Available online on www.ijcpr.com

International Journal of Current Pharmaceutical Review and Research

Volume 1, Issue 1, May 2010 – July 2010, Page 33-58

Research Article

Need for Hormonisation of Labelling of OTC drugs

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ABSTRACT

Over the counter (OTC) drugs are medicine that may be sold without a prescription and without a visit to a medical professional in contrast to prescription drugs. Reading the product label is the most important part of taking care of when using OTC medicines. There is increasing need for consumer to have easily readable and understandable information about OTC drugs. Information on active ingredients, warnings, indications, storage conditions, contraindications, directions, purposes and other information, must be legible and accessible as OTC drug products are now widely available and used without medical supervision. This is particularly important because many potent drugs which have been switched from prescription to OTC status. Consumers are becoming more actively involved in there own health care, and are practicing self-diagnosis and self-medication with OTC drug products. Thus, it is extremely important that OTC drug product be clearly and uniformly labeled in a simple manner so as to ensure there safe and effective use by consumers.

Keywords: OTC, Labeling, Regulatory authority, FDA

Introduction

The drug is used by consumers as an OTC product without professional supervision, but with adequate directions for use and warnings against unsafe use. The drug will provide a clinically significant benefit of the type claimed in labeling, for a significant

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proportion of the consumers who use the product.[1] All OTCs can be safely sold by anyone because the manufacturers of most of these products are required to put adequate labels (warnings, dosage, and usage instructions) on them.[2]

The OTC switch is an advantage for health care systems as medicinal products which are sold for self-medication are not reimbursed and the patients are not consulting a doctor for minor diseases they can treat on their own. OTC products are therefore saving money both directly and indirectly.[3] The Food and Drug Administration (FDA) is overhauling the format and content of prescription drug labels. Since the 1970s, drug labels - often referred to as the package insert - have expanded in length, detail and complexity.[4]

Table 1:- List of some OTC products[7,8,9]

S.No.	Generic Drug Name	Strength and Dosage form	Therapeutic category
1	Acetaminophen	325mg tablet,160mg/5ml suspension	Analgesic
2	Aspirin	81 mg chewable tablet	Analgesic and anti-inflammatory
3	Ibuprofen	200 mg tablet , 100mg/5ml suspension	Analgesic and anti-inflammatory
4	Bismuth subsalicylate	262 mg, 262mg/15ml suspension	Travellers diarrhea
5	Calcium carbonate	500 mg chewable tablet	Antacids
6	Famotidine	10 mg tablets	Anti -ulcer
7	Loperamide	2 mg capsule,1 mg /5 ml solution	Colostomy
8	Omeprazole	20 mg tablet	Anti-ulcer
9	Brompheniramie	Elixir	Antihistaminic
10	Cepacol	Oral lozenge	Antitissive
11	Chlorphenirmine	4 mg tablet	Sedatives and cough
12	Diphenhydramine	25 mg capsule, 12.5 mg/5 ml	Antiemetic and cough

FDA concluded that the increasingly cluttered label hampered communication of risk information and suffered from ‘over-warning’ of clinically insignificant and often unsubstantiated risks.[5] Recently there has been increasing interest in enabling consumers to more easily acquire information from over-the-counter (OTC) nonprescription pharmaceutical labels. Standardization of label formatting is being considered by industry, government, and health related professional organizations as a

way to facilitate their usability [6] The FDA wants to receive prescription product labeling electronically in XML format. So pharmaceutical companies now face the challenge of converting existing labeling to SPL format, producing new labels that comply, and managing the information they contain at a much greater level of detail.

Objectives of OTC Products Labeling [10]

1. To provide basic product information (including common name, list of ingredients, net quantity, durable life date, grade/quality, country of origin and name and address of manufacturer, dealer or importer).

2. To provide health, safety, and nutrition information. This includes instructions for safe storage and handling, nutrition information such as the quantity of fats, proteins, carbohydrates, vitamins and minerals present per serving of stated size of the food and specific information on products for special dietary use.

3. ToProtection against physical impact on object - The objects enclosed in the package may require protection from, among other things, damage caused by physical force, rain, heat, cold, sunlight, pressure, airborne contamination, automated handling devices, or any combination of one or more of these.

4. Information transmission - Information on how to use, transport, or dispose of the product is often contained on the package or label. An example is pharmaceutical products, where some types of information by governments.

5. To apprise about the risks and benefits to the patient or environment associated with the uses of the OTC.

Comparisons between Prescription and Non Prescription Medicine [11, 12]

Prescription (Rx) refers to medicines that are safe and effective when used under a doctor's care. Nonprescription or OTC drugs are medicines FDA decides are safe and effective for use without a doctor's prescription. The choice of nonprescription, over-the-counter (OTC) medicines to treat an expanding range of ailments is increasing. OTC medicines often do more than relieve aches, pains and itches. Some can prevent diseases like tooth decay, cure diseases like athlete's foot and, with a doctor's guidance, help manage recurring conditions like vaginal yeast infection, migraine and minor pain in arthritis. Over-the-counter drugs have to be primarily used to treat a

condition that does not require the direct supervision of a doctor and must be proven to be reasonably safe and well-tolerated.

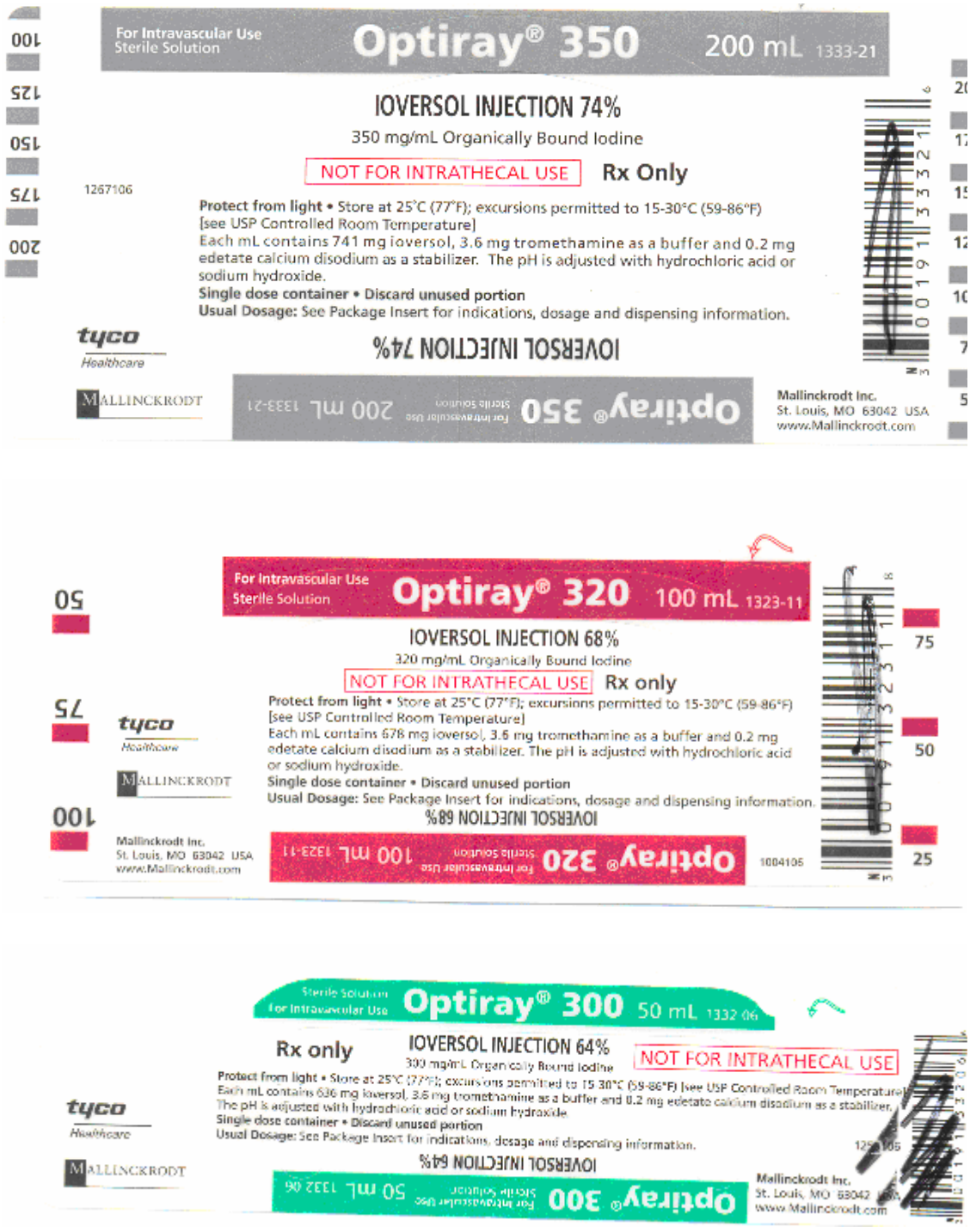


Figure 1:- **Prescription parental labels in U.S.A**

OTC drugs are usually also required to have little or no abuse potential, although in some areas drugs such as codeine are available OTC (usually in strictly limited

formulations or requiring paperwork or identification to be submitted during purchase). One of the oldest OTC drugs is aspirin

Drugs that prove themselves safe and appropriate for self-medication, may be switched from prescription to OTC. An example of this is diphenhydramine (Benadryl®) which once required a prescription but now is available OTC nearly everywhere. More recent examples are cimetidine and loratadine in the United States and ibuprofen (Herron Blue/Nurofen®) in Australia. Recently many U.S. [13,14]

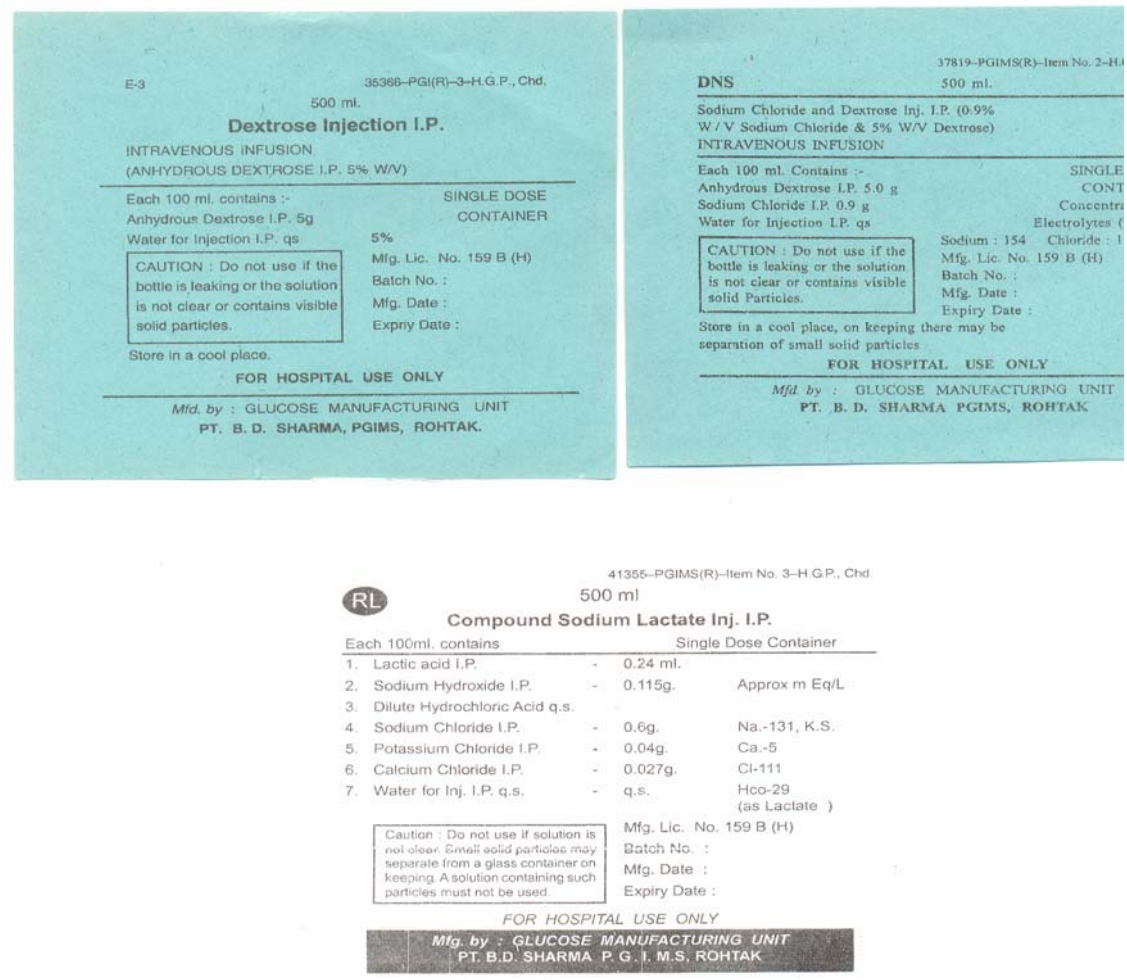


Figure 2:- **Prescription parental labels in India**

A prescription is not required; the change is allegedly being made in an effort to reduce methamphetamine production. Since the passage of the Methamphetamine Precursor Control Act the purchase of pseudo ephedrine in the United State is restricted and the identity of the purchaser is required to be obtained and recorded.[12] Nonetheless, these products are still considered OTC since no prescription is required, although this class is also called BTC, as in Behind-the-Counter, but not requiring prescription.

The FDA has approved the switch of a number of drugs from prescription to OTC status under new drug applications (NDA's). These include: antidiarrheals (loperamide), topical antifungals (clotrimazole, terbinafine HCL), antihistamines (clemastine fumarate), vaginal antifungals (clotrimazole, miconazole nitrate) analgesics (ketoprofen, naproxen sodium), acid reducers (cimetidine, famotidine) hair growth treatments (minoxidil) and smoking cessation drugs (nicotine polacrilex). [15]

Figure 3:- Non- Prescription (OTC) drugs labels in India

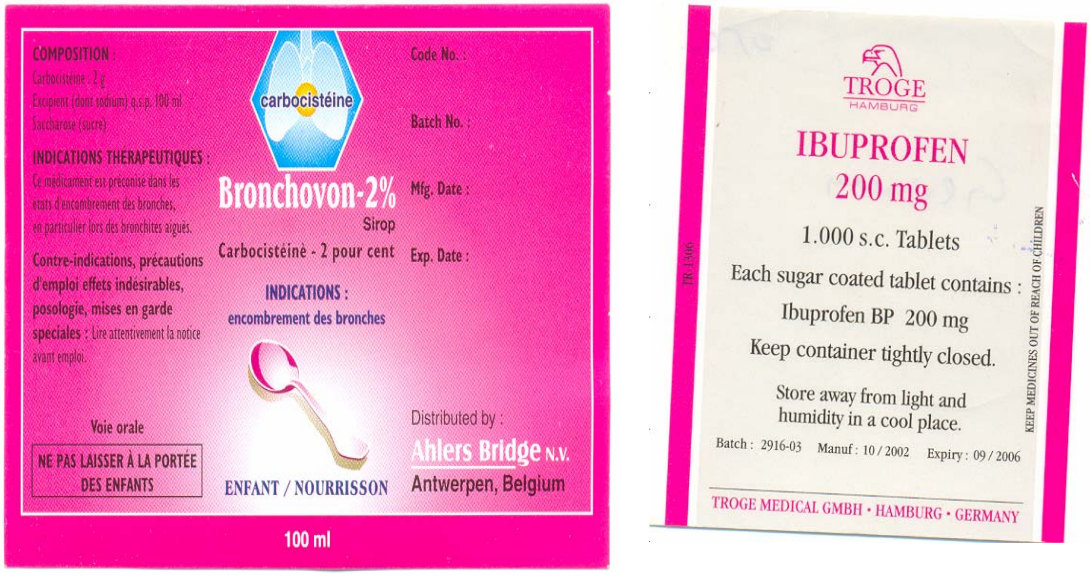


Figure 4:- Non- Prescription (OTC) drugs labels in USA and Europe

Standardization of OTC Drug Labeling

The Food and Drug Administration's (FDA) standardized format and content requirements for labeling of over-the-counter (O-T-C) drugs is designed to help consumers read and understand O-T-C drug product labeling so they use the products safely and effectively. FDA requires O-T-C drug products to include specific

headings and subheadings presented in a standardized order, with standardized graphical features and minimum standards for type size and spacing. The most contentious pertained to small packages-that is, packages sold in unit doses, convenient sizes, samples, minimal content packages, analgesic products with less than 6 square inches of usable labeling space, uniquely shaped containers, tubes, roll packs and bottles without any outer cartons.[16,17,18,19]

Indian label of Ibuprofen tablets **Germany label of Ibuprofen tablets**

Figure 5:-Difference between Indian and Germany label

FDA defines a *small* package as one that needs more than 60% of the total surface area available to bear the required labeling on the outside container or wrapper or the immediate container label if there is no outside container or wrapper.

Industry has contended that the format--and especially type size requirements--is impractical for many small containers, but FDA has refused to budge on the minimum 6 point type size regardless of the package's small size or unusual shape. FDA contends that that minimum size is needed for readability.

Clearly, for products sold without prescriptions, labeling plays an even more significant role since the patient or consumer must be able to read and understand the information when deciding which medication to use. In fact, the proposed product label and leaflet are important elements of a switch application. The emphasis should be on ensuring the delivery of comprehensive information that can effectively protect patients from any safety hazards

Information on a medicine label should be in "plain English" and larger type and should emphasize side effects and warnings with boldface type and bullets.

-There are about 100,000 OTC drug products on the market.

-Consumers self-treat four times more health problems than doctors treat.

-Sixty to 95 percent of all illnesses are initially treated with self-care, including self-treatment with OTC drugs.

An Ideal requirement for OTC Labeling [13,14]

There is need of the mandatory requirements for over the counter labeling in most countries including the EU, USA, Canada, New-Zealand and Japan. These mandatory elements are-

- **Active Ingredient**- Amount of active ingredient per unit.
- **Uses**- Symptoms or diseases the product will treat or prevent.
- **Warnings**.- When not to use the product; conditions that may require advice from a doctor before taking the product; possible interactions or side effects; when to stop taking the product and when contact a doctor; if pregnant or breastfeeding, case seek guidance from a health care professional; keep product out of children's reach.
- **Inactive Ingredients**-. Substances such as colors or flavors.
- **Purpose**. - Product action or category (such as antihistamine, antacid etc.)
- **Directions**- Specific age categories, how much to take, how to take, and how often and how long to take.
- **Other Information**- How to store the product properly and required information about certain ingredients.
- **The expiration date**- When applicable (date after which not use the product).
- **Lot or batch code** - Manufacturer information to help identify the product.
- **Name and address of manufacturer, packer, or distributor**
- **Net quantity of contents-** How much of the product is in each package
- **Bar Codes** -FDA is considering a number of issues as it formulate the regulation including which products should be bar-coded, what information the codes should include, what bar code symbols should be used, where the bar code should be placed on the package, and how soon the requirements should become effective.

Indian label of Metronidazole

European label of Metronidazole

Figure 6:-Difference between Indian and European label

Bilingual Labeling

Multilingualism on product labels is a widely extended practice. Distribution logistics mean that it is not exclusively limited to one linguistic community or particular country or state, but that multilingual labeling enables no differentiation to be made in stock in accordance with the functional dynamics of distributors and the market. This means that the languages present on the label of a product are often not only those present or official or widely used at the place of purchase, or even those used by potential purchasers from other linguistic communities that trave or move to that area, but the languages are often without any or almost any representation in the place where the purchase is made.[20]

A product purchased in Lisbon could, for example, be labelled in Spanish, Portuguese, Greek and English all at the same time. Sometimes the basic or obligatory information about the product may be displayed in more than twenty different languages on the same label or package. Governed by the commercial interest of this distribution, manufacturers have found practical solutions to fit a whole series of languages on the label, and therefore, for the time being, this does not imply any impediment to the sale of the product, in any case an advantage that enables reducing control over the distribution of stock to make it mandatory on pharmaceutical units to use bilingual labels on drug packs. Currently, most of the medicines are packaged in strips, bottles, vials and cartons with list of ingredients, directions for use and other details only in English.[21] and it is almost impossible to read these directions and information without a magnifying glass. Considering the volume of information and directions for use to be printed in English itself in the limited space available on strips, bottles and tiny injection vials, pharma companies are doing their best. Now, as

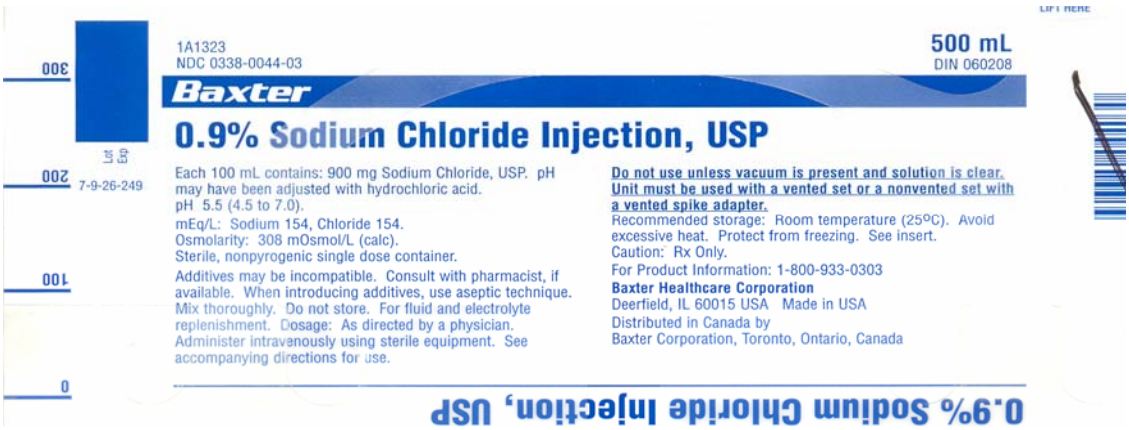
per the minister's proposal, pharma companies have to print this entire information both in English and state language.

Table 2:- Official Language(s) used in labels in various countries [22, 23, 24, 25]

Country	Language specified	Mandatory requirements	Regulatory authority
Austria	German	Requires use of national language.	EMEA(European medicine evaluation agency)
Belgium	Dutch,French,or German	Any one of the above as required by the professional user and all three for patient use.	EMEA
Brazil	Portuguese, Bororo, Canela, Carajá, Guarani	Requires use of national language	Agencia nacional de vigilancia sanitarious(ANVISA)
Canada	English, French	Requires use of national language.	HEALTH CANADA
China	Chinese	Requires use of national language	State Drug Administration (SDA)
Denmark	Danish	Requires use of national language	EMEA
France	French	Requires use of national language.	EMEA
Germany	German	Other EU languages may be used for nonsafety data.	
Iceland	Icelandic	Other languages (e.g., Finnish, Swedish, English) understandable to professional user may be used.	EMEA
India	Hindi, English	Requires use of national language	Ministry of Health and Family Welfare
Italy	Italian	Requires use of national language.	EMEA
Japan	Japanese, English	Requires use of national language	Ministry of Health Labour and Welfare(MHLW)
Netherlands	Dutch	Patient information must be in Dutch. English may be negotiated for professional use.	EMEA
Pakistan	Hindi , English, Urdu	Requires use of national language	The Pakistan Standard and Quality Control Authority
Russia	Russian,Tatar,Bashkir,Chuvash	Requires use of national language	Drug medical technology agency(AMTA)
Spain	Spanish	Requires use of national language.	EMEA
Sweden	Swedish	Generally requires use of national language. English may be negotiated for professional use.	EMEA
Switzerland	French, German, and/or Italian	Product information may need to be written in all three languages for patients. The manufacturer decides whether language requirements have been met.	EMEA
United Kingdom	English	Requires use of national language.	EMEA
U.S.A	English	Requires use of national language	Food and drug Administration(FDA)

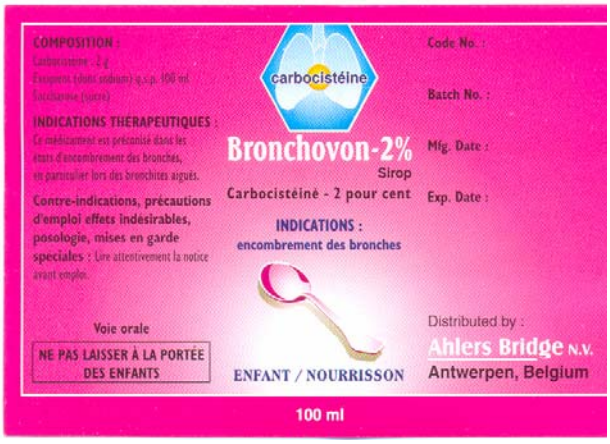
World Wide Global Scenario OTC Labeling [26,27,28]

The national requirements on OTC products are all based on the WHO Guideline for the regulatory assessment of medicinal products for use in self-medication and are mainly focusing on the safety of the drug product. Further on special requirements

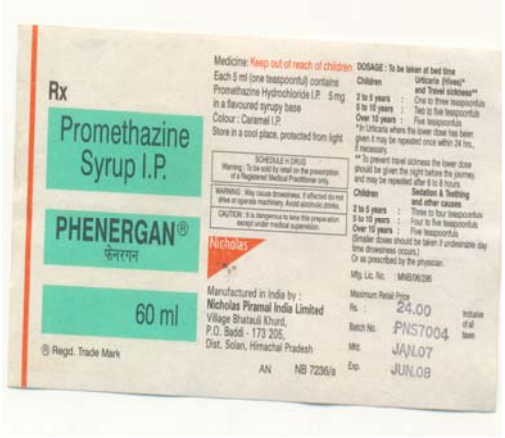


United State Labels

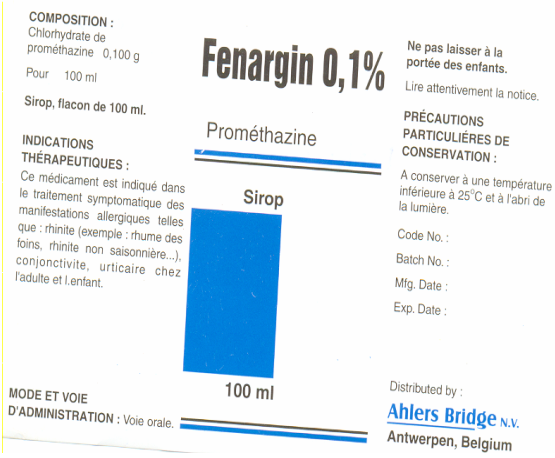
Russian Label



European label



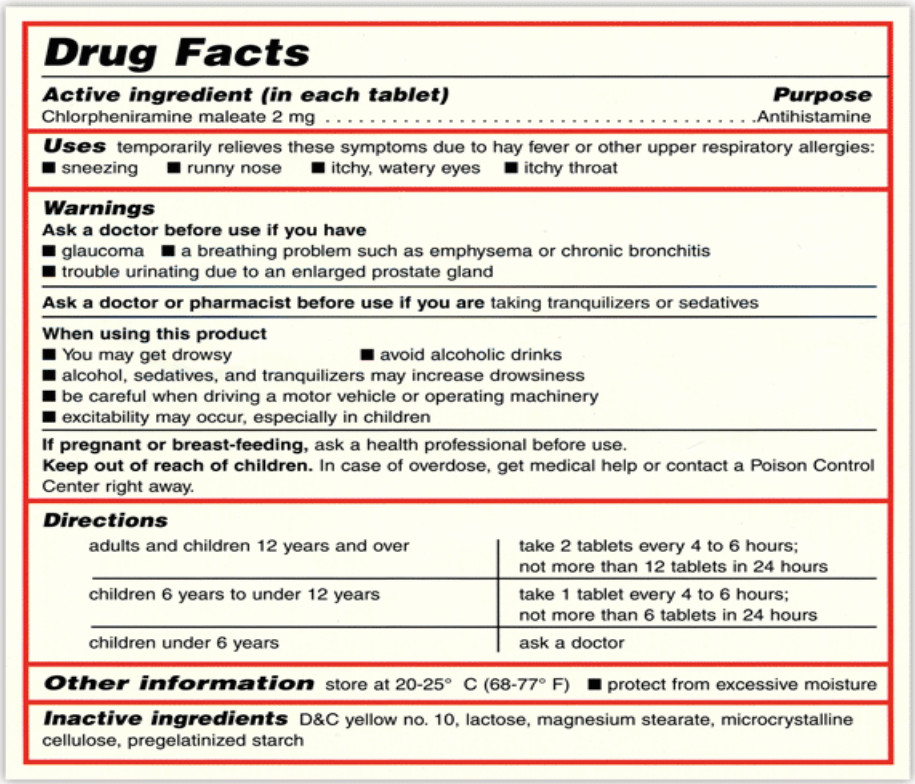
Indian label of Promethazine Syrup



European label of Promethazine Syrup

Figure 7:-Different types of various countries labels

regarding the labeling of an OTC drug product are formulated. The FDA conducted two studies to evaluate the effects these parameters have on the drug label readability, and after evaluating the studies concluded that a minimum type size of 6.7point is required to ensure that people over the age of 60 can read the label. Recognizing the space constraints, however, the FDA chose to allow type size as small as 6.0 point.



Drug Facts

Active ingredient (in each tablet) — **Purpose**
Chlorpheniramine maleate 2 mg ..... Antihistamine

Uses temporarily relieves these symptoms due to hay fever or other upper respiratory allergies:
■ sneezing ■ runny nose ■ itchy, watery eyes ■ itchy throat

Warnings
Ask a doctor before use if you have
■ glaucoma ■ a breathing problem such as emphysema or chronic bronchitis
■ trouble urinating due to an enlarged prostate gland

Ask a doctor or pharmacist before use if you are taking tranquilizers or sedatives

When using this product
■ You may get drowsy ■ avoid alcoholic drinks
■ alcohol, sedatives, and tranquilizers may increase drowsiness
■ be careful when driving a motor vehicle or operating machinery
■ excitability may occur, especially in children

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

adults and children 12 years and over	take 2 tablets every 4 to 6 hours; not more than 12 tablets in 24 hours
children 6 years to under 12 years	take 1 tablet every 4 to 6 hours; not more than 6 tablets in 24 hours
children under 6 years	ask a doctor

Other information store at 20-25° C (68-77° F) ■ protect from excessive moisture

Inactive ingredients D&C yellow no. 10, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch

Figure 8:- Drug Facts label

Moreover, the survey provides a snapshot of what kind of information could help consumers be more "OTC literate." Of special significance is the drug's active ingredient, which must be stated at the top of the standardized "Drug Facts" panel. As the new label goes into effect, the survey finds that only 34 percent of Americans can identify the active ingredient in common brands of OTC pain relievers. Also, the poll found that because Americans do not recognize the potential risks of taking OTC medicines incorrectly, as many one in three adults – over 64 million consumers—say they have taken more than the recommended dose.

In addition to the safety concerns the effectiveness of the drug product is stated as one requirement for an OTC switch in the USA. In Europe a proof of the effectiveness of a drug product is not covered by the requirements for an OTC switch as this is an essential requirement for the approval of an MAA. Even if the general requirements to switch the legal status of a medicinal product from Rx-to-OTC are comparable in Germany, the UK and in the USA, the lists of drugs which can be sold without a prescription from a practitioner in the three regions are very inhomogeneous. [29]

The procedure of an OTC switch is substantially different in the three regions compared . While in Germany and in the UK a switching application always deals with a drug substance, in the USA a switching application might deal either with a group of drug substances indicated for the same or for a comparable indication (OTC Drug Review) or it might deal with one special drug product (OTC NDA). [30]

Figure 9:- Specimen Russian label

Supervision of OTC Drugs Labeling in India

In 2005 the Indian OTC segment is Rs 4500 crore it could be considered as Rest 17000 cores if cosmeceuticals & neutraceuticals are also included. The global OTC market is projected to be USD 75 billion (roughly INR 375,000 crore) with a cumulative annual growth rate (CAGR) of 4.5%. The CAGR for Indian OTC markets is currently hovering between 12 and 15% and this is much faster than OTC market growth of most development countries. The label of any drug should include, at least, the name of the drug, its contents expressed in the metric system, the contents of the active ingredients, the name, address and license number of the manufacturer, the batch number, and the dates of date of manufacture and expiry. [31]

In India the prescription drugs are listed under Schedule H. There are about 570 molecules in this category that are stocked in a total of 5 to 8 lakh retail chemists. Currently, non pharmacy stores can sell a few drugs on the Schedule K of the Drugs & Cosmetics Act in rural areas in villages whose population is below 1,000.

Rule 106 of the Drugs Rules, 1945, provides that, no drug may convey to the intending user thereof any idea that it may prevent or cure one or more of the diseases or ailments specified in Schedule J. This schedule includes: Blindness, Bright disease,

cancer, cataract, deafness, delayed menstruation, diabetes, epilepsy, hydrocele, infantile paralysis, leprosy, leucoderma, lockjaw, locomotor ataxia, insanity, tuberculosis, tumours, venereal diseases (in general), female diseases (in general), fevers (in general), fits, glaucoma, goiter, gonorrhea, soft cancer, heart diseases, high blood pressure, lupus, obesity, paralysis, plague, rupture, sexual impotence and small pox.[32]

Despite having 5-8 lakh retail chemists in the country.By placing widely used painkillers, balms and cough syrups under OTC, they can be sold at the counters of grocery stores and other shops without a drug licence. Numbers of such trade channels are considerably larger and widespread than retail chemists shops. For pharmaceutical companies and some of the FMCG corporations, marketing of OTC medicines is thus going to be a huge business opportunity. [33]

The issues pertaining to OTC drugs' safe usage are many in India: Drastic change in the labeling practices of DTC medicines have to be compulsorily enforced if they have to be sold outside medical shops. Firstly, labeling of OTC medicines has to be in local languages and all the instruction have to be in simple and easily understandable words. At present, very few pharma companies are printing labels in local languages.

Generally labels on OTC products also do not indicate specified doses for children. It has to be ensured that all OTC drugs specify the correct needs for children in terms of quantities, frequency and duration of their intake.

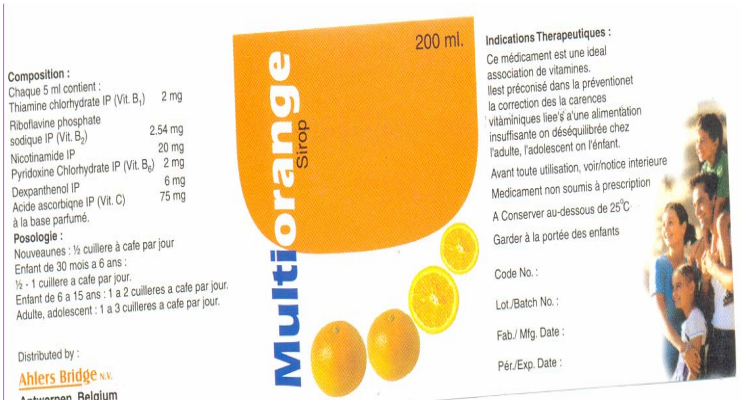


Figure 10:- U.K. multiorange syrup label

Supervision of OTC Drugs Labeling in Canada

OTC and Rx in battle over ageing Canadians in need of medication .Older Canadians continue to provide a solid consumer base for over-the-counter medication. However,

retail sales of OTC drugs showed much slower growth compared to the booming market for prescription drugs, as older people still turn to prescription drugs more often. Rx medications are usually seen as more effective and are covered under provincial healthcare plans. Although, in 2005 OTC pain relief medications managed to steal the show from prescription pain killers due to the recall of Vioxx and the subsequent concerns over side-effects of some arthritis pain prescription drugs. [34]

Drugstores/parapharmacies remained the leading distribution channel for OTC drugs in Canada, although the share of sales of the independent pharmacists/chemists declined. Drugstores increased the number of outlets and expanded their selection of products and services far beyond medications, thereby increasing flow of consumer traffic into their stores. At the same time, grocery outlets continued to gain ground in sales of over-the-counter drugs, as they opened more in-store pharmacies, expanded their self-service OTC aisles and the number of their store brands.

The *NHP (*Natural Health Products) *Regulations* , the labeling requirements include recommended conditions of use, the common and proper name of each medicinal ingredient, a listing of the non-medicinal ingredients, storage conditions, a description of the source material of a medicinal ingredient, a lot number, and expiry date. [35]

Product labeling is the major method by which manufacturers of nonprescription drugs communicate information about their products to consumers. survey revealed that while 87% of consumers read nonprescription product labels, only 80% find the information easy to understand and 74% find the information easy to read. The Drugs Directorate has indicated that it will support changes to label copy, on a voluntary basis, as long as NDMAC is able to provide proof that the recommended standard copy changes represent an improvement over the existing wording. NDMAC plans to engage the expertise of the Canadian Public Health Association's National Literacy and Health Program, the National Literacy Secretariat and Office of Learning Technology of Human Resource Development Canada, and the Consumer Association of Canada USPDI Literacy Program. NDMAC expects to implement its new, voluntary, labeling standard in 2005. [36]. Private label products showed fairly good growth in virtually all areas of OTC healthcare, and grew particularly strongly in grocery outlets. This tendency was largely due to the fact that grocery OTC store brands are fairly new, compared to more established private labels in drugstores. In fact, store brands for some medications, such vaginal antifungals, only started

appearing in Canadian food stores towards the end of the review period as more grocery outlets were opening in-store pharmacies, thereby circumventing Canadian regulations that allowed sales of these products in pharmacies only. [37]

Supervision of OTC Drugs Labeling in Europe

Europe's six largest markets for non-prescription and OTC self-medication skincare. Markets covered are - France, Germany, Italy, Poland,and Spain . The European market for non-prescription skincare is entering a period of considerable change particularly in areas of regulation, reimbursement, innovation and competition. In an increasingly competitive and maturing market. Successful companies are adapting their brand marketing strategies to meet new challenges and seize new opportunities. Skincare in OTC Self-medication in Europe is an in-depth market report that explores the issues and attractiveness of opportunities in this dynamic market sector. [38]

1.Six country profiles - European non-prescription and OTC medicines market includes: regulatory issues, distribution channels, innovation, companies and market data and trends from 1999 to 2010 .

2. Analysis of the European market for non-prescription and OTC self-medication skincare, consumption trends, innovation and evolving brand marketing models

3.European sales data by country for non-prescription and OTC Self-medication skincare including-Acne treatments, Antiseptics and Skin disinfectants, Topical antihistamines and Topical relief for Bites and Stings, Anti-fungal treatments, Anti-pruritics and Counter Irritation Skincare medication, Emollients and Skin protection and treatments for Itchy Dry Skin, Cold Sores, Topical Steroids, Wound Healing Products, and Corn, Wart and Verucca Removers

4. Descriptions of leading brands and companies in each category and country in Europe's non-prescription skincare market

All medicines are required by Community law to be accompanied by outer/inner labelingtext and a Package Leaflet setting out comprehensive information which is accessible to and understandable by those who receive it, so that they can use their medicine safely andappropriately. The safe and correct use of all medicines depends on users reading thelabeling and packaging carefully and accurately and being able to understand and act on the information presented. According to Article 54, Article 55

and Article 59 of Directive 2001/83/EC medicinal products must be accompanied by outer or immediate packaging information (labeling) and a package leaflet. Article 58 allows for the omission of a package leaflet where all the required information can be directly conveyed on the packaging. Article 56 of Directive 2001/83/EC requires that the label text shall be easily legible, clearly comprehensible and indelible. [39]

Article 56a of Directive 2001/83/EC requires the name of the medicinal product to be expressed in Braille format on the packaging, and the marketing authorisation holder to ensure that the package leaflet is made available on request from patients' organisations in formats appropriate for the blind and partially-sighted. Article 59(3) of Directive 2001/83/EC provides that the package leaflet shall reflect the results of consultations with target patient groups to ensure that it is legible, clear and easy to use. Article 61(1) and 8(3)(j) of Directive 2001/83/EC specify that one or more mock-ups of the outer packaging and the immediate packaging of a medicinal product, together with the draft package leaflet, shall be submitted to the competent authority at the time of marketing authorisation application. The results of assessments carried out in cooperation with target patient groups shall also be provided. [40]

Article 63(1) requires that the labeling and package leaflet shall be provided in the official language of the member state where the product is placed on the market. Additional languages can be included provided the information presented is the same in all languages and it does not impact adversely on the legibility, clarity and comprehensibility of the text. Article 63(2) of Directive 2001/83/EC requires that the package leaflet must be written and designed to be clear and understandable, enabling the users to act appropriately, when necessary with the help of health professionals. The package leaflet must be clearly legible in the official language or languages of the member state(s) in which the medicinal product is placed on the market. This guideline is published in accordance with Article 65 of Directive 2001/83/EC, which provides for the development of guidelines concerning, amongst other things, the legibility of particulars on the labeling and package leaflet. [41]

Supervision of OTC Drugs Labeling in Japan

OTC medicines sales in the first half of the year 2006 (April ~ September 2006) were 99% as compared with the same period of the previous year. As for the therapeutic category relating to a common cold, the unseasonable weather during the first quarter was responsible for an increase in the incidence of a common cold characterized by

the symptoms developed in the throat. Thus Multi-symptoms cold remedies registered a two-digit growth in April, May, and June consecutively. During the same period, Anti-tussives & expectorants, and Oral cavity drugs also recorded favorable sales. Also during September, the month of a change of season, many people under the weather with a cold contributed to a growth of the sales of the therapeutic category relating to a common cold. All in all, the first half of the year saw sales, as compared with the same period of the previous year, of 108%, 105% and 102% in Multi-symptoms cold remedies, Anti-tussives & expectorants, and Oral cavity drugs respectively. [42]

Indian label multivitamin syrup **European label multivitamin syrup**

Figure 11- Difference between Indian and European labels of multivitamin syrup

The OTC healthcare market is expected to post healthy growth over the forecast period despite a stiff competitive environment. Key growth areas will be vitamins and dietary supplements, smoking cessation aids and calming and sleeping products -- ie remedies that promote and maintain good health. Topical analgesics, topical antifungal, hair loss treatments and allergy-related products are also expected to grow due to an expanding consumer base. Growth is also expected on the back of rising consumer awareness of self-medication, and regulatory boosts when revisions to the Pharmaceutical Affairs Law take effect in 2006. [43]

The MHLW(Ministry of Health labour and Welfare) issued notifications in August 1999 on entry methods for Precautions and information that should be included on the outer containers. The information supplied includes information on package inserts of prescription drugs, safety information disseminated by the MHLW, cases of suspected adverse reactions collected by the MHLW Labeling requirements of excipients of

non-prescription drugs are the same as those for prescription drugs according to a voluntary agreement of the JPMA (Notification No. 165 of the JPMA dated March 27, 1991) and Office Communication of the Safety Division, PAB dated June 3, 1991. Based on a voluntary agreement of the JPMA (Notification No. 170 of the JPMA dated March 13, 2002), all ingredients must be included in package inserts by March 31, 2004 and the names of excipients including voluntarily designated ingredients must be included on the outer container (or its equivalent). [44]

The most basic tool for supplying information on drugs to health professionals is package inserts, and the contents of package inserts for prescription drugs have been specified by the Pharmaceutical Affairs Law. These package inserts are public documents that pharmaceutical manufacturers and distributors are obliged to prepare for the purpose of supplying to physicians, dentists and pharmacists the information necessary to assure the safety of patients administered the drug and to promote the proper use of the drug concerned based on the provisions of the Pharmaceutical Affairs Law. [45]

The Law specifies items which must be included in the package inserts, points to consider when preparing the package inserts and items which are prohibited in package inserts. It also specifies penalties for not complying with these provisions and for including false or exaggerated information in package inserts. The MHLW has also issued notifications that provide guidelines on the actual items to be included and the order of their inclusion in package inserts, as well as guidelines on the preparation of Precautions for package inserts. Important information on adverse reactions, etc. obtained and evaluated in post-marketing surveillance on product safety must be reflected in package inserts. Because of the limitations on space and the amount of information that can be presented in package inserts, manufacturers and distributors may prepare various types of information to supplement the package inserts. [46]

Supervision of OTC Drugs Labeling in U.S.A

FDA has finalized its regulation that will require nonprescription drugs to carry clear, simple and readable labeling. This action also will make it easier for consumers to understand information about products, benefits and risks and how the drugs should be used most effectively.[47] It will also help ensure that consumers select the right product to meet their needs. The new format will enable consumers to more readily and easily determine whether a product contains ingredients that they need or do not

need or should not take. It will also make it easier to compare similar products to determine which ingredients are right for them based on their symptoms and personal health situation. [48]

- Minimum type size

  Title = a type size larger than the largest type size
  Headings = at least 8 point or 2 points larger than text
  Text and subheadings = at least 6 point

- **A clear, easy-to-read type style, such as** Helvetica or Universe, with no more than 39 characters per inch.
- **Left justified text**
- **Leading** - at least 0.5 point (minimum space between lines)
- **Kerning** - letters cannot touch
- **Clearly marked sections with hairlines between sections**
- **Bold line surrounding Drug Facts information**
- **Upper and lower case letters only** - no all caps
- **Bullets** - solid square or circle, 5 point type
- **Directions table** - if three or more categories
- **Other graphical highlights** - contrast, white space, etc.

There are also special provisions which allow modifications when the information does not fit on small or unusually shaped packages:

- These exemptions may be used if 60% of available label space is insufficient to bear required labeling information.
- If more than one bulleted statement is on a line, the second bullet may start on one line and continue to the next line. Also bulleted statements need not be vertically aligned.
- Surrounding box may be omitted if information is offset using color contrast.
- Less than 0.5 point leading may be used.
- Headings may be presented using a 7-point minimum type size.

The national requirements on OTC products are all based on the WHO Guideline for the Regulatory Assessment of Medicinal Products for use in Self-medication and are mainly focussing on the safety of the drug product and on the question whether the product is appropriate for self-medication. Furtheron special requirements regarding the labeling of an OTC drug product are formulated. In addition to the safety concerns the effectiveness of the drug product is stated as one requirement for an OTC switch in the USA. [49]

The OTC labeling rule applies to more than 100,000 OTC drug products.

Before simplifying the OTC label, the FDA conducted extensive research on how consumers use OTC drug product labels. One major problem has been the readability of the labels, especially for older Americans, who purchase almost 30 percent of the OTC drugs sold in the United States. The FDA also found that consumers thought words like "indications," "precautions," and "contraindications" were confusing and not easily understood.

Previously, information about product directions, warnings, and approved uses appeared in different places on the label depending on the OTC product and brand. Finding information about inactive ingredients has also been a challenge for those who may be allergic to an ingredient in a drug product.

Patterned after the Nutrition Facts food label, the Drug Facts label uses simple language and an easy-to-read format to help people compare and select OTC medicines and follow dosage instructions. The following information must appear in this order [50]

1 The product's active ingredients, including the amount in each dosage unit.

2 The purpose of the product.

3 The uses (indications) for the product.

4 Specific warnings, including when the product should not be used under any circumstances, and when it is appropriate to consult with a doctor or pharmacist. This section also describes side effects that could occur and substances or activities to avoid.[51]

5 Dosage instructions--when, how, and how often to take the product.

6 The product's inactive ingredients, important information to help consumers avoid

ingredients that may cause an allergic reaction. [52]

Supervision of OTC Drugs Labeling in China

Packagings of pharmaceuticals are regulated under the State Pharmaceutical Administration of China (SPAC) the packaging and information notice of the pharmaceuticals should be in Chinese language. The Pharmaceutical Administration Law sets forth the specific requirements on package insert: the name and strength of the product, name of the manufacturer, the PRC government certification number, the lot number, principal ingredients, indications, dosage, contra-indications, adverse reactions and precautions in using. Trademark information must be marked on the package. [53]

China is a large and fast-growing pharmaceuticals industry. The estimated value of the domestic industry in China, at the end of 2005, will be in the region of RMB288.74bn (US$34.89bn), and will have grown by over 140% since 1998.For the domestic industry in China, the problem is that, although it is one of the world's largest bulk manufacturers of raw drugs ingredients.[54] China has yet to develop a real capability to develop its own proprietary drugs. This means that 99% of the over-the-counter drugs sold in pharmacies in China were developed by foreign companies. This means that China continues to pay a royalty to these developers, for drugs it could easily be developing for itself. Given the huge size of the domestic market, both for OTC and prescription drugs, the value of the royalties paid must be huge - which is why foreign drugs makers are so keen to corner the market for themselves. However, the Chinese manufacturers are at last beginning to work together to develop their own patent drugs, in order to begin reaping real profits.[55]

The market for OTC healthcare in China saw growth of approaching 11% in current value terms in 2005, underpinned by the continued rise in the preference of consumers to self-medicate. According to the Survey of State Hygiene Service in 2003, almost 45% of the population in Chinese cities and towns, and 79% of the population in rural areas, have no medical insurance, which means they cannot reimburse their medical costs.

Thus these consumers tend to purchase medicines themselves instead of seeing a doctor’s advice, mainly due to the lower cost in the retail channel. On the other hand,

while consumers in cities are able to reimburse the medical expenses, they are also willing to purchase medicines on an OTC basis for added convenience

The *Pharmaceutical Administration Law* sets forth the specific requirements on package insert, namely:

- Name and strength of the product
- Name of the manufacturer
- PRC government certification number
- Lot number
- Principal ingredients
- Indications
- Dosage
- Contra-indications
- Adverse reactions

Conclusion

Wide variation in labeling requirements of various countries poses numerous problems in an era of globalization. As a consequence, there is strong use for empowering WHO to harmonize uniform labeling requirement need for all the countries in the world. Rapidly changing global scenario necessitates urgent for complete harmonization in the present day regulatory environment

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