,585 million USD.The term "Latin America" was first used in 1861 in *La revue des races Latines*, a magazine "dedicated to the cause of Pan-Latinism"[14]. The filing strategies for identified latam region countries are listed in TABLE 4.

BRAZIL

Overview

The Brazilian pharmaceutical market remains our favorites regional market in Latin America due to its large market size and strong domestic demand for innovative, high-tech products. The government i s increasingly investing in the healthcare sector and pharmaceutical industry to reduce the financial burden of diseases, and the country's private healthcare sectors provide opportunities for foreign companies. However, the increasing d rug rebate level has significantly undermined the profits recorded by generic drug makers. The more aggressive government technology transfer deals with multinationals as well as the drug approval delays due to bureaucracy and staff shortages at ANVISA have also dampened multinationals' revenue-generating opportunities

VENEZULA

OVERVIEW

The population of Venezuela grew from 27.7 million in 2008 to 29.8 million in 2013, mainly due to increasing life expectancy. Domestic production of medicines meets approximately 50% of the total demand of the Venezuelan population. The government has introduced the Mision Barrio Adentro program to provide universal healthcare access and Farm patria to provide medicines on a discount up to 54%. The future growth in the pharmaceutical market will be dependent on the resolution of concerns related to inefficient patent protection laws, drug pricing policy, and dependency on imports. The country's pharmaceutical market was approximately $10 billion in 2013 and is projected to reach $22.2 billion by 2020 at a CAGR of 12%.

Table1. Country and their MOH.

S.No	Name of the Country	Name of MOH	Country Website
Africa			
1	Kenya	Pharmacy and poisons Board	http://www.pharmacyboardkenya.org/
2	Uganda	NDA: National Drug Authority	http://www.nda.or.ug/
3	Tanzania	TFDA: Tanzania and Food and drug Administration	http://www.tfda.or.tz/

ASIA			
4	Malaysia	National Pharmaceutical Control Bureau, Drug Control Authority (Registration Certificate Issuing Authority), Ministry of Health (MoH)	http://portal.bpfk.gov.mg/index.cfm http://www.pharmacy.gov.my/index.cfm
CIS			
5	Kazakhstan	The National Centre of expertise of medicines, medical devices and medical equipment(Agency of Republic of Kazakhstan for Health Affairs)	http:/www.dari.kz/?lang=rus
6	Ukraine	State Pharmacological Center of the Ministry of Health of Ukraine.	http://www.pharma-center.kiey.ua/view/en/index
LATAM			
7	Brazil	Agencia Nacional de Vigiloncia Sanitaria/National Health Surveillance Agency (ANVISA)	http://www.anvisa.gov.br/eng/index.htm
8	Venezuela	InstitutoNacional de Higiene "Rafael Rangel"	http://www.inhrr.gov.ve/

Table 2. Filing strategy for African region countries

AFRICA COUNTRIES				
Country		**Kenya**	**Uganda**	**Tanzania**
MOH		Pharmacy and poisons Board(PPB)	NDA: National Drug Authority	TFDA: Tanzania and Food and drug Administration
Dossier Format		CTD	CTD	CTD-Country specific
Submission Details		Number of copies to be submitted to MOH is two (1 Original & 1 Duplicate).application forms (Original and Duplicate) and an electronic copy (a summary of the dossier contents) in MS Word on a CD-ROM of Modules	Dossier to be submitted in English, 2. Number of copies of the dossier to be submitted is one (1).3. Each application must contain appendices.	Application shall be in English, Number of copies of the Dossier required for submission to MOH = 01 (original), 10. Dossier should be submitted both as hard-copy and on CD-ROM
Plant	**cGMP Inspection**	Required	Required	Required
	Fee	4000USD	6000USD	6000USD
	Validity period	3	3	5
Admin Documents		MFg.Lic., GMP (Notary), CPP (Original)	MFg. Lic (Notarized)., FSC, CPP (Notarized)	MFg. Lic., FSC, GMP, CPP
Artworks		English/ Anglofrench	English/ Anglofrench	English/ Anglofrench
Sample requirements		8 Packs	5 packs	6 packs
Stability data		30/65(6M)	30/65(6M)	30/65(6M)
Product	**Registration fee**	USD 1000.00	USD 1250.00	750 USD
	Registration lead time	12 - 18 Months	12 - 18 months	6 - 9 M(Fast track), 9-18M(Normal)
	Reg.Validity	1(Every year retention fee should be submitted)	1(Every year retention fee should be submitted)	5
	Retention Fees	300USD	300 USD	100 USD

Table 3. Filing strategy for CIS Asian region Countries

CIS Countries				Asian Countries
Country		**Ukrain**	**Kazakhstan**	**Malaysia**
MOH		State Pharmacological Center of the Ministry of Health of Ukraine.	National drug expertise center, Ministry of Health, Kazakhstan	National Pharmaceutical Control Bureau
Dossier Format		CTD	CTD	ACTD
Submission Details		Normitive document required	Normitive document required	CD+ Hard copy (Not complete dossier)
Plant	**cGMP Inspection**	Required or PIC/S GMP	PIC/S	PIC/S Certificate(Plant accredation required)
	Fee	12000	-	-
	Validity period	3	-	-
Admin documents		• MFg.Lic., GMP, CPP,FSC	• MFg.Lic, GMP, CPP	Mfg.lic(Notarized)., FSC(Notarized), COPP(Original)
Artworks		**Ukrainian**	**Russian/Kazak**	**English/Official native language**
Sample Requirements		500 tablets,200 inj.	500 tablets,200 inj.-300 inj.	Not Required
Stability Data		25/60	25/60	30/75(12m)
Product	**Registration fee**	8000USD to 10000USD	7500 USD - 10,000 USD	2200 Malaysian ringgets, two or more API-4000MR
	Registration lead time	9-12 Months	9-12 Months	210 working days
	Reg. Validity	5	5	5
	Renewal fee	-	-	333USD
	Renewal validity	Lifetime	-	5
	Retention fees			NA

Table 4. Filing strategy for Latam region countries

Latam Countries			
Country		**Brazil**	**Venezuela**
MOH		AgenciaNacional de Vigiloncia Sanitaria/National Health Surveillance Agency (ANVISA)	InstitutoNacional de Higiene "Rafael Rangel"
Dossier Format		CTD-Country specific	CTD-Country specific
Submission Details			
Plant	**cGMP Inspection**	Required	Not required
	Fee		
	Validity period		
Admin documents		Mf.lic, WHO GMP, FSC(Legalized), CPP(Legalized)	Mf.lic, WHO GMP, FSC(Legalized), CPP(Legalized)
Artworks		Portuguese	English/Spanish
Sample requirements			2-5 packs
Be studies		ANVISA approved lab BE studies is approved, brazil reference product	Required
Stability Data		30/75	30/75
Product	**Registration fee**	5100 Rias	175 USD
	Registration lead time	12-18 months	12-18 months
	Reg. Validity	5 years	7 years

Table 5. Communication received from various regulatory authorities			
1	**Malaysia –APL**	ASEAN	Please find attached BE application form for M-KAST 4 & 5 (Montelukast Chewable Tablets 4 mg & 5 mg).
2	**Kazakhstan –APL**	CIS	Please find attached following Appostille documents for M-KAST 4 & 5 (Montelukast Chewable tablets 4 mg & 5 mg) •Montelukast SodiumAPIMfg.Lic(Lauruslabs) •APIPlantGMP(Laurus labs) • M-KAST 4 & 5 Mfg.lic • M-KAST 4 & 5 GMP • M-KAST 4 & 5 FSc
3	**Ukraine-APL**	UKRAINE	Please find attached following documents for Montelukast chewable Tablets 4 mg & 5 mg (M-KAST 4 & 5) •Pharmacology •Pharmacokinetics •Toxiology study's.
			Please find the following registration certificates for Montelukast chewable Tablets 4 mg & 5 mg (M-KAST 4 & 5), •Netherlands •Ireland • USA
			Please find attached the placebo label with CoA.
			Please find attached the updated CoAs for working standards.
			please find attached the CoA for FP.
			please send documents (section 3.2.P.5.1, section 3.2.P.5.2 section 3.2.P.5.6 & section 3.2.P.8.3).
			please provide stability data.
4	**Venezuela-PFIZER**	LATAM AMERICA	Provide Legalized CPP and QQF inline to the submitted CPP.
			Please provide at least 3 batches with complete accelerated stability data and 3 batches of long term stability data at least with 12 months for each batch
			Please provide the following COAs for Montelukast4mg , 5mg chew tabs . • COAs Working Standard •COAs for Raw Material (API – Montelukast) the same batch that was used for produce the finish product.
			Could you please update about the availability of the registration samples.
			Updation documentations are submitted for new API
5	**BRAZIL**	BRAZIL	We are not Change of API source but Including one more API source The following documentation for API required.
			Please can you send the Validation Report of Residual Solvents and Particle size?
			in photostability data, is it possible to put the information about the Drug Substance MFG. Location, as you put in stability data
			Validation Report of Residual Solvents and Particle size, as Analytical Method Transfer Document
			In the initial process for MONTELUCAST CHEWABLE the specification and STP are different from the last specification and STP
			Can you clarify the results from photostability studies for montelukast chewable and tablets
		Pfizer	The dossier was filed in Nov-12 and it is still awaiting HA review and feedback The only strengths are 4mg and 5mg chewable tabs BE study has been performed with a batch manufactured with

			current API. The comparative dissolution profile needs to be performed by a Brazilian lab accredited by ANVISA. We need to know if there will be any change in FP specification and/or analytical method
			Please, kindly share the FP specifications and analytical method for our QC evaluation.
			Shipping 60 mg of Montelukast Cis-Isomer impurity as soon as possible
			Could you please send us the re-test CoAs
			Since our intention is to submit those variations before approval please, kindly share the FP specifications and analytical method for our QC evaluation.
			Please report about the standard solution stability
			Please, inform the estimated date to provide the photostability data.
			please, send a formal letter explaining this situation
			Please, provide the DDR
			Please, provide the updated General Test Procedures
			Please, inform the estimated date to provide regarding new API mfg site (APL).
			Stability of the API: pending
			Are there stability study data for the batches
			please send us the re-test CoA with purity and expiration date to quantitative analysis
			please, send us the CoAs and Standard's CoAs.
6	**Kenya**	AFRICA	Sec1.9.1 Pharmacotherapeutic group provided in this section is: Anti-Retroviral whereas in SPC it is indicated as Anti-Asthmatic drug, kindly amend and provide the correct.
			Provide the adventitious safety agents of Magnesium Stearate.
7	**Uganda**		1. A number of sections that are not supposed to be in the QIS were included. Please use the guideline on QIS and re-submit the revised QIS with version history. Some of the sections not to be included in the QIS are: 2.3.P.4. 2. The summaries of each section should be included in the respective sections of the QIS. References to the dossier are not acceptable. 3. The API option indicated in the QIS was full details in the PD but in the QOS you indicated APIMF. Please clarify. 4. Please clearly indicate the API option selected for submission of the API data and submit the full information as per the Registration guidelines including the details in the restricted part of the Dossier. 5. Please clearly indicate the block(s)/unit(s) used for the manufacture of the API. The relevant section of the QIS should be revised.
			6. please revise API Specifications 7. The relevant section of QIS should be revised 8. Please submit the revised, signed, dated and version controlled API Specifications.
			9. Please submit the stress studies carried out on the API.
			10. Please provide the executed BMR for the batch used in the biowavier studies (biolot) batch No. MSSA10001.
			11.Please provide blank master production documents for each strength 12. Regarding the QIS; Section 2.3.P.1 of the QIS, the table should

			be filled in with the composition of Montelukast 4 mg tablets and not the 5 mg strength. Section 2.3.P.2.2.1 (c) of the QIS, the table should be filled in with the composition of the batches used in the comparative bioavailability, stability, process validation and commercial batch. 15. Section 2.3.P.3.3 of the QIS, please include; a. Flow diagram of the manufacturing process b. Narrative description of the manufacturing process, including equipment type and working capacity, process parameters 16. Please include all the critical steps in section 2.3.P.3.4 of the QIS including the drying stage. The limits and frequency of testing for all the controls should be included. Section 2.3.P.3.5 of the QIS please include the document code(s) for the process validation protocol(s) and/or report(s) (including reference number/version/date). Section 2.3.P.8.2 (b): in the table, under the row for batch number indicate that three commercial batch sizes. Delete 'One batch (if manufactured) per year'.

CONCLUSION

Based on the IMS data and market survey by project management team & business potential survey by business development team identified following countries to register. Montelukast Chewable Tablets, Kenya, Tanzania, Uganda, Malaysia, Ukraine, Kazakhstan, Brazil, Venezuela,

After studying the regulatory requirements to register a pharmaceutical product for human use and after analyzing the communications received from respective regulatory authorities, the above countries are classified as regulated and semi- regulated countries.

Regulated countries	Semi- regulated countries
Malaysia	Ukraine
Brazil	Venezuela
Kenya	Kazakhstan
Uganda	
Tanzania	

Based on the experience gained from this product registration above said countries regulatory filing strategy has been developed to improve the quality of the submission file which helps to reduce the number of deficiencies received from each regulatory authority.

It also helps to reduce the product registration lead time which allows commercial team to launch the product at the earliest.

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