Republic of Korea

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Korea has a centuries-long tradition as an industrious, technically advanced and proudly independent nation. For much of this century the country was occupied by Japan. In 1948, Korea was divided along the 38th parallel to form the People's Democratic Republic of Korea (North Korea) and the Republic of Korea (South Korea).

North Korea still remains a strictly socialist country with centralised control of government and social services including healthcare (similar to Eastern Europe prior to the significant political changes of the 1990s). This chapter deals exclusively with South Korea, which prides itself in embracing liberal democracy and free market economy. President Kim Dae Jung was democratically elected in 1997 and inaugurated as President of the Republic of Korea on February 25, 1998.

For a long time, pharmaceutical regulation was a strongly controlled matter and the formation of the Korea Food and Drugs Administration (KFDA) in 1998 has further strengthened this.

COUNTRY DESCRIPTION

Geographical Location

The Republic of Korea lies south of the 38th parallel on the Korean peninsula with North Korea as its immediate neighbour. On the mainland, Korea is dwarfed by the enormous countries of the People's Republic of China and the Russian Federation. Across the East China Sea lies the island nation of Japan, which occupied all of Korea for much of this century.

The capital city of the Republic of Korea, Seoul, is situated just south of the dividing line with North Korea. The country has a population of over 45 million.

Korea is a densely populated country with few natural resources. The well-educated and self-motivated population have contributed to Korea's becoming one of the fastest growing economies in Asia. In 1996, it became a member of the Organisation of Economically Developed Countries (OEDC).

Economic Status

Despite economic difficulties common to many Asian states in late 1997 and early 1998, the country optimistically maintains a political stability for future growth. According to the International Monetary Fund (IMF) figures in 1998, the inflation rate was 10.5 percent with 4.3 percent projected for 1999. The growth rate, previously over 8 percent, was less than 1 percent in 1998, but was anticipated to recuperate to approximately 4 to 6 percent in July 1999. The Gross National Product (GNP) is over US $10,000 per capita with about 7.5 percent of the GNP currently spent on healthcare. The exchange rate of the national currency (the Won) has fallen to about 1204 Won to the US $ (Status July 1999, Bank of Korea).

OVERVIEW OF REGULATORY ENVIRONMENT/BACKGROUND

General

For centuries Korea has been culturally developed, with considerable educational advances propagated by emperors who ruled over several dynasties. One example of these advances is the "simplified" Korean alphabet derived from the more complex Chinese characters of similar linguistic origins (Koreans originally emigrated from Mongolia).

Traditional Chinese and Korean medicines have been utilised for centuries and are still a significant facet of medicine in Korea. Ginseng is one well-known remedy. There is a separate system for Chinese medical doctors' therapy in Korea.

The Medical Insurance System covers around 95 percent of the total population, the remaining 5 percent, mainly a low-income population, are covered by the Medical Aid Programme.

There are several thousand pharmaceutical companies in the country with indigenous Korean companies still playing a dominant role in a highly competitive market. Without local Korean representation, it is not possible to enter the market as a local company since registration is required prior to product registration (whether for import or local manufacture).

Until recently there has been no over-the-counter (OTC) market as such in Korea, with the market divided between hospital sales (46 percent) and pharmacy sales (36 percent). The remaining 18 percent is covered by clinics, dental surgeries, etc. New legislation now being implemented will effectively lead to the rise of a more OTC-like status by 1999.

Good manufacturing practice (GMPs) were introduced in 1985 and have been stringently applied in recent controls. Good clinical practice (GCPs), whilst officially issued in 1987, have only been effected in the last couple of years.

Pricing

Pharmaceutical pricing is controlled either by

- medical insurance price system (MIP) for reimbursed products
- standard retail price system (SRP) for OTC products

The Ministry of Health Guidelines on pricing are very strict. It is extremely difficult to obtain price increases in either the MIP or SRP systems.

Advertising

Both prescription and OTC products can be advertised. OTC advertisements must, however, include the price and the statement "Not to be misused or overused".

Many categories of pharmaceuticals are excluded from advertising including: antibiotics, anti-arrhythmics, anti-arteriosclerotics, anti-cancer preparations, anticoagulants, antihypertensives, artificial kidney dialysis agents, anaesthetics, capillary stabilsers, diabetic preparations, diuretics, epileptic drugs, hormone preparations, injectables, muscle relaxants, oxytoxics, plasma substitutes, radiopharmaceuticals, stimulants, synthetic antibacterials, urinary antiseptics, vasoconstrictors and vasodilators.

REGULATORY AUTHORITIES

The responsible regulatory authorities for pharmaceutical registration in Korea are:

Korea Ministry of Health and Welfare Administration (MOWH)
1 JungAng-dong, KwaChun,
KyoungGi-do, Korea 427-760
Telephone: + 82-2- 503 7513, Fax: + 82-2-503 7568

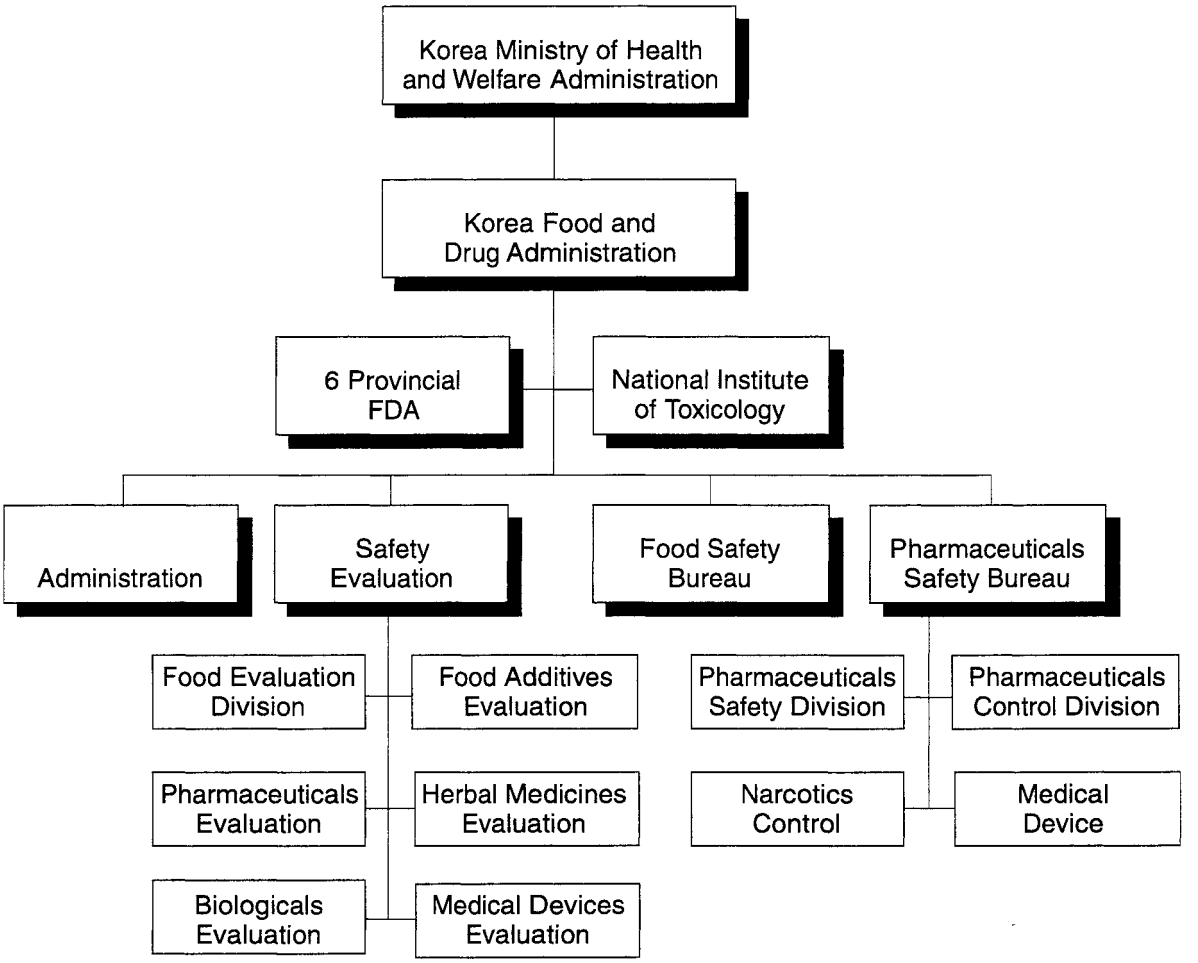
Korea Food and Drug Administration (KFDA)
5 NokBun-dong
Eun-Pyung-Ku
Seoul, Korea
Telephone: + 82-2-380 1800, Fax: + 81-2- 357 4737

See Figure 1 for chart.

REGULATORY REQUIREMENTS AND PROCEDURES

Pharmaceutical registration is required for all pharmaceutical specialties. The nationally controlled drugs include narcotics, biologicals and contraceptives. Herbal medicines, narcotics, diagnostics and vitamins are all subject to registration, as are generics.

Figure 1. Organisation chart MOHW/FDA.



Documentation and Other Requirements

1. Free Sales Certificate issued by the government authority of originating country, legalised and authorised by the corresponding Korean embassy or consulate. Essential components are:

   - manufacturers name and location
   - trade name of product
   - statement confirming that the product is duly registered, manufactured and sold in the country of origin
   - qualitative and quantitative composition

- product information
- shelf life

2. Technical documentation includes:
   - full qualitative and quantitative composition
   - specifications for dosage form, active ingredient and excipients
   - stability data supporting shelf life of the product
   - outline of manufacturing and formulation
   - outline of machinery and equipment required
3. Scientific documentation includes:
   - background on the origin and development of the drug
   - active substance data: structural formula, analysis and results
   - stability data
   - toxicity data: full range of standard data
   - pharmacology data: general, efficacy and pharmacokinetic studies
   - clinical data (See also section 4)
   - international registration status
   - local status (comparison with existing products)
4. Clinical data components:
   - Locally conducted trials are desired. These are conducted at a minimum of three general hospitals selected by the Ministry of Health and Welfare (MOHW) (A minimum of 90 patients is required. Study design may be open, double blind or comparative.).
   - One local study should be conducted after conditional approval of product manufacturing or importation licence if:
     - less than 3 years from the approval date in country of original development have passed, or
     - more than 3 years from the approval date have passed if the product is registered and marketed only in the country of origin.

5. Samples

   - Finished product and active substance samples, reference and impurity standards and special reagents, if appropriate, are to be provided with analytical certificates in all cases. In general, sufficient quantities for about three analyses are to be supplied.

6. Package leaflets

   - These are compulsory for all products and are professional– and patient-oriented. Items incorporated include: product name, name and address of manufacturer, composition, indications, dosage and administration, side effects, warnings and precautions, expiration date, storage instructions and content in package, Korean *Pharmacopoeia* reference (if listed) and advice (if habit forming).

7. Packaging materials

   - Although not essential prior to registration, these will be verified subsequently. All the items mentioned under item 6 should be included with the price to the public.

REGISTRATION PROCEDURES

1. Prerequisite approval

   - This is the first step and involves submitting the technical and scientific documents to the Korea Food and Drug Administration (KFDA). After review and approval, it is possible to proceed with the second step (See Figure 2).

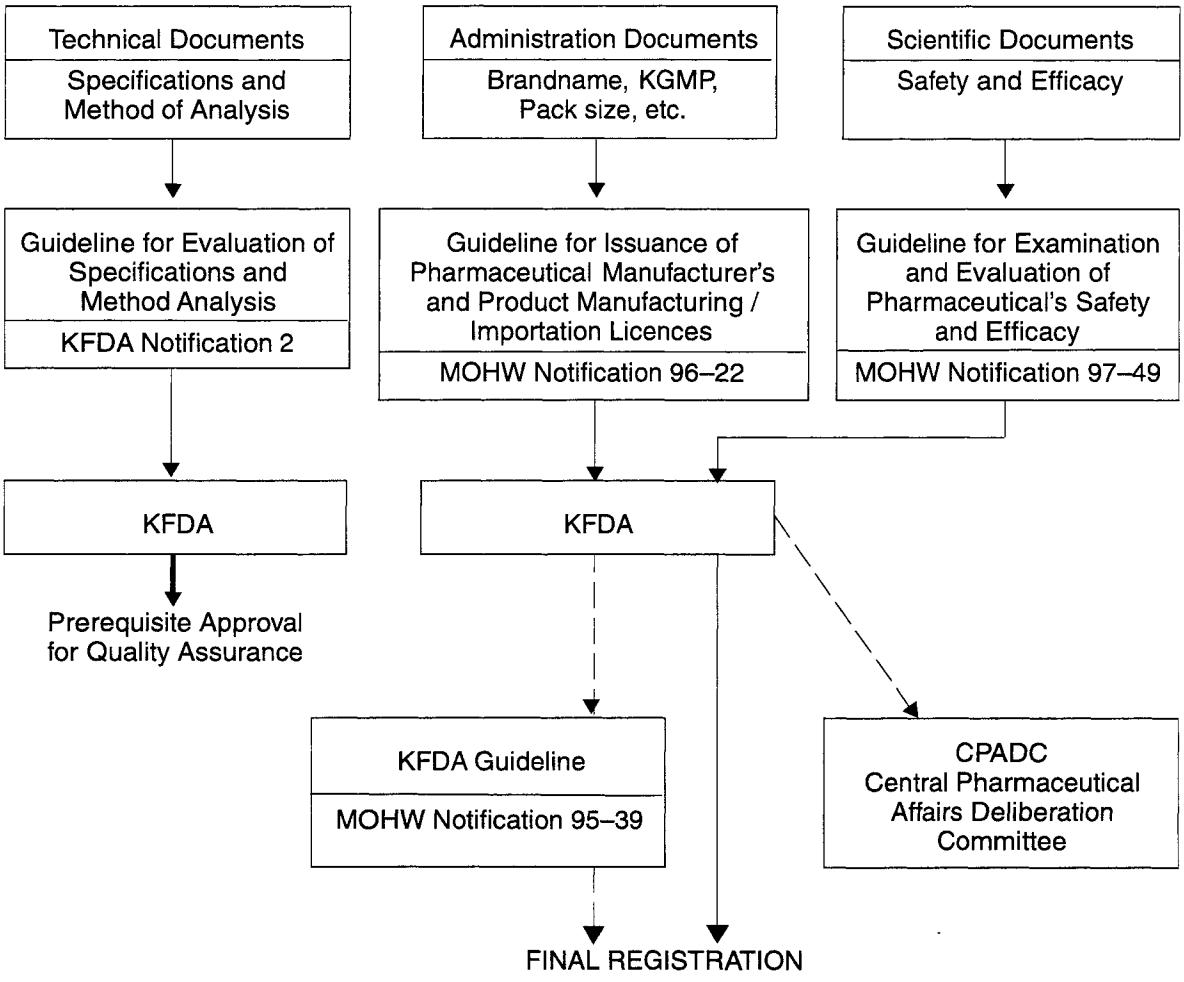
2. KFDA registration

   - With the approvals from step 1, the administrative registration for import or local manufacture is granted. For new drugs, a conditional approval for local clinical trials is simultaneously granted, which becomes step 3.

3. Local trials

   - The clinical trial protocols have to be approved beforehand as do the results of the study prior to final marketing authorisation. (See also Figure 3)

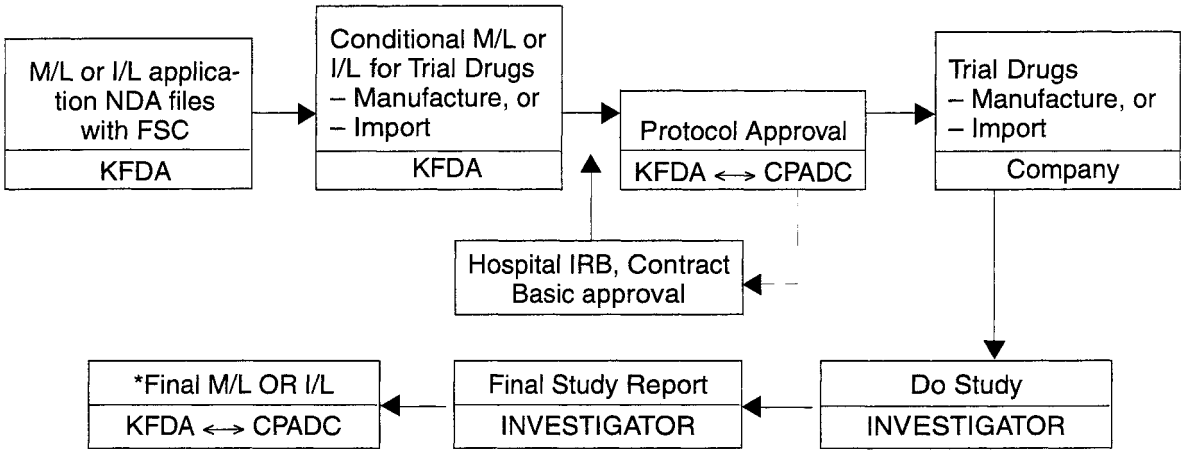
Figure 2. Basic guidelines for registration.



Generics

The registration of generics is comparatively easy in Korea. No scientific documentation as defined previously is required, only the technical pharmaceutical documentation. The prescribing information is identical to that of the original product. Patent protection in Korea is 15 years (with a possible extension of 5 years).

Figure 3. Clinical study for registration purpose in Korea.



M/L: Product Manufacturing Licence
I/L: Product Import Licence
CPADC: Central Pharmaceutical Affairs Deliberation Committee
KFDA: Korea Food and Drug Safety Administration

*Marketing Authorization either local manufacturing or import as finished dosage forms.

Revalidation Procedures

All variations to composition, standards and labelling require ongoing approval. In addition, there are regulations covering revalidation, which came into effect January 1, 1995.

In general, revalidation is required within 6 years from approval for the following:

- new drugs
- new combinations
- new routes of administration

Revalidation within 4 years from approval is required for evidently different indications to those previously established and also other products at the discretion of the MOHW.

PRACTICAL ASPECTS

The Korean authorities place great emphasis on published data. This applies not only to the clinical data, but also to preclinical data. An alternative is to request the regulatory authorities in the country of origin to provide an attestation of the original documentation submitted and on the basis of which approval had been made.

All documentation must be submitted in Korean, which is time-consuming and costly in preparing translations. The need for local representatives is crucial.

The guidelines as such are subject to frequent review and revision. There are strict demands to provide raw data and confirmatory evidence as well as published data (as mentioned previously). It is somewhat difficult to estimate effective time frames due to these aspects and as a result of the conservative officialdom. Figure 4 contains time frame estimates.

Figure 4. Time period for product registration.

	Category	Product Licence KFDA	Local Clinical Trials	Price Registration HIP	Price Registration SRP	Registration Period	Remarks
Local Manufacturing Product	– Generics in Pharmacopoeia	10D	–	6–12M	(IM)	6–12M	– New Indication (Registration change): 1–6 mos. – NDA File: Translated into Korean – HIP: Health Insurance Price – SRP: Standard Retail Price (= Label Price)
	– Generics	1M	–	6–12M	(IM)	7–13M	
	– Drugs requiring S&E evaluation	5–6M	–	6–12M	(IM)	11M–18M	
	– NEW DRUGS > 3 years, 2 countries	6–8M	–	–	(IM)	12M–20M	
	– NEW DRUGS: < 3 years, 1 country	6–8M (Conditional)	14M–33M	6–12M	(IM)	26M–53M	
Imported Product	– Generics in Pharmacopoeia	10D	–	–	IW	6–12M	
	– Generics	1M	–	–	IW	7–13M	
	– Drugs requiring S&E evaluation	6M	–	–	IW	11M–18M	
	– NEW DRUGS: > 3 years, 2 countries	6–8M	–	–	IW	12M–20M	
	– NEW DRUGS: < 3 years, 1 country	6–8M (Conditional)	14M–33M	–	IW	26M–53M	

* KFDA Approval for "Specifications and Method of Analysis", around 3–4 months, is not included in the time period for product registration

FUTURE TRENDS

Registration Changes

Following the reorganisation of the KFDA in 1998, further changes in the guidelines and procedures for registration are anticipated. These will be reviewed in subsequent editions of *International Pharmaceutical Registration.*

Drug Dispensing and Medical Practice

Between 1999 and 2005, it is foreseen that drug dispensing and medical practice will be separate:

- 1st step 1999: products of abuse
- 2nd step 2002: ethical drugs, except injections
- 3rd step 2005: all ethical drugs

OTC Sales

OTC sales will take place in convenience stores and supermarkets as well as pharmacies. This is due to be implemented as of July 1, 1999 following an amendment of the Pharmaceutical Affairs Law in 1998. Late 1998 classification standards of "Simple Drugs" are to be established:

- 1st step: drinks, tonics, nutritional products, vitamins, calcium preparations, external topical anti-infectives
- 2nd step: antacids, digestives, antiulcerants, cough suppressants, some NSAIDS

Pricing Changes

The current guidelines for Standard Retail Price system (SRP) are planned to be abolished.

From July 1, 1999 the lowest price control would be abolished for OTC products and in a second step from the year 2000 the SRP itself would be abolished, paving the way for an open price system.

A further change indicates reimbursement of imported products from July 1, 1999.

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Alan A. Chalmers has a BSc and PhD in pharmacy. He has 25 years of industrial pharmacy experience, beginning with Allen & Hanburys Research Ltd., United Kingdom (part of Glaxo). He subsequently worked for Ciba–Geigy Ltd. (latterly Novartis), mainly in Switzerland, where he gained extensive regulatory experience in all global markets. For the last 10 years Dr. Chalmers was Head of Regulatory Affairs for international markets including Central and Eastern Europe, the Middle East, Asia Pacific, Africa and Latin America. He is currently an international pharmaceutical consultant. Dr. Chalmers is a member of the Royal Pharmaceutical Society of Great Britain, the Association of Swiss Industrial Pharmacists, the Drug Information Association and several other professional bodies. He has been a guest speaker at numerous international conferences.