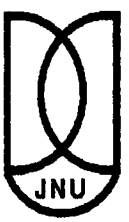
ETHICAL ISSUES IN MEDICINAL DRUG PROMOTION - AN ANALYSIS OF THE SITUATION IN NEPAL

Dissertation submitted to Jawaharlal Nehru University in partial fulfillment of the requirements for the award of the degree of

MASTER OF PHILOSOPHY

AVANIENDRA CHAKRAVARTTY



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NEW DELHI - 110 067

DECLARATION BY THE CANDIDATE

This dissertation titled "**ETHICAL ISSUES IN MEDICINAL DRUG PROMOTION – AN ANALYSIS OF THE SITUATION IN NEPAL**", submitted by me, in partial fulfillment for the award of the degree of MASTER OF PHILOSOPHY, is an original work and has not been submitted so far in part or in full, for any other degree or diploma of this University or any other University or Institution.

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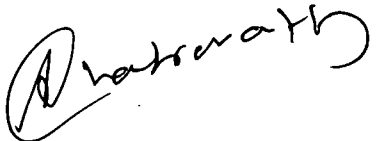

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CERTIFICATE

This dissertation entitled "**ETHICAL ISSUES IN MEDICINAL DRUG PROMOTION – AN ANALYSIS OF THE SITUATION IN NEPAL**" is submitted in partial fulfilment of six credits for the award of the Degree of MASTER OF PHILOSOPHY of Jawaharlal Nehru University. This dissertation has not been submitted for the award of any other degree of this university or any other university and is my original work.

Avaniendra Chakravartty

We recommend that this dissertation be placed before the examiners for evaluation.

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Chapter -1

Background

The distribution of imported medicines in Nepal started much earlier than the manufacturing of allopathic medicine in Nepal. It is only after 1950's efforts to start manufacturing allopathic medicine in Nepal has begun. The geographical market integration of the country brought by the construction of the east-west highway and other link roads paved the way for opening of scope for pharmaceutical companies (Subedi 2006). A total of 5488 foreign and 3006 domestic pharmaceutical products are authorized for marketing in Nepal (DDA, Drug bulletin Nepal 2009). The Drug Act of 1978 was promulgated in Nepal to prohibit the misuse or abuse of allied pharmaceutical materials as well as the false or misleading information relating to efficacy and use of drugs and to regulate and control the production marketing, distribution, export-import, storage and utilization of those drugs which are not safe for the use of the people efficacious and of standard quality. In accordance with objectives of the National Health Policy 1991, the National Drug Policy 1995 has been implemented.

In 1986, eight years after the Drug Act, the Government of Nepal published the National List of Essential Drugs based on the country's disease pattern as well as the relative merit of selected drugs in terms of cost, safety, and efficacy. Further, this step was taken in response to the request of WHO to all member countries to have a list of essential drugs as per the country's need. This list was revised in 1992, 1997 and 2002 respectively. Similarly, Standards for Pharmaceutical Regulation and Care was prepared and implemented in 2002 to measure performance and to meet the requirement of people by ensuring quality in the services provided by applying indicators for monitoring. This document adapted the WHO/SEARO framework for developing health care standards. The major focus has been given to quality characteristics and standards for drug regulatory control, drug supply and management, rational drug use and safe disposal. This framework highlighted the principles for regularly controlling pharmaceutical sales promotion and advertisement by measuring the level of promotional activities, and to prevent and monitor perverse incentives for prescribers and dispensers.

The pharmaceutical sector in Nepal comprises of several key stakeholders, Association of Pharmaceuticals Producers of Nepal (APPON), Nepal Medical Council (NMC), Nepal Pharmaceutical Association (NPA), Graduate Pharmacist Association-Nepal (GPAN), Nepal Chemist and Druggist Association (NCDA), Nepal Medical Association (NMA), Nepal Pharmacy Council and Nepal Medical and Sales Representative Association (NMSRA), and Department of Drug Administration (DDA).

Nepal's rapid integration into the world economy after 1950 has ushered in an era of privatisation, deregulation and other tenets of Free-Trade. In a laissez-faire

system the interest usually lies on economic profit and this affects all aspects of human life.

Drugs/medicines that are sold and used by the people of Nepal, as in other nations, reach them after many steps involving various actors at different levels who have their own interests. Drugs/medicines available to the people cannot be looked in isolation from the larger social, political, economical and cultural factors. Reports about counterfeit, over priced drugs, irrational and harmful drugs/medicines are rampant in many countries . Who are the victims of such drugs/medicines that harm them and push them further to poverty? Which class of people suffer from such harmful practices? Though, these questions are not part of the study I think it's important to know about the pattern of use of drugs/medicines amongst people at different strata's of society.

Allopathic drugs/medicines in Nepal-

Through the activities of Capuchine missionaries, modern Western medicine was already known in Nepal in the middle of the 18th century (Strbefland, 1985). Its prevalence in the country increased rapidly, however, during the first half of the 19th century (Dixit 1974). Labour-migration abroad and contacts of the Nepalese elite with the culture of the British, who established a Residency in Kathmandu after the Anglo-Nepali War of 1814-1816, formed the basis of this process. In 1890 the first of a number of government hospitals was built in Kathmandu. This initial period of building curative facilities was concluded in the middle of the 1930's after 22 general hospitals, a Cholera hospital, and a sanatorium had been constructed (Dixit 1966). In the 1950's when the country was going through fundamental political and administrative changes and, consequently, became much more accessible for people and influences from outside, a considerable acceleration in the spreading of modern Western medicine set in. In an UNCTAD (United Nations convention on trade and development) report it was estimated that 90% of the drugs were imported from India. Further, it was stated that "the private sector -pharmaceutical market appears to be an extension of the Indian market" and that "the private sector carries out very intensive promotional activity, and Indian manufacturers employ "detail men" (salesmen) to promote their products in Nepal. Fifty of them were stationed permanently in Nepal, while another 50 to 60 representatives visit the country periodically" (UNCTAD 1980). Until about 1970 the Nepal market was dominated by Indian companies, when Royal Drugs Nepal was set up. Presently, the DDA estimates that about 35 % of the country's drugs/medicines comes from the domestic sector (DDA, Drug bulletin Nepal 2009).

The pharmaceutical sector in Nepal from the retailers to the manufacturers claim that their main interest is to provide better access to medicines, which are safe, cheap and suit the epidemiological profile of the country . The geographical distribution of retailers and whole sellers of Allopathic medicines/drugs is very unequal. The number of retailers and whole sellers of drugs/medicines were more

in the Districts that figured higher in the socio-economic index. The table below shows the different districts along with its Human development index (HDI) ranking, life-expectancy at birth and the number of registered pharmacy outlets (allopathic) . In all the districts the allopathic medicine sector was dominant. Districts like Humla, Mugu, Jajarkot and Kalikot the poorerst districts had no other systems of medicines apart from allopathic.

Table-1.1- Human Development Index ranking of districts and availability of registered pharmacy outlets.

District	HDI Rank	Life expectancy at birth.		Registered pharmacy outlets, allopathy		Total (includes, AllopathyVeterinary Ayurved Homeo Unani) retailers and whole-sellers)
		Male	Females	Retailers	Wholesellers	
Nepal		61.5	60.5			
Morang	10	67.78	66.85	316	87	449
Sunsari	20	63.03	60.78	196	17	261
Rolpa	66	58.19	57.95	15	0	15
Rukum	63	57.76	55.90	10	0	10
Jajarkot	69	52.98	50.91	4	0	4
Bajhang	72	51.09	48.39	7	0	11
Bajura	73	46.24	45.16	4	0	5
Doti	62	56.75	59.99	12	1	13
Humla	68	58.68	58.11	2	0	2
Mugu	75	45.27	42.95	6	0	6
Kalilot	74	47.21	46.18	2	0	2
Dolpa	67	52.92	59.99	2	0	3

The above data was compiled from Human development report and from DRUG BULLETIN OF NEPAL volume 18 2006.

In the above table 1, I am trying to argue that in a capitalist economy, under the present neo-liberal policies, concentration of necessities of life, amongst which access to medicines is an important aspect too, is situated in areas which have more purchasing power and which are higher up in the Human Development Index. Though simply access to drugs/medicines will not improve the public health situation, it has important implications for overall public health improvement. The consumption of allopathic medicine is 90.8% when compared to other systems of medicines (DDA 2008).

On July 17th 2007, the Government of Nepal, through its Department of Drug Administration (DDA) released its Guidelines on Ethical Promotion of Medicine. The editorial of the August – November issue of the Drug Bulletin of Nepal, published by the DDA and entitled "Ethical promotion of medicine: Benefit to consumers". Acknowledging that the pharmaceutical industry has to promote its products as it is a business, the editorial locates the tensions between this and an "ethical" practice of rational prescribing. Acknowledging that what is ethical to one group may not be so to another the guidelines have been produced (after consultation with unnamed "stakeholders") to clarify this. Although starting as guidelines, the editorial goes on to state that these will need to be enforced by law and thereon will go on to become a "code" (Thapa 2006).

After the DDA released its Guidelines on Ethical Promotion of Medicine in 2007, the guidelines on medicinal drugs promotion, was opposed by various organisations existing at different levels. Nepal Chemist and Druggists Association (NCDA), one of the major stakeholders supposed to follow the Guidelines, forwarded a 12-point demand to the concerned authority to nullify the guidelines. Though NCDA is a non-governmental organization, it represents the interests of the importers, wholesalers and retailers. On August 6th 2007, NCDA announced that it would stop import of drugs from the very next day, as part of its protest. This sensitized the issue in the public sphere. In a complex system such as pharmaceutical trade, there are so many vested interests and players blame to another groups but not reflect critically on one's own practice (Harper, 2009).

Nepal being a small market with prospects for good scope in replacing imports has resulted in the development of industries, and the concept of bonus and special incentives has played a major role on promotional practices.. This has also resulted in some unethical practices by most of the companies, including Indian companies. At this juncture DDA proposed a study about the current promotional practices of the pharmaceutical companies in Nepal, a study that was supported by WHO. The main objective of the study was to identify the current

promotional practices of pharmaceutical products available in Nepal and assess the existing practices in context of WHO criteria for medicinal drug promotion and its compliance for ethical promotion.

In this regard, Graduate Pharmacy Association of Nepal (GPAN) conducted a study on promotional practices in the Nepalese pharmaceutical market in collaboration with DDA and WHO. A total of 30 pharmaceutical companies were selected consisting of 15 domestic and 15 Indian. The findings were presented in a seminar on Based on the research findings, the concerned stakeholders felt the need for the guidelines on ethical promotion of medicine. The study found a wide variation in bonus schemes offered by the companies. In some products, for example, cardiac were found without bonus. The products like Amoxicillin and Ciprofloxacin were in the market with a free offer which ranged from 10 percent to 100 percent. Albendazole 400 mg was another product in the market with a wide bonus range from 20 percent to 100 percent. Vitamin B complexes were in the market with as high as 60 percent bonus offer especially for 200 ml packs. The 100 ml packs were sold at the bonus offer half to that offered for 200 ml packs. Even products such as cough formula, anti ORS were having a bonus system. The most commonly used bonus by every company was a 10 percent offer, and 70-100 percent as exceptional cases with certain products. However, some companies had been practicing no offer system in the sale of some selected products.

In response to the relationship between WHO-GMP (good manufacturing practice) certified companies and bonus offer, the study did not find any relationship; the bonus offer was equally being practiced by WHO-GMP certified companies as well as other companies. Some WHO-GMP certified companies even have been seen to offer good gift items such as TV to the prescribers. However, some of the WHO GMP certified companies are found to have the maximum bonus offer of 20 percent with no bonus offer in certain selected products. The gift items being offered were carpets, pens, blankets, bed sheets, iron, calculator, TV, etc. The companies are also found to have practiced offering a good bonus for products that DDA had already decided an irrational combination. The companies had gone beyond ethical norms to provide a special incentive of personal benefit from the sale of products in quantity, while

forgetting the issues of quality and patients' benefit. It was very clear that the maximum benefit is being taken by the retailers enjoying bonus offer and long term credit limits. The study highlighted that the substitution by the retailers on prescription to go for products with more offer had resulted some set back on turnover growth of some companies focusing their promotion on ethical prescription base. The study results indicated the need for implementation of guidelines on ethical promotion in Nepal. Guidelines on the Ethical Promotion of Medicine was drafted and discussed with various stakeholders like Association of the Pharmaceutical Producers of Nepal (APPON), Nepal Medical Council (NMC), Nepal pharmaceutical Association (NPA), Graduate Pharmacy Association of Nepal (GPAN), Nepal Chemists and Druggists Association (NCDA), Nepal Medical Association (NMA), Nepal Pharmacy Council (NPC) and Nepal Medical and Sales Representative Association (NMSRA), and DDA implemented them from July 17, 2007. It is further mentioned that the criteria do not constitute legal obligations; governments may adopt legislation or other measures based on them as they deem fit.

The APPON welcomed the Ethical Guidelines and argued that this policy would help the long term benefit to the nation and its people towards making a stronger and self-reliant Nepal. NCDA, a key player in the distribution of drugs, voiced its reservation. Members of NCDA argued that some handful people, including the DDA, were trying to denigrate the reputation of NCDA by raising the issue of deal bonus in a bad light. They argued that the Ethical Guidelines talk about scraping deal bonus, but just by bringing out the Ethical Guidelines, one could not be sure that the deal bonus scheme. would be halted and the result will not be that drug price go down. They argue that profit will be transmitted straight to the producers, not to the general people. They see DDA and APPON have been making conspiracy to victimize the retailers and argue that such regulation cannot be implemented unilaterally focusing against NCDA but rather requires more debate and discussion.

Medicinal drugs regulation in Nepal- An overview

Government of Nepal has promulgated the Drug Act 1978, to prohibit the misuse or abuse of drugs and allied pharmaceutical materials as well as the false or misleading information relating to efficacy and use of drugs and to regulate and control the production, marketing, distribution, export-import, storage and utilization of those drugs which are not safe for the use of the people, efficacious and of standard quality. To implement and fulfill the aim of Drug Act 1978 and various regulations under it Government of Nepal established Department of Drug Administration (DDA) in 1979. In accordance with the objectives of the National Health Policy 1991, to improve and manage by establishing co-ordination among governmental, non-governmental and private organizations involved in the activities related to drug production, import, export, storage, supply, sales, distribution, quality assessment, regulatory control, rational use and information flow, the National Drug Policy 1995 has been implemented. Achieving the aim and objectives of National drug Policy is another important area for DDA. Under the Drug Act 1978, the following rules and regulation and codes have been implemented as supporting tools for the active enforcement of Drug Act 1978.

- Regulation on Constitution of Drug Consultative Council and Drug Advisory Committee, 2037
- Drug Registration Regulation, 2038
- Interrogation and Inspection Regulation, 2040
- Codes on Drug Manufacturing, 2041
- Drug Standard Regulation, 2043

In Nepal, monitoring and evaluation of drugs starting from the production, marketing, distribution, export-import, storage to use of safe and efficacious drug is done by the Department of Drug Administration (DDA). Manufacturer has to register their individual product to the DDA before marketing their product. Department of Drug Administration (DDA) has been implementing the Drug Act 1979 and its regulations. The DDA since then has been responsible for regulating the Nepalese market regarding medicinal Drug Promotionfrom different systems of medicine like, allopathy, ayurvedic, homeopathy and Unani. The focus of this study is on allopathic medicines.

The objectives of DDA is to regulate all functions relating drug like misuse and abuse of drugs and its raw materials, to stop false and misleading advertisement and make available safe, efficacious and quality drug to the general public by controlling the production, marketing, distribution, sale, export-import, storage and use of drugs.

Strategies

- Selection of essential drug to promote rational use of drugs
- Establishment of regional offices at all five regions for effective decentralization
- Strengthening of National Medicine Laboratory as an Independent National Drug Control Laboratory
- Drug Registration on scientific facts
- Promotion of rational drug use
- Development of an efficient drug information system to disseminate the relevant information
- Encouragement to promote and establish pharmaceutical industries to achieve self-reliance in the production of essential drugs
- Effective inspection to ensure the quality of marketed products
- Prevent misuse of antibiotic to combat antimicrobial resistance
- Strengthen national industry to comply with WHO-GMP

Sections and Branch Office of Department of Drug Administration and its functions-

The Branch offices of DDA exist in Biratnagar, Birgunj and Nepalgunj. All the three places are border towns close to the Indian border.

Drug Import and Export Section-

- To register the foreign drug manufacturing company and
- products for import in a scientific manner and issue the recommendation letter for import.
- To issue the recommendation letter for export of drugs.
- To renew the recommendation letter for import-export and cancel or ban the unnecessary products as required.

Drug Industry Section-

- To issue recommendation letter for the establishment of pharmaceutical industry and issue Product Manufacturing License and renew them.
- Check and approve the pharmaceutical manufacturing plant layout.
- Check and approve the products labels and issue the certificate for the sale and distribution.

- Issue letter of recommendation for the import of raw materials and renew them.

Pharmacy Registration Section-

- To register and issue pharmacy registration certificate to open retail / wholesale outlets of drugs and renew them.
- Issue and renew certificate of professionalist i.e. person authorized to sale drugs.
- Update the record of pharmacies.

Training and Drug Information Section-

- Conduct the refresher training to drug sellers.
- Disseminate information about drugs particularly side effects, contraindication, drug interaction, availability and storage condition and other necessary information regarding drugs.
- Publish Drug Bulletin of Nepal (DBN) three times every year and distribute them to health institutions, industries, medical doctors, health personnel's, pharmacists and others concerned person and institutions.
- Publish National List of Essential Drugs, Standard Treatment Schedule and Nepalese National Formulary and update them from time to time.
- Focal point for Drug Information Network of Nepal (DINoN).
- Co-ordinate training program for sale of drugs

Inspection Section-

- Inspect drug industries, wholesale and retail pharmacies regularly.
- Take legal and administrative action on cases of non-compliance as per the prevision of Drug Act and its Regulations.
- Control of sales and distribution of psychotropic and narcotic drugs.
- Co-ordinate Good Manufacturing Practice Audit.

National Medicine Laboratory (NML)-

National Medicines Laboratory, formally Royal Drug Research Laboratory (RDRL), is the principal body of Government of Nepal for testing and analysis of drugs. It is a National Drug Control Laboratory. It has various sections like chemical analysis, microbiology, pharmacology and instrumental analysis. The main functions of NML are :

- Test and analyze the quality of drug as empowered according to the Drug Act 1978.
- Check and evaluate the standard of drug testing laboratories in the country.
- Develop Reference Standard and make available to the pharmaceutical industries and laboratories
- Conduct training on Good Laboratory Practices.
- Audit laboratories of National pharmaceutical industries.

Regulating medicinal Drug Promotion by Department of Drug Administration- Information to physicians and health-related professionals-

The wording and illustrations in information to physicians and related health professionals should be fully consistent with the approved scientific data sheet for the medicine concerned or other source of information with similar content. The text should be fully legible. Information that make a promotional claim should at least contain summary scientific information. Information should usually contain, among others(DDA, Guidelines on Ethical Promotion of Medicine, , 2007):

- The name(s) of the active ingredient(s) using either international non proprietary names or the approved generic name of the drug;
- The brand name;
- Content of active ingredient(s) per dosage form or regimen;
- Name of all the excipients and their role in the dosage form;
- Approved therapeutic uses;
- Dosage form or regimen;
- Side-effects and major adverse drug reactions;
- Precautions, contra-indications and warnings;
- Major interactions;
- Name and address of manufacturer, and distributor, where applicable;
- Reference to scientific literature as appropriate.
- Date of production of the information;

CHAPTER-2

Research Framework and Methodology –

2.1- Rationale of the study-

Medicinal drug promotion is an integral part of pharmaceutical marketing. The World Health Organization (WHO) defines, "promotion as all the informational and persuasive activities by manufacturers and distributors, the effect of which influence the prescription, supply, purchase and/or use of medicinal drugs". There are various methods by which pharmaceutical companies promote their drugs. The most common methods are drug promotion using medical representatives (MR), distributing free samples, advertisement through pamphlets, radio, TV and sponsoring medical events". (Thapa, 2007). In a free market guided by pecuniary incentives in the forefront, drug companies have indulged in unethical practices at different stages ranging from manufacturing of drugs, drugs promotion to suppression of adverse drug effect findings.

The pharmaceutical sectors just like any other commercial sectors have their focus on economic profit. In the present era of neo-liberalism the dictates of free trade the pharmaceutical sector along with other health care institutions have become highly commoditised. With increasing pressure to capture the market different commercial sectors have indulged in various unethical practices, to say the least. The poorer the country the higher percentage of expenditure on pharmaceuticals is from out of pocket. The WHO Essential Drug Program has failed in most countries because of personal financial interests at local, national and foreign levels or a black market (Chattopadhyay, 1999). Studies indicate that a country's capacity to restrict dangerous drugs depends heavily on its wealth (Menkes, 1997). Nepal comes under the 'least developed countries' catergory as per the United Nations and ranks 142 in terms of human development indicator as per the human development report. Unnecessary, Irrational Drug use leads to iatrogenic poverty, adverse drug effects (ADD), drug resistance (DR). The issues of ADD, DR occur only after the consumption of the drug. For the consumption of the drug by the patients require that the medicinal drugs be prescribed by the doctors, registered in the country. Use of allopathic/western medicinal drugs has been more significant for different ailments then other drugs provided by other alternative medicines. The major medicine use problems in Nepal are

polypharmacy and misuse of antibiotics. Self medication is a common practice in Nepal (Nepal,2000), (Kafle KK, 1993). Use of vitamins and tonics, irrational fixed dose combinations and unethical and aggressive drug promotion are other common practices. (INRUD, 2003).

2.2 Conceptual Framework-

This study deals with the ethical issues pertaining in the pharmaceutical sector. The present study uses few concepts like the, concept of ethics, Medicinal Drug Promotion, the concept of double standards, (An ethical or moral code that applies more strictly to one group than to another).

The international pharmaceutical manufacturing sector is a continuous source of polemic and divisive debate. It is a sector unlike most in that its products have the potential to significantly improve deteriorating health conditions, and in many cases save lives. Unlike other products offered in the market (apparels, electronics etc) with the sole purpose of profit motive, pharmaceutical products when left to the market forces becomes a matter of life and death for the poor globally. The idea of medical markets has been described as a "theoretical anomaly" (Donald, 2000a). as medical markets often do not meet many of the elements in classical definitions of a competitive marketplace. "Asymmetry of information" and "uncertainty in the definition, recognition, and diagnosis of disease states" in particular distinguish medical markets from other "consumer" markets" (Montagne, 1992). To understand the present state of pharmaceutical sector it is necessary, to have an understanding of the history of pharmaceutical sectors. Healing or to heal is the foremost function of the pharmaceutical sector. All communities around the world had their specific healing procedures through, out history. Colonialism in the past and the present system of a free market economy has changed healing practices throughout the world. From a practice guided by benevolence, healing practices seem to be guided by malevolence where pecuniary objectives are at the forefront.

2.2.1- Conceptualising ethics in the pharmaceutical sector-

Religious and cultural laws as well as ethics have always been important in Medicine. The Code of Hammurabi, a Babylonian king of 18th century BC, included laws relating to the practice of medicine and the penalties for which were severe (Britannica). The earliest existing documents regulating the practice of medicine are records of Egyptian laws from the sixteenth century B.C. and the Babylonian Code of Hammurabi dated about 2000 B.C. These legal documents included guidance on what fees could be charged, what constituted competent medical care, the conditions under which a physician could be held accountable for malpractice, and what sanctions would apply. The first significant statement on medical morality, however, is the Hippocratic Oath (fourth century B.C.).

In terms of the pharmaceutical sector the question of ethics is both a pragmatic and rational issue. Since the 1960's, the study of ethics has seen the growth of interest among philosophers in practical, or applied ethics; i.e. the application of normative theories to practical moral problems.

The free market is all about profit seeking and the maximising of potential returns. Exploitation of the market at once brings personal or corporate gain, but also facilitates the notion of the invisible hand to achieve the common good of increasing wealth. For Adam Smith, the invisible hand is essentially the unseen outcome of individual rational choices supporting the common good serendipitously rather than arising from any moral motives by the actor to achieve the goal, apart from self interest. In straightforward terms it might be considered ethical to act upon selfishly as that is what is required to make the market fully functional. Any deviation from this course could be construed as damping down the market's potential. This leads to the philosophical questions which concern the meaning of ethics, intentionality and the meaning of the common good. On the basis of arguments derived from Adam Smith to Friedrich von Hayek and others belonging to the same school of thought, the Neo-Liberals can hold that ethics has no place in the market and in fact could ultimately lead to negative rather than positive outcomes. While neo-liberals may be able to rationalize self-maximizing strategies as part of the essential workings of the market, they fall into the apparition of assuming that the market and society are one and the same. This approach operates on the assumption that rights are one-dimensional, while

in fact they comprise of two poles–entitlements and obligations. It is not just a case of the rational actor exploiting his or her autonomous rights, but as Kant outlined in The Metaphysics of Morals they are also obligated to act responsibly. This is drawn out in his second formulation of the categorical imperative: 'so act that you always treat humanity, whether in your own person or in the person of any other, never merely as a means but always at the same time as an end' (Kant, 1991).

Though there always was the existence of alternative systems of medicine, the interest of the "market" had not entered the markets in a significant way in the developing countries largely in Asia, Africa and Latin America until the end of the Second World War. With countries getting free from the colonial rulers the people had their own governments. During the period between 1950's till date policies have changed and the whole idea of the role of the state has changed from being a welfare state to a state where it starts viewing its citizens as consumers.

Due to the "Asymmetry of information", the competitive nature of the market, profit maximisation that the pharmaceutical sectors have been involved in violation of ethical standards and which has been a recurring issue.

2.2.2 Conceptualising pharmaceutical promotion within the pharmaceutical sector-

The WHO guidelines on Ethical Criteria for Medicinal Drug Promotion and the Guidelines on Ethical Promotion of Medicine, 2007 published by the Department of Drug administration Nepal has been used as the yardstick to study the promotional activities and adherence to ethical standards through which medicinal Drug Promotionare marketed.

The pharmaceutical sector is a wide and complex sector also referred to as the 'medicines chain'. The medicines chain refers to the steps required for the creation, regulation, management and consumption of pharmaceuticals (WHO, Measuring transparency in the public pharmaceutical sector: assessment instrument., 2009). The medicines chain includes the following steps: (WHO, A Framework for Good Governance in the Public Pharmaceutical Sector., 2008).

1. Research and development of new medicines or chemical entities
2. Conducting clinical trials
3. Filing patents
4. Manufacturing
5. Registration
6. Price fixing
7. Licensing of professionals and establishments
8. Selection of essential medicines
9. Procurement
10. Distribution
11. Inspection of establishments
12. Prescription
13. Dispensing
14. Pharmacovigilance
15. Medicines promotion

Each step is vulnerable to corruption and involves different professional expertise, such as the medical profession (nurses, pharmacists, physicians, etc.), economists, lawyers and researchers (WHO, 2008). Transparency International defines corruption as: "the abuse of entrusted power for private gain□ (Transparency International).

Drug promotion is one part of the 15 different issues in the medicines chain that are vulnerable to corruption. A comparative analysis of the various national assessments reveals that control of medicines promotion is often identified as the function most vulnerable to corruption (Serhan, 2010). Drug promotion has many different facets such as- Advertisements, Sales representatives, Sponsored conferences and seminars, Promotional 'research, Gifts, Industry-funded medical or scientific journals, Use of 'opinion leaders', Industry-funded research published in peer-reviewed journals, Free samples, Use of the Internet for promotion (Mintzes, 2005). Two different ways of drug

promotion exist in Nepal, promotion to the healthcare professionals and to the general public. In this study promotion of medicinal Drug Promotion to health care professionals has been dealt with. The exploration of drug promotion and the concurrent issues that come up in this stage has been studied. They are various ways through which promotion to health care professionals take place some are covert in nature and some are overt in nature. Promotional brochures given to health care professionals by different pharmaceutical companies are overt in nature and hence these brochures will be analysed to assess the extent of adherence to prescribed ethical guidelines.

2.2.3- Banned, withdrawn, not approved drugs-

The consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not approved by governments is part of a continuing effort in the United Nations systems aimed at disseminating information on products harmful to health and the environment. It constitutes a tool which helps governments to keep current with regulatory decisions taken by other governments and assists them in considering the scope for their own eventual regulatory action. It enables government agencies which review applications for product registration to ascertain easily restrictive regulatory decisions made in other countries. It complements and consolidates other information on the subject produced within the United Nations system, including data received from United Nations Environment programme (UNEP) and Food and Agriculture organisation of the United (FAO) on chemicals and from World Health Organization (WHO) on pharmaceuticals. The main source of information on chemicals is the Prior Informed Consent (PIC) circulars issued by the the secretariat which is maintained jointly by UNEP and FAO, of the Rotterdam Convention on the Prior Informed Consent on the Prior Informed Consent procedure for certain hazardous chemicals and pesticides in International trade. The list also contains information previously received under the original PIC procedure as well as the Notification Scheme for Banned and Severely Restricted Chemicals. The source on pharmaceuticals is WHO Drug Information, circulars and pharmaceuticals, Newsletters which contain information, received from Member States on the safety and efficacy of drugs including information gathered through drug monitoring programmes as well as

certification scheme on the quality of pharmaceutical products moving in international commerce.

2.3- Research questions-

- What are the different ethical issues in theMedicinal drug promotion?
- What are the different drugs that are being marketed despite being removed, banned or not approved by governments in developed and developing countries?
- Do drug promotional materials adhere to WHO guidelines on ethical promotion?
- What has been the role of regulatory bodies in maintaining ethical standards at various levels of drug promotion?

2.4- Objectives of the Study-

The objectives of this study are as follows-

1. To identify the ethical issues relevant to medicinal Drug promotion.
2. To identify whether medicinal drugs that have been banned, withdrawn or not approved by governments according to the "*Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted or not Approved by governments*" are available in Nepal.
3. To study the ethical standards of medicinal drug promotion through which pharmaceutical medicines are marketed and whether they adhered to WHO guidelines on ethical promotion of medicines?
4. To study the role of regulatory authorities in ensuring safe and rational use of drugs/medicines.

2.5- Operational definitions-

- **Medicinal drugs** - Medicinal drugs are chemical substances that affect the functioning of living things and organisms that affect them. The term 'medicinal drug' has been used by the World Health Organisation in its "Ethical Criteria for Medicinal Drug promotion. Geneva: World Health Organization" which was published in 1988.
- **Promotion-** In this context, "promotion" refers to all informational and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs.

- **Promotional materials-** Promotional materials distributed to medicinal drug prescribers by different companies.
- **Banned-** A product that has been withdrawn from use and/or sale nationally in one or more countries by order of the competent national authority, having regard to its safety in relation to its intended use (UNO, 2009).
- **Withdrawn-** A product formerly in commerce that has been withdrawn for all uses nationally in one or more countries by final voluntary action of the manufacturer because of health or environmental reasons (UNO, 2009). For the purpose of this study "withdrawn" will refer to only medicinal Drug Promotionwithdrawn due to health reasons.
- **Not approved-** A product that has been formally submitted for registration by a manufacturer to a national competent authority and which has been rejected on grounds of safety (UNO, 2009).
- **Medicinal drug retailers-** The point where selling of goods to consumers is done directly.

2.6 Research Design-

Both primary and secondary sources were utilised during the study. The attempted study uses secondary data, through a literature review to identify medicinal drugs that are banned, withdrawn or not approved and it uses a check list to identify the availability of these medicinal drugs in medicinal drug retail shops. For studying medicinal drug promotion and adherence to ethical guidelines it uses data available from different pharmaceutical companies in the form of promotional brochures and compares these promotional brochures to the criteria prescribed by WHO criteria for ethical promotion of medicinal drugs.

2.6.1- Study Area-

The study was conducted in Biratnagar a city in Eastern Nepal bordering India. Biratnagar is the second largest city in Nepal. According to the DDA Branch office, there are 242 medicinal drug retailers in Biratnagar. Morang District of which Biratnagar is the headquarter has 316 medicinal drug retailers.

2.6.2- Sampling-

The study uses secondary sources for sampling. For identifying medicinal drugs that are banned, withdrawn or not approved the study uses the, United Nations report on "Consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not approved by governments"(14th issue 2005) and "Pharmaceuticals: restrictions in use and availability"(2010) published by the World Health Organisation, which is prepared within ,the context of the "Consolidated List of Products whose Consumption and/or Sale have been Banned, Withdrawn, Severely Restricted or Not Approved by Governments" which is also an update of the 14th issue. Medicinal drugs that have been banned, withdrawn or not approved in two or more countries were selected for study. The reason for choosing medicinal drugs banned, withdrawn or not approved in at least two countries is to be certain about its status. Moreover pharmaceutical industries have also claimed that some medicinal drugs have been banned, withdrawn or not approved with insufficient proof. Medicinal drugs that were banned, withdrawn or not approved according to the above mentioned criteria were then searched for in the "List of Manufacture with product(s) including Ingredient" published by the Department of Drug Administration, Nepal in the year 2007. Banned, withdrawn or not approved medicinal drugs that were present in the, List of Manufacture with product(s) including Ingredient were sorted out. These medicinal drugs were then identified by their brand names (See table 4.1) and then medicinal drug retails shops were visited and then enquired about the availability status of these medicinal drugs. A total of 30 medicinal drug retailers were given a check list with the brand name and generic names mentioned. The 30 medicinal drug retailers were chosen by the following criteria-

- 10 medicinal drug retailers were chosen based on their proximity to Koshi Zonal Hospital which is a government hospital and also the oldest in Biratnagar.
- 10 medicinal drug retailers were chosen based on their proximity to Nobel Medical College which is a private medical college.
- 10 medicinal drugs retailers were chosen based on their proximity to two different private run hospitals, Awadh Narayan Nursing Home and Birat Nursing Home.

The medicinal drugs chosen for studying, medicinal drug promotion and adherence to ethical guidelines were based on the level of consumption.

Promotional materials of 'antibiotic' medicinal drug promotion were chosen. The total consumption of antibiotics in 2005/06 was Rs.2 billion 717million. Of which, 48.7% was shared by domestic industries. About 30% of total consumption of drugs was covered by antibiotics. (DDA 2007).

Promotional materials printed only after 2008 were selected since, Nepal issued its guidelines on ethical promotion of medicines only in 2007. They are two different criteria for advertisements to healthcare professionals and to the general public. In this study advertisements to physicians and health care professionals were selected. The top 3 antibiotics sold were chosen for the study. These top 3 antibiotics are available from both the domestic and foreign companies. For assessing the different promotional brochures the first step was to choose the manufacturers. Amoxicillin was produced by 53 manufacturers, Ciprofloxacin by 59 manufacturers and Cefadroxil by 20 manufacturers. Since 10 promotional brochures was to be selected from each category, I decided to select the promotional materials of those 10 companies based on the price of their products (High to low) which is mentioned in the, 'List of manufacture with products'. If the promotional brochures of any product was not available then the next product was selected.

2.6.3- Tools for data collection-

Both primary and secondary sources were utilised during the data collection exercise. The study begins by looking at the primary data available on medicinal drug promotion such as promotional materials of the different medicinal drugs available at the the Biratnagar branch office of the DDA. For identifying banned medicinal drugs available secondary sources such as the "List of Manufacturers with product(s) including Ingredients" published in June 2007 (Jestha 2064) and The Consolidated List of Products whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted or Not Approved by Governments were used. Medicinal drugs that were banned according to the "Consolidated List of Products whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted or Not Approved by Governments" but were mentioned in the List of Manufacturers with product(s) including Ingredients" were selected. These availability of these medicinal drugs were then further checked by visiting medicinal drug retailers.

To study the *first* objective, "identifying ethical issues relevant to medicinal Drug promotion, a literature review was done. Google Scholar was used to avail the literature available on medicinal drug promotion. Rather than using specific search engines like Pub Med, Meds cape which limits the searches, 'Scholar's great breadth of coverage makes it a handy tool for searching those topics that do not instantly lend themselves to specific subject indexes (e.g., "brain drain"). Google Scholar is a handy tool for verifying citations, extending the limits of Pub Med's Single Citation Matcher'.A user study among students at Uppsala University in Sweden measurin g the effect of training for Google Scholar showed that students may be enabled to retrieve full text peer-reviewed documents, relevant for their assignment (Haya, 2007). Using Google Scholar had a positive effect and increased their degree of information literacy according to the aspects of locating and using information. Google Scholar has been referred as a new paradigm in academic research (Drewry, 2007).

The key words searched for the literature review, were, *drug promotion/advertising, medicine promotion/advertising, Monetary involvement in medicinal drug promotion, medicinal drug promotion to Physicians or Prescribers, Regulating drugs/medicine promotion, ethical issues in drug promotion, unethical and aggressive drug promotion, irrational use of drugs and developing nations*. The inclusion criteria for the relevant literature were whether 'conflict of interest was mentioned'. This is because in the pharmaceutical industry many papers are funded by the industry which can be biased. The 'exclusion criteria' were those literatures that did not state 'conflict of interest' or were funded by the pharmaceutical industry.

Differences exist between different stake-holders, regarding subtle changes in definitions, concepts and practices. These differences exist within the "medicines chain". The pharmaceutical companies run by huge corporate bodies have been shrouded due to lack of free access to information because of patent and copyright issues. Chapter one discusses about the intricate relation between pharmaceutical companies and their promotional practices.

To study the *second* objective, 'medicinal drugs that have been banned, withdrawn or not approved by governments' I have reviewed the 'Consolidated

list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not approved by governments' and Pharmaceuticals: restrictions in use and availability.

From the United Nations List of Consolidated products and and the WHO report on pharmaceuticals: restrictions in use and availability medicinal drugs that were banned withdrawn or not approved in other nations were identified and searched for in the "List of Manufacturers with product(s) including Ingredients" published in June 2007 (Jestha 2064) by the Department of Drug Administration (DDA), Nepal". A total of twenty different medicinal drugs were found that are banned or withdrawn according to the list published by the United Nations. Some medicinal Drugs like nimesulide, Phenylpropanolamine, Chloramphenicol are marketed by many companies both domestic and foreign. Some drugs like Thioridazine, Cyclandelate, Nandrolone decanoate, Nandrolone phenylpropionate were marketed by only a single company.

To study the *third* objective, different promotional tactics through which pharmaceutical medicines are marketed and whether they adhered to WHO guidelines. Since domestic industries in Nepal have a small share of market compared to foreign pharmaceutical products, both domestic and foreign products were selected for the study. Drug company representatives visiting the doctors leave promotional materials for them. Drug promotional materials are also available at the branch offices of the Department of Drug Administration (DDA) and the Drug Information Centre. The promotional materials present in the Biratnagar branch office of the DDA were analysed. Promotional materials of antibiotics were studied. Promotional materials printed only after 2008 were selected since, Nepal issued its guidelines on ethical promotion of medicines only in 2007. They are two different criteria for advertisements to healthcare professionals and to the general public. In this study advertisements to physicians and health care professionals were selected. WHO guidelines for advertisements to physician and health care professionals states that the advertisement should include the name of the active ingredient, brand name, content of active ingredient per dosage form or regimen, other ingredients known to cause problems, approved therapeutic uses, dosage form or regimen, side effects, contra-indications, major interactions, management in case of overdose or toxicity, storage conditions, pharmacokinetic profile, use in pregnancy and

lactation, name and address of manufacturers or distributor, and reference to scientific literature (HAI, 2005). The top three selling anti-biotics were selected for the study.

The fourth objective of the study is to understand the role of regulatory bodies in maintaining ethical standards at various levels of drug promotion. Documents available from the Department of Drug Administration (DDA), Nepal will be studied. DDA is the principal organisation whose main objective is to ensure safe and rational medicinal drug to the people. Its publications will be reviewed and their role will be assessed. Regarding this part, DDA's role in control of medicinal drugs that have been removed banned or not approved by governments in developed and developing countries will be assessed . DDA comes out with newsletters, notices and bulletins that provide information on medicinal drugs, efficacy, safety, rationality, precautions etc,. It also provides information on adverse drug reactions and irrational use.

2.6.4- Data analysis-

The data available on medicinal drugs banned, withdrawn or not approved from the thirty medicinal drug retailers were scrutinised and medicinal drugs that were marked as available by 10 or more medicinal retailers were selected and these medicinal drugs were further studied.

The data available from medicinal drug promotional were checked as to whether they had provided relevant information as per the WHO guidelines. The promotional materials were searched for the following information's-

Manufacturing industry

Brand Name

Price

Name of active ingredient(s)

Reference to scientific literature

Name and address of manufacturers or distributor

Dosage form or regimen

Storage conditions

Approved therapeutic use

Pharmacokinetic profile

Side effects/ adverse drug reactions

Precautions, Contra-indications, Warnings

Major interactions

Management in case of over dose/toxicity

Use in pregnancy and lactation

2.6.5-Limitations of the study-

This study has certain limitations since, chapters 2 & 3, were based on the, "List of Manufacturers with product(s) including ingredient" published in June 2007 (Jestha 2064) by the Department of Drug Administration (DDA), Nepal". Since this list was the latest list available there is a probability of new medicines that are available presently in the market are not mentioned in the list. Also, some companies for example, 'Royal Drugs limited' which has closed down and whose products are no more available are also mentioned in the list.

Chapter-3

Pharmaceutical Companies and medicinal drug promotion- A literature review.

This chapter deals with the different ethical issues regarding medicinal drug promotion.

3.1- Monetary involvement in medicinal drug promotion

Though significant development in the study of applied ethics (i.e. the application of normative principles to practical problems) since 1960's has occurred, it was not a new phenomenon since from the times of Plato onwards there has been concerns with practical questions like, suicide, the exposure of infants, the treatment of women. Under the rapid progress of medicine from the 20th century onwards, no longer an individual could work in isolation. With greater specialisation came increased team work and also a series of steps beginning from which medicines to manufacture to medicine consumption. In a laissez faire economy, intense competition began occurring between the different pharmaceutical companies and with monetary profit as principle inspiration; promotion, advertising and marketing became an important way to increase sales. The monetary involvement in medicinal drug promotion is quite high. A study suggests that the amount of money involved in medicinal drug promotion by the manufacturers is at least 30 times more than the money spent on drug information by the government (CMA, Editorial 2003). Advertisements in medical journals are the visible 'tip of the iceberg' of a much larger promotional campaign. In 2002, the pharmaceutical industry spent $21 billion promoting its products in the U.S., of which only $480 million, or 2%, was on ads in medical journals (Health 2002). These figures include the retail value of free samples although the cost to manufacturers is much less. In the entire economy, firms spend an average of 2% of their revenues on promotion. For pharmaceutical firms this percentage is much higher; estimates imply that around 15%-25% of their revenues are spent on promotion (Windmeijer 2004). With the rapid growth of pharmaceutical market combined with competitive and aggressive medicinal drug promotion by pharmaceutical companies there is every possibility of the promotion being unethical. The ethics of medicinal drug promotion practices remain zealously

contested in North America and Europe, Asia and Africa and has become a global public concern, as also evidenced by the fact that the 2007 World Consumer Rights Day was dedicated to the theme of unethical medicinal Drug promotion. In the developing world, there have been concerns about inappropriate medicinal drug promotion and the impact on public health for at least four decades. In a study carried out by the Institute for Evidence-Based Medicine in Germany, it was found that 94% of the information contained contained in the promotional literature sent to doctors by the pharmaceutical companies was either distorted or exaggerated. For example, the study quotes that treatment effects were exaggerated, study results were suppressed, and risks were manipulated. Many effects of the drugs were actually dawn from animal studies rather than human studies, even though the drugs were intended for human consumption. (Chris 2004)

3.2- Disinformation and medicinal Drug promotion-

The most important distinction between information and mis-information and dis-information is the question of truth. Where information is true, misinformation or disinformation are untrue.. Disinformation is also wrong information but unlike misinformation, it is a known falsehood. Misinformation that is deliberately disseminated in order to influence or confuse rivals (foreign enemies or business competitors etc.) is disinformation.

The accuracy and usefulness of drug advertisements has been the subject of debate for more than a century now (Anonymous 1894). Excessive promotion of pharmaceuticals has been associated in many countries with serious problems of irrational drug use. Unethical medicines promotion activities often convey misleading information about drugs to the different target audiences. Disinformation can be in the form of an expansion of indications or an exaggeration of efficacy but can also present itself as downplaying the seriousness or the incidence of adverse reactions. Such misleading information will create a wrong perception of the efficacy and safety of medicine's among prescribers and consumers and it will lead to a significant increased demand for drugs(Lembit 2008). A crucial component to promote the appropriate use of medicine is accurate information on medicines to healthcare professionals and consumers. While the pharmaceutical industry plays a central role in developing and

producing medicines, there can be a tension between industry's need to expand product sales through the promotion of its products and the public health priority of rational use. In fact, the World Health Organization (WHO) has called it "an inherent conflict of interest between the legitimate business goals of manufacturers and the social, medical and economic needs of providers and the public to select and use drugs in the most rational way"(WHO, Clinical Pharmacological Evaluation of Drug Control. 1993). Cases of false promotion of medicines and its terrible effects on the consumers have been experienced by millions. Thalidomide a drug that caused severe congenital disabilities was promoted during the 1950's. Thalidomide was withdrawn in 1961 in Germany where it first originated following reports of births of malformed babies, and side effects of peripheral neuritis in adults but was still available in other countries. Pharmaceutical companies have promoted their drugs in irresponsible ways, for example misrepresenting the safety of medicines. In June 2004 GlaxoSmithKline was accused of hiding research data suggesting that its anti-depressant drug Paxil was ineffective and unsafe for children and adolescents, increasing the risk of suicide(Financial June 3, 2004). There have also been cases of celebrities that were paid large fees to mention the benefits of specific brand-name drugs in TV programmes, without disclosing they received a financial reward for these stories. Novartis, for instance, used this type of unethical advertisement for its drug Visudyne In March 2002 (Zammit 2003). According to Braithwaite, who wrote of pharmaceutical companies; "The moral failure of the transnational's lies in their willingness to settle for much lower standards abroad than at home"(Braithwaite 1988.). Unethical medicinal drug promotion encompasses practices that deviate from these normative criteria, e.g. by misleading patients and doctors as to the utility or the efficacy of a particular drug, and that can then lead to inappropriate use of medicines, which can have a large socio-ethical significance for the global society. Yet while it may be easy to identify egregious violations as unethical (e.g. lying or blatant misrepresentation of scientific data), it is much more challenging to parse the grey zone between positively and justifiably promoting a drug and engaging in unethical marketing practices, such as misrepresentation or fear mongering and promoting drugs under the garb continuing medical education and educational activities. Medicinal drug promotion creates demand for medicines in various ways such as, defining illness conditions that need treatment, promote the

idea that medicines are the best remedy as opposed to non-drug alternatives and tends to emphasize a medicine's efficacy while minimizing possible health risks. Companies spend vast amounts of money (an estimated one-third of sales revenues) on marketing. This is often more than double the amount spent on research and development (Mintzes, 1998).Medicinal drug promotion to consumers is becoming an increasingly important component of drug companies marketing strategies (Mintzes,1998.). In the past, most consumer advertisements promoted over-the-counter medicines. More recently, companies have started promoting prescription drugs to consumers. Direct-to-consumer advertising (DTCA) for prescription drugs is allowed in the United States and New Zealand. It is now under consideration by regulatory authorities elsewhere. The pharmaceutical industry has devised ways to create consumer demand for prescription products even where DTCA for prescription medicines remains illegal (Mintzes 2002). In a few countries, notably the US, direct-to-consumer advertising for prescription drugs is allowed. This form of advertising has been heavily criticized for its inappropriate and unethical nature (HAI 2003). One study in the U.K. cites television advertising as being primarily responsible for a 24% increase in the sale of cough medicines (Chetley 1989)(Silverman 1979). The accuracy and fairness of promotional claims in advertisements has been studied in the past. Codes of conduct are often reported to be breached with respect to the accuracy and fairness of promotional claims in advertising (International 2005). In developing countries, promotional claims are often presented in an inadequate way (Vlassov 2001).

"If you sleep less than six hours a night, you're increasing your risk of developing or dying from heart disease by 48 percent. At least, that's what U.S.-based pharmaceutical giant Abbott would have 1.2 billion people in India believe". (Joelvin 2011).

The above example is just one example of medicinal drug promotion indulged in by the pharmaceutical companies. The above advertisement which appeared in an Indian newspaper has been criticized according to the source (Reuters) of this information. According to an article published

["Doctors say the grim message, which appeared in a newspaper ad in India earlier this year, is baseless. In fact, they worry Abbott's marketing campaign may

be the bigger threat, scaring healthy people into buying potentially harmful sleeping pills they don't need -- such as the company's own drug Zolfresh. "They are implying that taking sleeping pills may help you live longer, whereas the data shows that taking sleeping pills is associated with increased mortality," said Dr. Daniel F. Kripke, a psychiatrist at the University of California, San Diego. Industry insiders say the ad points to a bigger problem: According to Benjamin England, an attorney formerly with the U.S. Food and Drug Administration (FDA), drug makers have lower standards for how they operate in emerging markets like India and China, where government oversight is poor. "You already feel like you are in the Wild West," said England, founder of the international consulting firm FDA Imports.com. "There is not likely to be anybody who is going to take them to task." "If there is nobody paying that much attention to what people are saying about the product, then they'll push the envelope and say things they would not have gotten away with here," he told Reuters Health". "Insomnia is an area where you will find a huge untapped market," said Ram Bala, a marketing expert at the Indian School of Business in Hyderabad, who has consulted for companies like Johnson & Johnson and AstraZeneca. He said drug makers appear to be stepping up their efforts to win over emerging markets, although it's an uphill battle as many Indians still prefer herbal remedies or are largely unaware of modern medicine. "There is a lot of public resistance to treating insomnia, because they don't think it is such an important condition," Bala told Reuters Health. "If you bombard them with enough information about insomnia, maybe they may at some point decide, 'Hey, you know what, there are so many people telling me that insomnia is important, maybe I should go to the doctor and check it out.'" Indeed, Abbott's ad encourages readers to see their doctor if they can tick off just one of 10 statements, including "I feel sleepy during the day" and "I have a feeling that my sleep is unrefreshing." "This is so dramatic and ridiculous," said Dr. Adriane Fugh-Berman of Georgetown University in Washington, D.C., who runs Pharmed Out, a think tank that studies drug makers' influence on prescribing. "It is really advertising, but it is disguised as education," she told Reuters Health. "Industry calls it disease awareness, those of us who are public health advocates call it disease-mongering -- making people believe that they are sick when they are normal"] (Joelvin 2011).

It is not unusual to find advertisement of dangerous drugs in both developed and developing countries. The side effects are not seldom given enough space in the commercial messages. The areas of indications are often wider than can be supported by clinical trials data (Lilja 1983). Studies from several countries classified as least developed, developing countries and also from the developed countries have shown the prevalence of unethical drug promotion in these countries. medicinal drug promotion practices in a developing country context raise several distinct socio-ethical issues. In developing countries, the sparse resources allocated to health care and education limit physician involvement in continuous medical education. Thus, pharmaceutical promotion often becomes the major source of information on new drugs, and ways to use them, for the majority of physicians in many countries (Bhutta 1996). When countries have poor or inadequate economic resources in health care and education, and also lack adequate regulatory measures to control medicinal medicinal drug promotion(or lack sufficient compliance if some form of regulation exists), their populations become even more vulnerable to aggressive medicinal drug promotion practices by the large pharmaceutical companies (Dal-Pizzol 2002) A study from Brazil noted that approximately 75% of the advertisements did not comply with regulations in Brazil (Wzorek LF 2007). Another study from Brazil showed that, 33% of promotional statements were either partially consistent or inconsistent. The study concluded that there was difficulty in accessing the references mentioned in the promotional materials and the messages on efficacy, safety and cost were not always supported by scientific studies (Mastroianni PC 2008). A study from Argentina identified only eighteen (60%) of the thirty promotional materials had statements supported by cited references. Adverse reactions, warnings about drug interactions and contraindications were absent from all promotional material (Mejía R 2001). Developing countries and the poor around the world have also been used to generate profit for pharmaceutical companies for example, the Swiss company Novartis announced free supplies of its cancer drug Glivec to people around the world that could not afford its costs of US$ 27,000 per year. Some estimated that this number of patients would be as high as 600,000. However, in the end only 1,500 patients outside the US benefited from these donations, of which just 11 in least developed countries. It became clear that Novartis had used Glivec as part of a marketing strategy, and even encouraged

patients benefiting from the donations to press public health systems to pay high prices for the drug (Zammit 2003). A study from Bangladesh showed that, Drug advertisements often lack scientific evidence to support their claims, The study reported that medical or pharmaceutical claims made in the drug advertisements in MIMS (Medi Media Index of Medical Specialities) Bangladesh are mostly not supported by scientific evidence (Islam 2008). In a critical analysis of advertisement content in Pakistan, 345 distinct advertisements, covering 182 drugs from different manufacturers, were critically analysed for information content. Out of 345, 62 (18%) of the reviewed advertisements were misleading and were again classified as exaggerated (32%), ambiguous (21%), false (26%) or controversial (21%). Most general practitioners considered pharmaceutical companies, in particular drug representatives, as their primary source of information on drugs. Furthermore, 110 (90%) of the general practitioners thought that drug promotion influenced their prescribing behaviour. (DK 2006). A 12-month survey of information content and standards of advertisements in 23 leading national medical journals in 18 countries demonstrated that 96% of the advertisements contained pictures, of which 58% were considered to be irrelevant. In developing countries, a significantly higher number of pictures were present in advertisements (Herxheimer A 1993). Pharmaceutical companies have often been criticized for the quality of their drug advertisements in developing countries. In 1990, a quantitative study was conducted on the content of advertisements, published in six medical and paramedical journals, aimed at Francophone health personnel in African countries. Only 41 out of 141 advertisements conformed to French standards for accuracy and objectivity. Indications were absent from five (3.5%) advertisements and exaggerated in 42 (29.8%). Side-effects were not mentioned at all in 37 (26.2%) advertisements and were incomplete in a further 20 (14.2%). Contraindications were absent from 30 (21.3%) advertisements and incomplete in 19 (13.5%). Pharmaceutical companies do not always follow a code of ethical conduct and frequently exploit the lack of effective controls in developing countries (P 1993). In a 1990 study, drug advertisements in the Ceylon Medical Journal in Sri Lanka were analysed and conformity with the WHO-ECPM and IFPMA Code was assessed. Of the 111 advertisements analysed, only 22% and 23%, respectively, provided information on adverse effects and contraindications (K 1990). A 2001 study stated that, over the past 20 years,

studies in countries with limited regulatory infrastructure have shown that pharmaceutical advertisements supply less information in the places where it is most needed. Even in developed countries where controls are stricter and resources more plentiful, there are serious problems with journal advertising (V 2001). In a 1998 study, the content of Indian advertisements, supplied by drug representatives, was evaluated using a checklist based on the WHO-ECPM. Information about adverse effects, precautions, warnings, major interactions, ingredients known to cause problems, pharmacology, drug overdose, references and drug storage was present in less than 40% of the advertisements (Lal 1998).

3.3- Medicinal Drug promotion and Physicians or Prescribers-

. Physicians are categorised into various categories, and the drug representative tries to work out to which category a physician is likely to belong. The representatives and the company have a different tactic for each category(Fugh-Berman A 2007). Personal friendship with the doctor is often exploited by the representative to push his/her products. Physicians tend to believe that promotion does not influence their own prescribing. For example, only 1% of 102 surveyed internal medicine residents believed that sales representatives had a lot of influence on their own prescribing; whereas 51% of the same respondents believed that sales representatives had a lot of influence on other physicians' prescribing(Steinman 2001). Another U.S. survey found that physicians were less likely than patients to believe that gifts such as pens, mugs, or meals were influential(Lal. 1992). Physicians at one hospital who attended an all-expenses paid trip to a luxurious resort were asked whether they believed that attendance would influence their prescribing practices. Evidence suggests that promotion affects attitudes and behaviours(HAI 2005). Aggressive promotion has been shown to influence the prescribing behaviour of doctors. Doctors relying on pharmaceutical-industry literature were more likely to prescribe three or more drugs which frequently cause adverse effects(Mapes 1977). A Dutch study found that physicians who reported seeing pharmaceutical sales representatives prescribed higher volumes of second-choice antibiotics for respiratory infections (Kuyvenhoven 2003). This is consistent with concentration of promotional spending on relatively new patented products(Kessler 1994). On the whole, they did not believe that they would be influenced. However, prescribing data showed

a strong influence. Pharmaceutical manufacturers are clearly in the business of influencing consumer behaviour in the direction of greater dependence on products the public is made to feel it cannot live without.

3.4- Regulating medicinal drugs promotion-

Lack of regulation of medicines was a major factor for the occurrence of the Thalidomide disaster. Henceforth, issues on regulating medicinal drug promotion and other unethical practices began to emerge. Regulatory bodies and regulations were set up and from 1980's, attention to the need for better regulation of medicinal drug promotion by HAI (Health Action International) formed as a network, called for an international code of pharmaceutical marketing, followed by IFPMA (International Federation of Pharmaceutical Manufacturers & Associations) which launched international self regulatory code in 1981. Many pharmaceutical companies favour this code on medicinal Drug promotion, the Code of pharmaceutical marketing practices of the International Federation of Pharmaceutical Manufacturers Associations (IFPMA 1994). This code was revised in 1994 and has a complaints procedure. It sets lower standards because it gives precedence to national legislation, and may therefore be insufficient in developing countries where legislation is weak(Oxfam 2002). WHO whose constitution came in to force on 7th April 1948 came up with, "Ethical Criteria for Medicinal drug promotion" in 1988, following a 1985 WHO Nairobi Conference on, Revised Drug Strategy – emphasis on rational drug use.

The WHO issued its Ethical Criteria for Medicinal drug promotionin 1988, but a 1997 WHO roundtable discussion concluded that inappropriate medicinal drug promotion is still a problem in developing and developed countries(WHO, Drug Promotion Database n.d.). Beginning in the late 1980s, the World Health Organization (WHO), industry groups and national medical associations began to produce guidelines for such relationships. In 1988, the WHO Assembly adopted a resolution endorsing a set of ethical criteria for medicinal medicinal Drug promotion(WHO, Ethical Criteria for Medicinal Drug Promotion. 1988). In 1991 the Canadian Medical Association adopted guidelines for physician–pharmaceutical industry relationships,(CMA, Canadian Medical association n.d.) followed by many other professional organisations, including the

American Medical Association in 1992 (AMA n.d.) the Israeli Medical Association in 2004(pharma-israel.org n.d.) and the World Medical Association in 2004(WMA n.d.). These guidelines deal with gifts to physicians, continuing medical education/professional development, industry-sponsored research and drug samples. Though their primary concern is to avoid conflicts of interest between physicians and patients, they are equally applicable to conflicts between the interests of physicians and those of society in general, for example regarding cost-effectiveness in prescribing drugs that are paid from public sources. The pharmaceutical companies must observe ethical criteria for medicinal drug promotion with clear responsibility for providing unbiased information about their own pharmaceutical products. Promotion of medicinal drugs must be in conformity with accepted ethical standards. Much has changed in pharmaceuticals since WHO began establishing international pharmaceutical standards and guidelines, and since the introduction of the essential drugs and national drug policy concepts. Nearly 160 countries now have national essential drugs lists; while over 100 countries have national drug policies in place or under development. Similarly, rational drug use concepts and teaching are spreading in all regions(WHO, Medicines Strategy: Framework for Action in Essential Drugs and Medicines Policy. 2000-2003).

WHO recommendations carry important political and ethical weight for member countries and so can play an important role in shaping global standards. The aim of the WHO ethical criteria was to improve health care and regulate medicinal drug promotion practices to ensure the rational use of medicinal drugs (with particular attention to promotion, advertising, drug representatives, free samples and medical education). But how does one classify a medicinal drug promotion practice as unethical? The WHO defines medicinal drug promotion as 'all informational and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs'(WHO, Ethical Criteria for Medicinal Drug Promotion. 1988).

3.5- Weakening of regulatory authorities-

Pharmaceutical industry and its allies, holds that the main function is to facilitate industry's efforts to develop new products and to approve them as quickly as

possible. In this view, medications are commodities and the regulatory authority exists to provide a service to the industry (Lexchin 2007). While consumer groups and health activists in developing and developed nations, concede that the drug companies are necessary to develop new products, but they are mainly focused on the quality of the products that emerge from the approval process, and are more interested in a thorough review than a rapid one. They also are in favor of transparency in the regulatory review process. Disease-focused groups which is seen more in the developed nations, sometimes differ from consumer groups on the question of the speed of drug approvals. While they still are concerned with safety, they often want what they see as new therapeutically important medications approved as quickly as possible. Drug regulation in the USA, the pluralist model, with its laissez-faire approach to the participation of private interests in decision making, has predominated. Despite their different origins, their different operating models, and differences in the financial resources and number of personnel, the regulatory decisions that these different authorities make are often quite similar and historically have favored the interests of the pharmaceutical industry (ME 2003). Abraham documented the situation in the USA in the mid-1970s involving a group of FDA reviewers. These reviewers told the US Congress that when they recommended the approval of a drug, their analyses were hardly ever challenged, but when they rejected an application their judgments were sometimes unjustifiably overruled. Furthermore, they claimed, that when they pointed out that applications had inadequate data to support approval, they experienced harassment and were removed from reviewing the file. A panel concluded that ''a non-adversarial philosophy vis-a` -vis drug companies ... brought a kind of pressure to approve drugs onmore adversarially inclined reviewers.'' (Abraham 1995). In Canada, Lexchin shows how influence can be seen by looking at regulatory decisions made in the 1960s and 1970s regarding the benzodiazepine class of drugs. These include products such as diazepam (Valium), triazolam (Halcion), and lorazepam (Ativan). Lexchin, examined this topic and showed that there is strong circumstantial evidence that these drugs were approved on the basis of inadequate clinical trials, resulting in them being indicated for conditions for which they were not useful, and that significant safety issues were ignored (J. Lexchin 1998). These deficiencies in the regulatory process were magnified in the advertising of these products to physicians, thus

contributing to inappropriate prescribing. Similarly, Medawar and Hardon exemplify how that philosophy was applied in the case of the selective serotonin reuptake inhibitor (SSRI) group of antidepressants, in particular paroxetine (Seroxat; in North America the trade name is Paxil). The Medicines Commission and its successors consistently refused to accept mounting evidence that this group of drugs had frequent and serious side effects, and was associated with significant symptoms when patients tried to withdraw from their use (Medawar C 2004). The Washington-based Public Citizen's Health Research Group (HRG) surveyed FDA reviewers in 1998 for their reaction to the changes in the agency. Nineteen out of 53 medical officers identified a total of 27 new drugs in the previous three years that they thought should not have been approved but were; and 17 said that standards were ''lower'' or ''much lower'' than they had been three years previously (Lurie P 1998). One former FDA reviewer is quoted as saying: ''When I joined [the FDA], there was an absolute emphasis on safety. It is very, very clear that the emphasis now is getting drugs approved. To justify not getting them approved is considerably more difficult.'' (Okie 2005)

3.6- Medicinal drug promotion in Developing nations-

The public health consequences of, and ethical responsibilities associated with, drug promotion are substantially larger when viewed through the prism of the realities faced by persons living in developing countries (Thomas 2010). Anti Microbial resistance is an emerging issue and which has been linked to drug promotion. "The emergence of resistance in microbes can be impetuous most evidently due to excess use of antimicrobials. Improper antimicrobial use can easily develop as a downstream effect of excessive drug promotion activities. Therefore, it is not startling that the use and prescription of antimicrobials, which escalated significantly until the mid-1990s, was immediately followed by an increase in antimicrobial resistance worldwide (McCaig 2002), (A Gaur 2006) . Other social factors that are widespread in developing countries – such as low-quality generic or counterfeit antimicrobials, ineffective distribution and inappropriate storage conditions of pharmaceuticals can also contribute to erratic or suboptimal drug use. And these factors can have even more drastic consequences when compounded by aggressive drug promotion practices.

A study conducted in India between July 1995 and June 1996 demonstrated that the majority of drug promotional material provided to physicians at the Guru Teg Bahadur Hospital in Delhi concerned antimicrobial agents, and at the same time, this study also showed that 60% of the promotional material encountered in Delhi did not conform with the WHO guidelines for drug promotion (Lal 1998). Similar studies in Latin America and South Asia further support the case that there is poor compliance with the WHO ethical guidelines for medicinal drug promotion in developing countries (Dal-Pizzol 2002), (Islam 2007). A particular concern with global drug promotion practices is the absence of concordance between the content of promotional messages concerning a particular drug and the evidence base in the scientific literature (B. Mintzes 2006).

Fixed dose combination [FDC] are highly popular in the pharmaceutical market and are particularly flourishing in the last few years. The pharmaceutical industry has been manufacturing and marketing fixed dose combinations (FDC's), many of them irrational and harmful for the last two decades. Initially not many in number, today they are in several thousands and a large number of them have no therapeutic rationale. The uncontrolled growth of such combinations more often than not has been the brainwave of marketing heads of pharmaceutical companies. Responding to the pressure for newer products, marketing heads of pharmacy companies used to invent combinations of two or more drugs, often launched without an assessment of their therapeutic benefits (Sreedhar, 2008).

Chapter- 4

Banned medicinal drugs and their availability in Nepal.

This chapter deals with the second objective of the study, To identify whether medicinal drugs that have been banned, withdrawn or not approved by governments according to the "*Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted or not Approved by governments*" are available in Nepal.

Medicinal drugs that are mentioned in the report published by United Nations, 'Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely restricted or not Approved by Governments' (12^{th} and 14^{th} issue) was reviewed and medicinal drugs which were banned, withdrawn or not approved by governments was sorted out from the report. These sorted medicinal drug promotion were then searched in the, " List of Manufacture with product(s) including ingredient" published in June 2007 (Jestha 2064) by the Department of Drug Adminstration (DDA), Nepal. Medicines that were banned, withdrawn or not approved according to the report published by the United Nations, but are found in Nepal according to the report were selected to study. Apart from the report by DDA, 10 medical shops were randomly selected and enquired about the medicines that according to the list by DDA were available in Nepal but were banned, withdrawn or not approved according the UN report.

Altogether 20 different banned medicinal drugs were found in the "List of Manufacture with product(s) including ingredient". The 20 different medicinal drugs that were banned, withdrawn or not approved by governments are as follows- see Table 4.1. These medicinal drugs were further enquired in medicinal drug retailer shops. Altogether 30 medicinal retail shops were chosen based on convenient sampling. Availability of the banned medicinal drugs as stated in table 4.1 were asked to the shop keepers.

Table- 4.1- Medicinal drugs banned along with their brand names and generic names.

1. **Cisapride**- Cizakin 10, Cisapro-10, Cispad 10, Cipride Tab, Ciza-10. ,
2. **Phenylpropanolamine**- Tuspress Cough Suppressant, Dolar Syrup, De-Cold Syp(60ml), Ascoril –D, Tussinol, Coldin-P, Coldin Tablet, Axil D Syr, Bronchodyne Syrup, C-Tab, Rinixin-Dx Syr, Coldchem Syr, Flucold Tablets, Coldflu Tablet, Cofril Syp, Rhinex Syrup, Meryl Linctus, Syn0hist Linctus, Breathex Bron Expectorant, TOPEX –CS
3. **NIMESULIDE** - Slide-100 Tab, Q-Nim, Soonil Tablet, Nimison Tab, Nimulid Transgel, Nimulid –Md, Anim 100 Cd, Neslide Tablet, Nimtech, Coxflam Tab, Coxflam Susp(60ml), Nimica Dt-100, Nimstal -100, Emsulide, Nise -100, Nimsel, Nibucid, C-Nim 50, Nimutab, Nilide, Inflatop 100, Remulide Tablet, Nims Tablet, Nimegesic Tablet.
4. **Clioquinol** - Betnovate –C, Himosone-C.
5. **IODOCHLORHYDROXYQUIN**- Staderm Cream. Himoderm Plus Cream
6. **THIORIDAZINE**- Zeneril- 25, Zeneril- 50
7. **BENZYLPENICILLIN**-Benzyl Penicillin Injection 5 Lacs, Benzylpencilin -10lac, Fortifide Procaina Penicillin Injection 20 Lacs Solution, New Bistrepen, Pencom -12 Lacs, Fortified Procaine Penicillin 4 Lac, Benzapen-0.5, Penidure La12,
8. **CHLORMEZANONE** - Dolobak Tablet, Cetozone Tablet
9. **CHLOROFORM** - Dentaik
10. **CYCLANDELATE** - Martispasmol- 200, Martispasmol- 400.
11. **CYPROHEPTADINE**- Practin Tablet, Aptiv(100ml), Apetamin Syrup, Apetone, Promeal (200ml/100ml, Apdine Syrup(110ml/200ml), Cypon Plain, Apet 4, Apet 2(200ml), Ciplactin -4, Cypotone Syp(200ml,
12. **ERYTHROMYCIN**- Althrocin -500, Althrocin Drops, Althrocin Kid Tab, Althrocin-250, Ardimycin Tabl, Ardimycin Susp, Clamycin Tablet, Erythrolar-500, Eltocin Tablet, Eltocin Kid Tablet, Ethro Ctl 500mg, Erythrokem- 500,
13. **LOPERAMIDE-** Imodium, , Eldoper,
14. **NANDROLONE DECANOATE**- Deca Durabolin -25, Durabolin,

15. **NANDROLONE PHENYLPROPIONATE** – Durabolin,
16. **NEOMYCINSULFATE**- Cindox -Forte (50gm/10gm), Flomex-N, Neosporin Antibiotic Powder, Himosone -N Ointment, Benezole Cream
17. **PHENYLBUTAZONE** - Algesin Injection
18. **SOMATROPIN**- Humatrope,
19. **TERFENADINE** - Ternep 60, Terfin-60.
20. **CHLORAMPHENICOL IN COMBINATION** - Euchlor-1000, Chloram Cap, Paramycetin 500, Phenicol 250 Caps, Nephenicol 125, Ramphen 250 Cap, Chloro-500, Cetacol, Comycetin 500, Larmycetin-250, Chloramphenicol Capsule-250, Chlorocin Suspension, G-Phenicol -250, Typhenicol 500, Chlora Ctl 500mg, Ocupol-D.

The table shows the names of medicinal drugs that are available in Nepal according to the, "List of Manufacture with product(s) including Ingredient". The Brand names along with the different Generic names under which these medicinal Drug Promotion are marketed. The difference between a brand-name product and a generic one is designed to be transparent. Once the patent life expires on a brand-name drug product, it is eligible to be made into a "generic drug." To do this, the generic drug manufacturer must ensure that the drug they are producing contains the same active ingredient(s) as the brand-name product, in the same dosage form, at the same dose or concentration, and for the same route of administration.

From the list of drugs mentioned in Table 4.1, the following medicinal drugs were found to be prevalent in the market. The availability of these medicinal drugs were enquired for in the medicinal retail shops. Information about the availability of these medicinal drugs were collected from February 2011 to March 2011. The banned medicinal drugs are as follows-

1- Cisapride
2- Phenylpropanolamine
3- Nimesulide.
4- Clioquinol
5- Iodochlorhydroxyquin
6- Benzylpenicillin-

7- Chlormezanone.
8- Cyproheptadine.
9- Erythromycin.
10- Loperamide.
11- Nandrolone decanoate
12- Nandrolone phenylpropionate
13- Neomycin sulfate

The above mentioned medicinal drugs that have been found in Nepal were further reviewed through a literature search. Drugs that have been banned decades ago in many nations were found in the study. How is it that these drugs pass the scrutiny of the government bodies? Cisapride a drug banned a decade ago or more in other nations was banned in India in January 2011 (Drug Information Bulletin, 2011).

Brief review of the medicinal drugs banned-

1- Cisapride-

C.A.S[1]. number 810968-60-4.

Scientific and common names, and synonyms- CIS-4-AMINO-5-CHLORO-N-(1-[3-(4-FLUOROPHENOXY)PROPYL]-3-METHOXY-4-PIPERIDYL)-2-ETHOXYBENZAMIDE MONOHYDRATE; CISAPRIDUM.

Legislative or regulative action-

The Department of Health Bureau of Food and Drugs of Philippines has banned the use of cisapride because of documented reports on adverse events including deaths associated with its use in the year 2000 (PHADO, 2000). Cisapride has been voluntarily withdrawn from the market because of the risk of rare but serious cardiac events associated with the drug. These include heart rhythm disorders associated with the drug. These include heart rhythm disorders and deaths associated mostly with the use of the drug in people who are either taking certain other medications or who have certain underlying conditions that are known risk factors (FDA, 2000). The Federal Institute for Drugs and Medical

[1] The Chemical Abstract Service is part of the American Chemical Society and maintains a database of chemical compounds and sequences. CAS Numbers are up to 10 digits long using the format xxxxxxx-yy-z. They are assigned to a compound as the CAS registers a new compound. The number has no significance to the chemistry, structure or chemical nature of the molecule.

Devices has suspended the marketing authorization of cisapride because of the association with cardiac arrhythmias and a number of deaths (DEUCFI, 2000). The Medicines Control Agency has withdrawn cisapride from the market because of rare but serious cardiac adverse effects (GBRMCA, 2000). Cisapride was withdrawn from the market following reports of adverse cardiac events published by the FDA (MUSMHQ, 2000). Cisapride was withdrawn from the local market in May 2001. The action was based on reports of serious cardiac events (BHRCW, 2001). Cisapride injections have been withdrawn due to concerns about life-threatening cardiac arrhythmias. This measure follows actions previously taken worldwide (SRBNPC, 2005).

Comments-

In the early 1990's with the advent of the discovery of sudden cardiac death from torsades de pointes associated with the very widely used cisapride.Cisapride and its formulations for human use has been recently banned in India according to a notification issued by the Ministry of Health and welfare (GOI, 2011). In Nepal out of the 5 manufacturing companies whose products containing cisapride were found in the List used for the study, 4 of the company's products were available in the market.(Annexure Table 1). Both domestic and foreign companies products were available in the market. As for Nepal, the website maintained by DDA for baaned drugs (http://www.dda.gov.np/band_drugs.php) does not have any information on cisapride. According to a bulletin (DBN),published by DDA in 2006 it mentioned that, High-profile drug safety issues, like those of cisapride has presented numerous challenges for drug regulators (DDA, 2006). No further information on cisapride is available from the DDA.

Table- 4.2

Cisapride manufacturing companies along with their generic name, price and availability-

MANUFACTURING COMPANY	GENERIC NAME	PRICE	CURRENT AVAILABILITY IN THE MARKET-
ASIAN PHARMACEUTICALS PVT.LTD. (D)	CIZAKIN-10	5.00 MRP (PER TABLET)	YES
CADILA HEALTH CARE LIMITED (INDIA)	CISAPRO-10	5.72 MRP (PER TABLET)	NO
CUREX PHARMACEUTICALS PVT.LTD. (INDIAN COM WITH MANUFACTURING UNIT IN NEPAL)	CISPAD 10	4.60 MRP (PER TABLET)	YES
INTAS PHARMACETICALS LTD (INDIA)	CIZA-10	4.66 MRP (PER TABLET)	YES
LOMUS PHARMACEUTICALS PVT. LTD (D)	CIPRIDE TAB – 10	4.00 MRP (PER TABLET)	YES

2- Phenylpropanolamine –

C.A.S. number 14838-15-4

Scientific and common names, and synonyms-BENEZENEMETHANOL, ALPHA-(1-AMINOETHYL)-,(R*,S*)-,(+/-)DL-ERYTHRO-2-AMINO-1-PHENYL-1-PROPANOL (+/-)-NOREPHEDRINE.

Legislative or regulative action-

In 2000 Phenylpropanolamine ingredient products Removed From Marketing or Distribution for Safety Reasons, With Identification/Evidence From Spontaneous or Case Reports, United States (Diane K. Wysowski, 2005). All Phenylpropanolamine (PHENYLPROPANOLAMINE)-containing products are banned and no longer marketed (CMRPCC, 2007). All preparations containing PHENYLPROPANOLAMINE are banned (NAFDAC, Communication,, 2007). The Portuguese regulatory body, Infarmed, has suspended cold and flu products containing the decongestant PHENYLPROPANOLAMINE , while it reviews PHENYLPROPANOLAMINE 'S risk/benefit profile following worldwide concerns of cerebral haemorrhage and other adverse reactions (PRTBFV, 2005). Phenylpropanolamine products to be gradually removed from the market due to risk of haemorrhagic stroke (TLSFR, 2005). The Centre for State Control of Drug Quality (CECMED) issued a resolution banning the use of Phenylpropanolamine products in Cuba (CUBCDQ, 2001). Due to its potential to cause stroke, Phenylpropanolamine (PHENYLPROPANOLAMINE) used in cold and cough remedies was banned in all North American countries including US and western Europe (Drug Information Bulletin, 2011).

Comments-

Phenylpropanolamine and its formulations for human use has been recently banned in India according to a notification issued by the Ministry of Health and welfare (GOI, 2011). In Nepal according to the DBN, ;Considering the adverse drug reaction, use of Phenylpropanolamine has already been stopped in Nepal'. It further goes on to state that 'Pseudoephedrine has become popular ingredient in cough and cold preparations, once use of Phenylpropanolamine was stopped. Since, these preparations are sold without prescriptions and many children take this medicine, we should be seriously thinking about the (DDA, 2007)rational use of Pseudoephedrine containing preparation'. According to the DDA list, of Phenylpropanolamine products from 28 different manufacturers were available in Nepal. Majority of the products are available in the market.

Table 4.3- Phenylpropanolamine manufacturing companies along with their generic name, price and availability

MANUFACTURING COMPANY	GENERIC NAME	PRICE	AVAILABILITY
ALEMBIC LIMITED, INDIA	EPHEDREX SYRUP ZEET EXPECTORANT TABLET	35.00 MRP (PER BOTTLE) 0.88 MRP (PER ABLET	YES
ALIVE PHARMACEUTICALS PVT. LTD (D)	ACTIVE ACTIVE-P TAB	1.70 MRP (PER TABLET 2.00 MRP (PER TABLET	NO NO
AMIE PHARMACEUTICALS PVT LTD (D)	MUCODIL SYP(100ML) MUCODIL SYP(60ML)	56.00 MRP (PER BOTTLE) 37.00 MRP (PER BOTTLE)	NO YES
APEX PHARMACEUTICALS PVT.LTD. (D)	COLATE SYP COLATE TAB	24.00 MRP (PER BOTTLE 1.50 MRP (PER TABLET)	YES YES
BIRAT PHARMA LAB PVT. LTD (D)	PALORMIN PALORMIN SYP	1.50 MRP (PER TABLET) 27.00 MRP (PER BOTTLE)	YES YES
BLUE CROSS LABORATORIES LIMITED (INDIA)	TUSQ P ORAL DROP TUSQ-D SYRUP	20.00 MRP (PER BOTTLE) 20.00 MRP (PER BOTTLE)	YES YES
CENTAUR PHARMACEUTICALS P.LTD (INDIA)	SINAREST SYP SINAREST TAB	21.77 MRP (PER BOTTLE) 1.26 MRP (PER TABLET)	YES YES
CHEMI DRUG INDUSTRIES PVT LTD. (D)	RINIXIN-DX SYR COLDCHEM SYR COLDCHEM TABLET CO-EXS SYP SYRUP	53.00 MRP (PER BOTTLE) 26.00 MRP (PER BOTTLE) 1.50 MRP (PER TABLET) 37.00 MRP (PER BOTTLE	YES YES YES YES
CTL PHARMACEUTICAL PVT. LTD (D)	C-TAB	2.00 MRP (PER TABLET)	NO
CUREX PHARMACEUTICALS PVT.LTD. (D)	BRONCHODYNE SYRUP	45.00 MRP (PER 100 ML)	NO
DENIUM LABORATORIES (P) LTD (D)	AXIL D SYR	46.00 MRP (PER BOTTLE)	YES

DEURALI-JANTA PHARMACEUTICALS PVT. LTD (D)	COLDIN SYRUP COLDIN TABLET COLDIN-P SYRUP	35.00 MRP (PER BOTTLE) 2.25 MRP (PER TABLET) 28.00 MRP (PER BOTTLE)	YES YES YES
G.D.PHARMACEUTICALS PVT.LTD. (D)	TUSSINOL SYRUP	26.00 MRP (PER BOTTLE)	NO
GLENMARK PHARMACEUTICAL LIMITED. (INDIA)	ASCORIL -D SYRUP	35.00 MRP (PER BOTTLE)	YES
INDOCO REMEDIES LIMITED. (INDIA)	TUSPRESS COUGH SUPPRESSANT	25.30 MRP (PER BOTTLE)	YES
LARK LABORATORIES LIMITED(INDIA)	DOLAR SYRUP	32.00 MRP (PER BOTTLE)	NO
LOMUS PHARMACEUTICALS PVT. LTD. (D)	DE-COLD SYP(60ML) SUSPENSION DECOLD TABLET LOMOHIST PAED (60ML) SOLUTION	28.00 MRP (PER BOTTLE) 1.50 MRP (PER TABLET) 28.00 MRP (PER BOTTLE)	YES YES YES
NEPAL PHARMACEUTICALS LAB. PVT. LTD. (D)	ACT TABLET BRONIT-P TABLET NEPEX-PAED SYRUP	1.50 MRP (PER TABLET)	YES YES YES
NICHOLAS PIRAMAL LIMITED. INDIA	DELETUS -D LIQUID SYRUP DELETUS -P EXPECTORANT SYRUP	43.00 MRP (Per bottle 41.35 MRP (Per bottle)	YES YES
OMNICA LABORATORIES PVT LTD	RINZ TAB	2.00 MRP (Per tablet	YES
OZONE PHARMACEUTICALS LIMITED	TOPEX –CS	36.56 MRP (Per bottle)	YES
PHARMACEUTICAL COMPANY OF NEPAL	CHERENA PAEDIATRIC	25.00 MRP (Per bottle)	NO
PHARMACO INDUSTRIES PVT. LTD	ALLAREX (60ML/120ML SOLUTION TRIREX (60ML) SOLUTION	28.42 MRP (PER 60ML) 27.84 MRP (Per bottle)	NO NO
S.R. DRUG LABORATORIES PVT. LTD.	COLDAREST TABLET	1.50 MRP (Per tablet	
SIDDHARTHA PHARMACEUTICALS PVT. LTD.	COFEND SYP	36.00 MRP (Per bottle	NO
SIMCA LABORATORIES PVT. LTD.	MERYL LINCTUS SOLUTION, RHINEX SYRUP	46.96 MRP (Per 100 ML) 24.95 MRP (Per bottle	YES YES
UNIQUE PHARMACEUTICALS (P)	COFRIL SYP. SYRUP	25.00 MRP (Per bottle)	YES

LTD.	COLDFLU	1.80 MRP (Per tablet)	YES
WALLACE PHARMACEUTICAL PVT. LIMITED	FLUCOLD TABLETS FLUCOLD SYRUP	1.20 MRP (Per tablet 18.00 MRP (Per bottle)	YES YES

3- Nimesulide-

C.A.S. number 51803-78-2.

Scientific and common names, and synonyms- AULIN, MESINE, ESULID,NIMULID.

Legislative or regulative action-

Nimesulide was banned in US, Britain, Canada, Sweden, Denmark, Australia, New Zealand, Japan and other 168 countries, the drug was freely available in Nepal and also in India, being aggressively marketed by prominent drug companies. Nimesulide containing products banned due to adverse health effects (NAFDAC, Communication, 2007), (NGRPCC, 2007). The Irish Medicines Board (IMB) has announced the suspension of the marketing and sale of nimesulide-containing medicinal products for oral use available in Ireland. The suspended products include Aulin (100 mg tablets and granules), Mesulid (100 mg tablets and granules) and Mesine (100 mg tablets). The IMB decision was based on new information from a National Liver Transplant Unit that six patients required liver transplant following treatment with nimesulide. The IMB has received 53 liver-related adverse reaction reports with nimesulide since the product was first approved for use in Ireland in 1995 (WHOPNL, 2007), (WHOIES, 2007), (IRLMB, 2007). The National Regulatory Agency (NRA) suspended the marketing authorization for nimesulide-containing products; a 'Dear Health-care Professional' letter was also issued based on the WHO Drug Alert No. 113 that highlighted the decision in the Republic of Ireland to withdraw these products from the Irish market (GHAFDB, 2008). In spite of several reports of its adverse drug reactions in India, the marketers of Nimesulide are unwilling to acknowledge any of its side effects. The prescription of this drug by doctors to children below 12 years of age continues. The marketers of Nimesulide allege that since Nimesulide is taking the market share for analgesics away from

Paracetamol and Ibuprofen, the marketers of Paracetamol and Ibuprofen are engaging in misrepresenting Nimesulide.

Comments-

Nimesulide has been banned in several countries but in Nepal about 25 different manufacturing comapany's products are available. Nimesulide use has been restricted and is not recommended to children below 12 years old. Majority of the banned products are available in Nepal. (See Annexure 3) In Nepal Nimesulide, is on the top ten selling medicines from domestic industries (DDA, 2007). Nimeuslide was discovered by an American Company, 3M Pharmaceuticals, but never got approval for use in the US, Canada, Britain, Australia, New Zealand and 140 other countries around the world. It was banned in Spain and England in 2001 on reports of its hepatotoxicity. Even in Sri Lanka and Bangladesh, it is not allowed to be marketed. In August 2003, the European Medicine Evaluation Agency (EMEA) had banned the use of nimesulide in all the 25-member countries. Its use for fever is not permitted (Sharma, 2007).

Table 4.4- Nimesulide manufacturing companies along with their generic name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
ALBERT DAVID LIMITED	NIMERIL	1.50 MRP (Per tablet)	Yes
ALEMBIC LIMITED, INDIA	NIMEGESIC TABLET	2.57 MRP per tablet	Yes
APEX PHARMACEUTICALS PVT.LTD.	NIMEX TAB	1.80 MRP (Per tablet)	Yes
ARISTO PHARMACEUTICALS LTD.	NIMODOL TABLET	2.40 MRP (Per tablet	NO
ASIAN PHARMACEUTICALS PVT.LTD.	NIMS TABLET	3.00 MRP (Per tablet)	YES
BANGALORE PHARMACEUTICALS & RESEARCH LABORATORIES (P) LTD.	REMULIDE TABLET	3.99 MRP (Per tablet)	NO
BIRAT PHARMA LAB PVT. LTD.	INFLATOP 100	3.00 MRP (Per tablet	YES
BROWN AND BURK PHARMACEUTICALS P.LTD.	NOVOLID TABLET	1.88 MRP (Per tablet)	YES
CADILA PHARMACEUTICALS LIMITED	NIMUTAB TABLET	2.00 MRP (Per tablet)	YES
CHEMI DRUG INDUSTRIES PVT	C-NIM 50	3.00 MRP	YES

LTD.	TABLET	(Per tablet)	
CTL PHARMACEUTICAL PVT. LTD.	NIBUCID TABLET	3.00 MRP (Per tablet)	NO
CUREX PHARMACEUTICALS PVT.LTD.	NIMSEL TABLET	3.00 MRP (Per tablet)	YES
DR. REDDY'S LABORATORIS LTD	NISE -100 TABLET	2.57 MRP (Per tablet)	YES
INDCHEMIE HEALTH SPECIALITIES P.LTD	NIMSTAL -100 TABLET	1.65 MRP (Per tablet)	NO
INTAS PHARMACETICALS LTD.	NIMOTAS CD TABLET	2.40 MRP (Per tablet)	YES
IPCA LABORATORIES LIMITED	NIMICA DT-100	2.56 MRP (Per tablet)	NO
LOMUS PHARMACEUTICALS PVT. LTD.	COXFLAM TAB. TABLET	3.00 MRP (Per tablet)	YES
MACLEODS PHARMACEUTICALS LTD	NIMTECH TABLET	2.75 MRP (Per tablet)	YES
NATIONAL HEALTH CARE PVT.LTD.	NESLIDE TABLET TABLET	2.00 MRP (Per tablet)	YES
NEPAL PHARMACEUTICALS LAB. PVT. LTD.	ANIM 100 CD TABLET	3.00 MRP (Per tablet)	YES
PANACEA BIOTEC LIMITED	NIMULID -MD TABLET	5.00 MRP (Per tablet)	YES
PHARMACO INDUSTRIES PVT. LTD	SLIDE-100 TAB TABLET	3.19 MRP (Per tablet)	YES
QUEST PHARMACEUTICALS PVT.LTD.	Q-NIM TABLET	2.50 MRP (Per tablet)	NO
UNICHEM LABORATORIES LIMITED	PRONIM TAB TABLET	2.00 MRP (Per tablet)	NO
UNIQUE PHARMACEUTICALS (P) LTD.	NIMISON TAB TABLET	2.00 MRP (Per tablet)	NO
WALLACE PHARMACEUTICAL PVT. LIMITED	SOONIL TABLET TABLET	1.90 MRP (Per tablet)	NO

4- Clioquinol –

C.A.S. number 130-26-7

Scientific and common names, and synonyms- 5-CHLORO-7-IODOQUINOLINOL, 5-CHLORO-7-IODO-8-QUINOLINOL, CHLOROIODOQUIN, CHINOFORM, IODOCHLORHYDROXYQUINOLINE, IODOCHLORHYDROXYQUIN.

Legislative or regulative action-

The Ministry of Heath and Welfare, Japan prohibited the sale of clioquinol and preparations containing them, following reports that clioquinol might be one of the causes of Subacute myelo-optic neuropathy (SMON) in 1970. In Norway in Jan 1974, Clioquinol withdrawn from the market. In 1978, Denmark products containing clioquinol withdrawn from the market (UGLAAD, 1978). In United Arab Emirates, since 1981 Pharmaceutical preparations containing Clioquinol were banned (UAEMD, 1981). In Bangladesh from 1982, Clioquinol was banned as a single ingredient or in combination due to its implication in SMON. In Spain The Ministry of Health and Consumer Protection has withdrawn approval for clioquinol in 1983 (ESPMC, 1983). Clioquinol, is a halogenated hydroxyquinoline derivative, was introduced into medicine around 1900 as a topical antiseptic and in 1934 oral preparations for the treatment of amoebic dysentery and simple diarrhoea became available. By 1964 its use in Japan had been associated with cases of SMON which reached epidemic proportions resulting in its withdrawal there in 1970. Although relatively few cases of SMON were documented elsewhere, clioquinol was subsequently withdrawn from use in many countries and placed under prescription control in others. It was phased out worldwide by the major manufacturer between 1983 and 1985 on grounds of obsolescence. No adequately controlled evidence was ever generated to demonstrate that clioquinol is effective in bacterial or viral diarrhoea. However, products containing clioquinol and related halogenated hydroxyquinolines continue to be used in some tropical and subtropical countries where Amoebiasis remains endemic (WHODI, 1977).

Comments-

Products containing clioquinol was also available in ointment form and was available from 2 companies one was Hindustan medicine products and Glaxo Smith Kline pharmaceuticals ltd.

Table 4.5- Clioquinol manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
GLAXO SMITH KLINE PHARMACEUTICALS LTD	BETNOVATE C OINTMENT	19.60 MRP (Per tube)	YES
HINDUSTAN MEDICINE PRODUCTS	HIMOSONE-C OINTMENT	33.57 MRP (Per tube)	YES

4 (b)- Iodochlorhydroxyquinoline –

Clioquinol and Iodochlorhydroxyquinoline are the same scientific and common names, or synonyms But According to the DBN 2006, In Nepal many medicines have been banned due to adverse effect based on the data available from foreign countries. We didn't have system to note the adverse effect. For example, iodochlorhydroxyquinoline was banned in Nepal long ago because serious adverse effect was observed in Japanese population. Products containing Iodochlorhydroxyquinoline were available in ointment form only from two companies.

Table 4.6- Iodochlorhydroxyquinoline manufacturing companies along with their brand name, price and availability

MANUFACTURING COMPANY	Brand Name	Price	Current availablity in the market-
HINDUSTAN MEDICINE PRODUCTS	HIMODERM PLUS CREAM CREAM	30.90 MRP (Per tube)	YES
NATIONAL MEDICINE CONCERN	STADERM CREAM CREAM	40.00 MRP (Per tube)	YES

5- Benzylpenicillin- Benzylpenicillin sodium (topical preparations)

C.A.S. number 69-57-8

Scientific and common names, and synonyms- BENZYLPENICILLIN CRYSTALLINE PENICILLIN G SODIUM MONOSODIUM (2S,5R,6R)-3,3-DIMETHYL-7-OXO-6-(2-PHENYLACETAMIDO)-4-THIA-

ZABICYCLO(3.2.0)HEPTANE-2-CARBOXYLATE PENICILLIN G PENICILLIN

Legislative or regulative action-

Topical preparations have been withdrawn from the market and are prohibited for export by the Food and Drug Administration due to the lack of effectiveness of these products and an unfavourable benefit-to-risk ratio (FEREAC, 1972).

Comments-

Benzylpenicillin sodium, one of the first penicillin derivatives to be used in medicine, was introduced in the early 1940s. Topical preparations intended for use on the skin have been associated with allergic rashes and are in general no longer acceptable. However, topical preparations for specialized use, in particular in the eye and on open wounds, are available in many countries. Injectable preparations of Benzylpenicillin are included in the WHO Model List of Essential Drugs (WHO, 1985). This drug is available in the market and products from 4 different manufacturers have been found in the market.

Table 4.7- Benzylpenicillin manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availablity in the market-
ALEMBIC LIMITED, INDIA	BENZYL PENICILLIN INJECTION 5 LACS SOLUTION,	5.81 MRP (PER vial)	YES
SHIV PHARMACEUTICALS LABORATORIES PVT. LTD.	FORTIFIED PROCAINE PENICILLIN 4 LAC SOLUTION,	9.20 MRP (PER vial)	YES
UMEDICA LABORATORIES PVT. LTD.	BENZAPEN-0.5 SOLUTION,	12.00 MRP (PER vial)	YES
WYETH LIMITED, INDIA	PENIDURE LA24 SOLUTION,	30.10 MRP (PER	YES

6- Chlormezanone-

C.A.S. number 80-77-3

Scientific and common names, and synonyms- CHLORMETHAZANONE 2-(P-CHLOROPHENYL)-TETRAHYDRO-3-METHYL-4H-1,3-THIAZIN-4-ONE1,1-IOXIDE.

Legislative or regulative action-

Because of severe cutaneous reactions including life-threatening toxic epidermal necrolysis, Stevens-Johnson syndrome, and fixed drug eruptions, the manufacturer of chlormezanone withdrew the drug worldwide. This coincided with local action undertaken in several countries. The withdrawal concerns chlormezanone used alone or in combination (SANOFI, 1996). The Ministry of Health has withdrawn marketing approval for pharmaceutical products containing chlormezanone because it has been associated with an unacceptable incidence of Stevens-Johnson syndrome (UAEDIB, 1997). The Medicines Control Authority has cancelled the registration of all chlormezanone containing products in the light of international actions taken on the basis of a safety evaluation of chlormezanone. This drug has been associated with an unacceptable incidence of Stevens-Johnson syndrome (ZWEDIB, 1998).

Comments-

Chlormezanone is available in tablets from two manufacturing companies, Brown and Burk Pharmaceuticals pvt.ltd and Lomus pharmaceuticals pvt. Ltd. They were sold under the brand names Dolobak tablet and Cetozone tablets. As per the DDA , List of Manufacture with product(s) including Ingredients

Table 4.8 Chlormezanone manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
BROWN AND BURK PHARMACEUTICALS P.LTD.	DOLOBAK TABLET TABLET	3.20 MRP (Per tablet)	YES
LOMUS PHARMACEUTICALS PVT. LTD.	CETOZONE TABLET TABLET	4.50 MRP (Per tablet)	YES

7- **Cyproheptadine-**

C.A.S. number 129-03-3

Scientific and common names, and synonyms - PIPERIDINE,4-(5H-DIBENZO(A,D)CYCLOHEPTEN-5-YLIDENE)-1-METHYLPIPERIDINE,4-(5H-DIBENZO[A,D]-CYCLOHEPTEN-5-YLIDENE)-1-METHYL-,HYDROCHLORIDE, ESQUIHYDRATE.

Legislative or regulative action-

Sale and use of preparations containing Cyproheptadine have been severely restricted due to abuse of its appetite stimulant effect (GHAPDR, 1979). Under the provisions of the Drugs (Control) Ordinance, Cyproheptadine was banned following unacceptable promotion encouraging its use as an appetite stimulant (BGDCO, The Drugs (Control) Ordinance, 1982)

Comments-

Cyproheptadine is available in Nepal and products from 4 manufactures are marketed. It is available in syrup form and other forms such as tablets and solutions. According to the DDA website combination of Cyproheptadine with Strychnine and combination of Cyproheptadine with another drug is banned.

Table 4.9- Cyproheptadine manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
CHEMI DRUG INDUSTRIES PVT LTD.	APETONE SUSPENSION,	34.96 MRP (Per 100 ML)	YES
CIPLA LIMITED	PRACTIN TABLET TABLET	1.12 MRP (Per tablet)	YES
DEURALI-JANTA PHARMACEUTICALS PVT. LTD.	PROMEAL (200ML/100ML) SUSPENSION,	60.00 MRP (Per bottle)	YES
GENO PHARMACEUTICALS LIMITED	PRACTIN TABLET TABLET	1.12 MRP (Per tablet)	YES
LOMUS PHARMACEUTICALS PVT. LTD.	APETONE SUSPENSION, 34.96	MRP (Per 100 ML)	YES
NATIONAL HEALTH	APETAMIN SYRUP SYRUP	42.95 MRP (Per bottle)	YES
NAXPAR LAB. PVT. LTD.CARE PVT.LTD.	APTIV(100ML) SOLUTION	32.00 MRP (Per 100 ML)	YES
SIMCA LABORATORIES PVT. LTD.	CYPOTONE SYP	(100ML) SYRUP 38.00 MRP (Per bottle)	YES
TABLETS (INDIA) LIMITED	APETAMIN SYRUP SYRUP	42.95 MRP (Per bottle)	YES
UNIQUE PHARMACEUTICALS PVT LTD.	APTIV(100ML) SOLUTION,)	32.00 MRP (Per 100 ML	YES

8- **Erythromycin Estolate-**

C.A.S. number 3521-62-8

Scientific and common names, and synonyms –

ERYTHROMYCIN, 2'PROPIONATE, DODECYL SULPHATE ERYTHROMYCIN PROPIONATE LAURYL SULPHATE ERYTHROMYCIN 2'-PROPANOATE DODECYL SULPHATE.

Legislative or regulative action-

Withdrawn from the market (GRAGA, 1977). The Ministry of Health of Sudan no longer allows registration of preparations containing erythromycin estolate since 1982. Under the Pharmacy and Poisons (Prohibitions of Harmful Drugs) Regulations, this drug is deemed "harmful" by the Ministry of Health and is prohibited for import, manufacture, storage, distribution, sale, possession, use,

export or other transaction (MPPHD, 1982). Registration has been cancelled (UGLAAD, 1974)

Comment-

In Nepal Erythromycin estolate is available in tablet, capsule and syrup form. Several products from different manufacturers are found in Nepal.

Table- 4.10 Erythromycin estolate manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
ALEMBIC LIMITED,	ALTHROCIN -500 TABLET	7.07 MRP (Per tablet)	YES
ALKEM LABORATORIES LIMITED	ERYTHROKEM- 250 TABLET	20.80 MRP (PER 10	YES
ASIAN PHARMACEUTICALS PVT.LTD.	KLARION 250 TABLET	25.00 MRP (Per tablet)	YES
BROWN AND BURK PHARMACEUTICALS P.LTD.	CLARIWIN-500 TABLET	30.00 MRP (Per tablet)	YES
CUREX PHARMACEUTICALS PVT.LTD.	ETHRO CTL 250MG TABLET	5.90 MRP (Per tablet)	NO
GENO PHARMACEUTICALS LIMITED	ULCICLAR-250 TABLET	24.90 MRP (Per tablet)	YES
INDCHEMIE HEALTH SPECIALITIES P.LTD	GERY OINTMENT OINTMENT,	26.68 MRP (Per tube)	YES
LARK LABORATORIES LIMITED	ELTOCIN DS. TABLET	9.27 MRP (Per tablet)	YES
IPCA LABORATORIES LIMITED	ERYTHROLAR TABLET-250 TABLET	4.25 MRP (Per tablet)	YES

9- Loperamide

C.A.S. number 53179-11-6

Scientific and common names, and synonyms

1-PIPERIDINEBUTANAMIDE, 4-(4-CHLOROPHENYL)-4-HYDROXY-N,N-DIMETHYL-ALPHA, ALPHA-DIPHENYL 4-(P-CHLOROPHENYL)-4-HYDROXY-N,N-DIMETHYL-ALPHA,ALPHA-DIPHENYL-1-PIPERIDINEBUTYRAMIDE.

Legislative or regulative action-

Drop formulations containing loperamide have been voluntarily withdrawn by the major manufacturer (LJJ, 1990). Drop and syrup formulations of products containing loperamide were banned (TURMH, 1991). Manufacture, import or sale of drop and syrup formulations of loperamide were prohibited (LKAGAZ, 1991). Drop and syrup formulations of products intended for paediatric use containing loperamide were voluntarily withdrawn by the manufacturer ((OMNCR, 1990)

Comments-

Liquid formulations of products containing loperamide either alone or in combination, and intended for the treatment of diarrhoea in children, were banned in Nepal. (DDA, 1992). In Nepal products from two manufacturers were found both in capsule form. The two company were Brown and Burk pharmaceuticals pvt.ltd and Encore healthcare pvt. Ltd.

Table- 4.11- Loperamide manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
BROWN AND BURK PHARMACEUTICALS P.LTD.	ELDOPER CAPSULE	1.38 MRP (Per capsule)	YES
ENCORE HEALTHCARE PVT. LTD.	IMODIUM CAPSULE	2.89 MRP (Per capsule)	YES

10.Nandrolone decanoate

C.A.S. number 360-70-

Scientific and common names, and synonyms- ESTR-4-EN-3-ONE, 17-((1-OXODECYL)OXY)-, (17BETA) NORTESTOSTERONE DECYLATE.

Legislative or regulative action-

Under the provisions of the Drugs (Control) Ordinance, low-strength preparations were banned following unacceptable promotion encouraging their use in children suffering from malnutrition (BGDCO, The Drugs (Control) Ordinance , 1982). The Medicines Agency has withdrawn from the market all Injectable formulations of the anabolic steroid, following a routine re-evaluation of the benefit/risk ratio showing a lack of clinical data to support the efficacy of the product in the claimed indication (confirmed osteoporosis in postmenopausal women) (FRAAMC, 1998).

Comments-

In Nepal, Nandrolone decanoate is available as injection and products from only one company are available. Organon (India) limited.

Table-4.12- Nandrolone decanoate manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
ORGANON (INDIA) LIMITED.	DECA DURABOLIN -25 SOLUTION, 25MG	128.49 MRP (PER vial)	YES
	DECA DURABOLIN -50 SOLUTION, 50MG	201.12 MRP (PER vial)	YES
	DECA DURABOLIN- 100 SOLUTION, 100MG	342.37 MRP (PER vial)	YES

11- Nandrolone phenylpropionate-

C.A.S. number 62-90-8

Scientific and common names, and synonyms- ESTR-4-EN-3-ONE, 17-(1-OXO-3-PHENYLPROPOXY)-, (17BETA)-NORTESTOSTERONE

PHENYLPROPIONATE NANDROLONE PHENPROPIONATE 17BETA-HYDROXYESTR-4-EN-3-ONE HYDROCINNAMATE.

Legislative or regulative action-

Under the provisions of the Drugs (Control) Ordinance, low-strength preparations were banned following unacceptable promotion encouraging their use in children suffering from malnutrition (BGDCO, The Drugs (Control) Ordinance, 1982)

Comments- Nandrolone phenylpropionate was available from only one company. The DDA has not issued any information on this medicinal drug.

Table- 4.13- Nandrolone phenylpropionate is available in Nepal from one company, Organon (India) limited.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
ORGANON (INDIA) LIMITED.	DURABOLIN SOLUTION,	61.46 MRP (PER vial)	YES

12. Neomycin sulfate-

C.A.S. number 1405-10-3

Legislative or regulative action-

Under the provisions of the Drugs (Control) Ordinance, this product has been banned since it has been shown to cause malabsorption in children and to be of little or no therapeutic value. (BGDCO, The Drugs (Control) Ordinance, 1982). All anti-diarrhoeal preparations for oral administration containing this product have been banned. Most cases of diarrhoea have been found to be resistant to the drug and its constant use promotes pseudomembranous colitis in infants and children. Neomycin can cause other serious adverse effects including renal damage, neuro-muscular blockage and ototoxicity, possibly leading to deafness in some patients (PHADO, Administrative Order, 1982).

Comments-

Products containing neomycin sulfate are available in Nepal in solution, ointment and powder form. These products were not available for diarrhoea.

Table 4.14- neomycin sulfate manufacturing companies along with their brand name, price and availability.

MANUFACTURING COMPANY	Brand Name	Price	Current availability in the market-
CIPLA LIMITED	CINDOX -FORTE (50GM/10GM) POWDER	217.95 MRP (Per 50 g)	YES
GLAXO SMITH KLINE PHARMACEUTICALS LTD.	FLOMEX-N SOLUTION, EYE	42.00 MRP (PER 5ML)	YES
HINDUSTAN MEDICINE PRODUCTS	NEOSPORIN ANTIBIOTIC POWDER POWDER	27.57 MRP (Per bottle)	YES
KARE LABS PVT LTD	HIMOSONE -N OINTMENT CREAM	14.07 MRP (PER 5gm)	YES
MICRO LABS LIMITED	BENEZOLE CREAM CREAM	30.90 MRP (Per tube)	YES
NATIONAL HEALTH CARE PVT.LTD.	POLYSPORIN OINTMENT (15GM/5GM) OINTMENT,	27.00 MRP (PER 5gm)	YES

Discussion-

Medicinal drugs that are banned are available in Nepal, In some cases medicinal drugs that were banned even by the DDA were available in Nepal. As a result of a profit enthused pharmaceutical industry, there is a immense misuse of medicines which causes ill health rather than better health. There are many products in our markets which are harmful, ineffective, inappropriate, irrational, useless or needlessly expensive. The scope of this chapter was to investigate a selected number of freely available harmful medicinal drugs in Nepal. Manufacturers who market harmful and non-essential products in poor countries invariably stress the differences in opinions and regulations that exist from one country to another. For example, within Europe medicines considered too

hazardous for sale in Britain and Scandinavian countries are still marketed in third world countries. Undoubtedly this complicates the issues as there can be as many opinions on the degree if risk of medicines as there are experts. The concept of self regulation has not been adhered by the companies. The "differences" argument forwarded by companies to 'prove' that they are doing all that can reasonably be expected of them and that it is up to the Third world governments both to decide which medicines they will allow on to the market, and to make sure they are used safely. But the argument needs to be considered as fundamental changes are required by the companies. Third world regulatory agencies rely on manufacturers for information on which to base their decisions. Inevitably manufacturers are in a position to convince governments and the prescribers that the advantages offered by their products outweigh possible hazards. As a result, medicines with known toxic side-effects are freely available in Third world countries like Nepal.

Chapter- 5

Medicinal drug promotion and adherence to ethical guidelines-

5.1- Introduction-

This chapter looks at different promotional tactics through which pharmaceutical medicinal drug promotion are marketed and whether they adhered to WHO guidelines which is the third objective of the study.

Advertisement or promotion has been a crucial factor in all types of economies. When we visualise a vegetable market, the fish market we hear them trying to grab our attention by giving us some information. This is not a recent phenomenon since markets have existed since ancient times [around 350 BC the existence of 'Silk road' (coined by German scholar, von Richthofen in nineteenth century) indicates that markets have existed since thousands of years]. History shows us that markets have changed and evolved over a period of time. Significant differences in the characteristics of markets started to occur with the onset of colonialism. Presently the market is predominantly follows the laissez-faire doctrine. Under the laissez-faire approach all utilities from education, health services to cosmetics and music industry are treated alike whose objectives usually are solely for the purpose of monetary profit motive. Asymmetry of information and "uncertainty in the definition, recognition, and diagnosis of disease states" in particular distinguish medical markets from other "consumer" markets" (Montagne, 1992). The establishment of more stringent acts regarding patents, copy rights, data-exclusivity have been vehemently pursued by pharmaceutical companies. These acts have ensured huge profits for the pharmaceutical industry on one side and slow and painful death more millions around the world. The contradiction is that millions die due to inaccessibility, unaffordability to medicines on the one hand and millions die due to consumption of irrational medicine use, adverse drug effects, counterfeit drugs, promotion of harmful drugs on the other hand.

5.2- Antibiotic resistance Nepal-

With so many different brands of antibiotics in Nepal, there is an intense competition to capture the market. Improvements in production have provided

increasingly less expensive compounds that encourage non prescription and off-label uses. In this study the three antibiotics selected, Amoxicillin, Ciprofloxacin and Cefadroxil are available from more than 130 different companies. Due to the laissez-faire economy approach there is intense competitiveness beteween different private-enterprises to increase market share and make monetory profit which makes the situation even more conducive for malpractices and unethical behaviour. In Nepal 30% of total consumption of drugs was covered by antibiotics(DDA 2007). This high consumption can be imputable to various factors, one of them being aggressive drug promotion.

One study conducted in 1998 showed that 68% of drug prescriptions/recommendations for diarrhea and 70% of prescriptions/recommendations for acute respiratory infection symptoms were for antimicrobials. Of all encounters at health facilities and with private-sector pharmacists, 50.7% resulted in antimicrobials being dispensed (Kafle KK, 1998).

A study conducted in Kathmandu in 1999 showed that unauthorized dispensing is clearly problematic. Drug retailers in the study did not demonstrate adequate understanding of the disease processes in question to justify their use of these drugs. Risks of such indiscretion include harm to individual patients as well as spread of antimicrobial resistance. antimicrobial medications without prescription, these agents are widely available over the counter, and are in fact readily given out by drug sellers without consumer solicitation or clinical indication. It is particularly notable that 97% of patients with a complaint of three episodes of loose stool were given antimicrobials (David A.Wachte,1999).

Nepalese are forced to rely on health assistants and pharmacy shopkeepers as their primary source of allopathic health care (CBS, 1997). Studies have documented that '<97% of the medications distributed by these pharmacies for routine symptoms, such as diarrhea, were antimicrobials (Walson, 2001). In Nepal, resistance rates in individuals were found to correlate more with the total community use of antibiotics than with the individual's own use. (Walson, 2001)

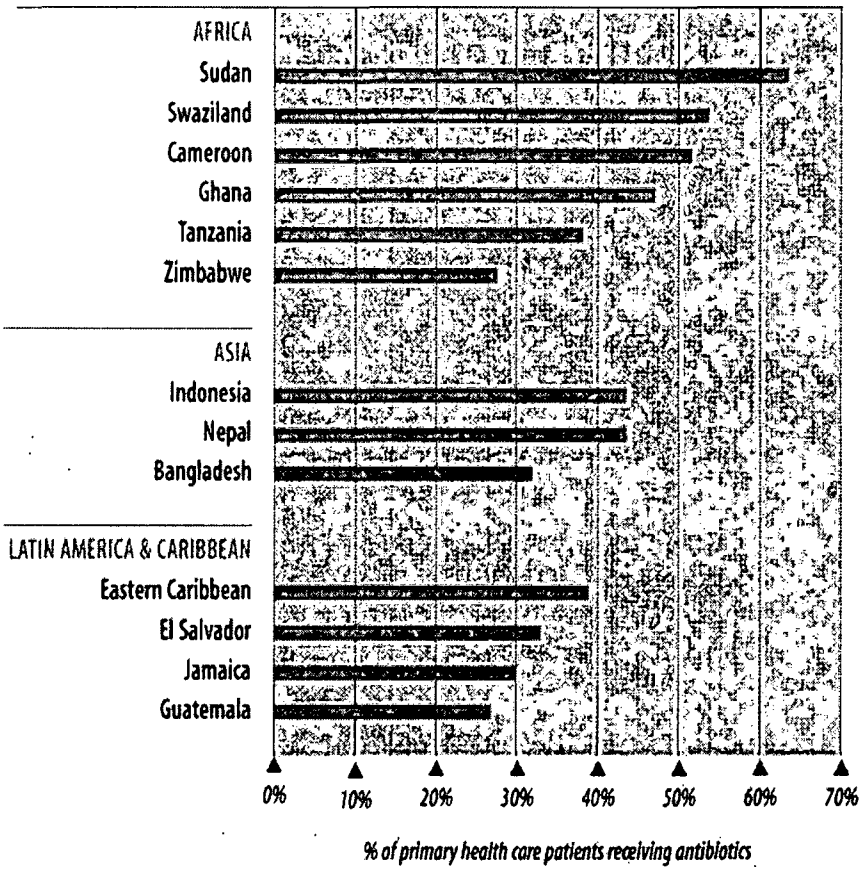
A study carried out in Nepal between 1993 and 2003 showed an increased susceptibility to first-line antibiotics comparing the first half of the

study (1993–1998) with the second half (1999–2003). Susceptibility increased for tetracycline from 77 to 92%, for amoxicillin from 72 to 94% and for chloramphenicol from 95 to 98%. However, isolates were all susceptible to ciprofloxacin until 1998 but from 1999 to 2003 resistance rates reached 13% (Maskey et al. 2008).

There have been reports of antimony resistance spreading to the Terai regions of Nepal, especially from the district adjoining hyperendemic areas of Bihar, where up to 24% of patients seem to be unresponsive, though in eastern Nepal a study showed that only 10% were unresponsive. (Rijal, 2004)

Table- 5.1

27 to 63% of patients in primary health care centres receive antibiotics —perhaps twice what is clinically justified.



(Hogerzeil 1993).

Typhi strains were first reported in Nepal in 2002 during Bharatpur outbreak of enteric fever in Chitwan, Nepal in May-June, 2002. This outbreak of enteric fever in Bharatpur, 2002 was reported to be a large single source outbreak

due to multidrug resistant S. typhi. (Lewis M 2003). Since then the necessity of monitoring the antimicrobial resistance in Salmonella initiated this study. In this study, the overall percentage of multi-drug resistant strains was 8.8%, however the yearly breakdown of the MDR strains showed a gradual decrease, 2002 (15.5%), 2003 (7.5%) and 2004 (3.5%). Ciprofloxacin is the drug of choice for multi drug resistant. S. typhi in Asia for the past decade. But acquired drug resistance to this drug has posed a serious problem for the treatment of enteric fever. In India 64.5% of S typhi was reported as being MDR in 1993. (Pillai 1993). Epidemic dysentery caused by multidrug-resistant *S.dysenteriae* serotype 1 has been a recurrent challenge in many parts of developing world. This organism caused an extensive epidemic of shigellosis in eastern India in 1984 (Pal 1984.) After a lapse of about 18 years, an outbreak of bacillary dysentery with high morbidity and mortality was reported in April 2002 among the laborers of tea gardens in the same region (Pazhani 2004). The strains were resistant to ampicillin, co-trimoxazole, nalidixic acid, and norfloxacin.Similar strains have also been reported from sporadic cases in Nepal and Bangladesh, leading to a regional alert in south Asia (Talukdar 2004).

Another study highlighted the emergence of penicillin resistant N. gonorrhoeae in Birgunj. In this study, resistance to penicillin was detected in 60.0% (18/30) of isolates, partially sensitive to penicillin was seen in 13.3% isolates and sensitive to 26.6% of isolated cases. The study concluded that Penicillin resistant *N. gonorrhoeae* was on the rise in and around Birgunj. (Bhargava, 2010).

5.3- Analysis of medicinal drug promotional materials-

This chapter looks at different promotional tactics through which pharmaceutical medicines are marketed and whether they adhered to WHO guidelines which is the third objective of the study. Since domestic industries in Nepal have a small share of market compared to foreign pharmaceutical products, both domestic and foreign products were selected for the study. Drug company representatives visiting the doctors leave promotional materials for them. Drug promotional materials are also available at the branch offices of the Department of Drug Administration (DDA) as per the code . I

identified the promotional materials present in the Biratnagar branch office of the DDA and also collected them from the Drug Information Centre. Promotional materials of antibiotic medicinal drug promotion were studied. Promotional materials printed only after 2008 were selected since, Nepal issued its guidelines on ethical promotion of medicines only in 2007. They are two different criteria for advertisements to healthcare professionals and to the general public. In this study advertisements to physicians and health care professionals were selected. WHO guidelines for advertisements to physician and health care professionals states that the advertisement should include the name of the active ingredient, brand name, content of active ingredient per dosage form or regimen, other ingredients known to cause problems, approved therapeutic uses, dosage form or regimen, side effects, contra-indications, major interactions, management in case of overdose or toxicity, storage conditions, pharmacokinetic profile, use in pregnancy and lactation, name and address of manufacturers or distributor, and reference to scientific literature (HAI 2005).

The total consumption of antibiotics in 2005/06 was Rs.2 billion 717million. Of which, 48.7% was shared by domestic industries. About 30% of total consumption of drugs was covered by antibiotics. (DDA 2007).

Top 15 Selling Antibiotics from Domestic Industries and import (DDA 2007).

1. Amoxicillin
2. Ciprofloxacin
3. Cefadroxil
4. Metronidazole + Diloxanide
5. Ampicillin + Cloxacillin
6. Ofloxacin
7. Metronidazole
8. Ceftriaxone*
9. Cephalexin
10. Cefixime
11. Chloramphenicol
12. Co-trimoxazole
13. Povidone Iodine

14. Azithromycin
15. Cefotaxime*

*Not available from domestic industries.

The following are the top 3 antibiotics sold and are available from both domestic and foreign companies-

AMOXICILLIN- From the, 'List of Manufacture with product(s) including Ingredient' published by the Department of Drug Adminstration 206 versions of Amoxicillin were found. They were available in capsule, tablet, syrup, powder, suspension and solution form. According to the DDA list 53 companies were marketing their products in Nepal which includes both domestic and foreign companies.

CIPROFLOXACIN- From the, 'List of Manufacture with product(s) including ingredient published by the Department of Drug Administration it was found that 111 different versions of Ciprofloxacin. They were available in tablet, capsule, solution (injection), solution eye and ear and infusion solution. According to DDA list there are 59 Ciprofloxacin manufacturers both domestic and foreign whose products are available in Nepal.

CEFADROXIL- From the, 'List of Manufacture with product(s) including ingredient published by the Department of Drug Administration it was found that 58 different versions of cefadroxil were available. They were available in tablet, powder form, syrup, capsule, suspension, dispersible. According to the DDA list there are 20 cefadroxil manufacturers both domestic and foreign whose products are available in Nepal.

5.4- Selecting the promotional brochures-

For assessing the different promotional brochures the first step was to choose the manufacturers. Amoxicillin was produced by 53 manufacturers, Ciprofloxacin by 59 manufacturers and Cefadroxil by 20 manufacturers. Since 10 promotional brochures was to be selected from each category, I decided to select the promotional materials of those 10 companies based on the price of their products (High to low) which is mentioned in the, 'List of manufacture with products'. If the promotional brochures of any product was not available then the next product was selected.

Abbreviations used in the table-

- MI- Manufacturing industry
- BN- Brand Name
- P-Price
- NAI- Name of active ingredient(s)
- RSL- Reference to scientific literature
- NAMD- Name and address of manufacturers or distributor
- DFR- Dosage form or regimen
- SC- Storage conditions
- PKP- Pharmacokinetic profile
- ATU- Approved therapeutic use
- SE/ADR- Side effects/ adverse drug reactions
- PCW- Precautions, Contra-indications, Warnings
- MI-Major interactions
- MODT- Management in case of over dose/toxicity
- UPL- Use in pregnancy and lactation.

Table 5.2- Promotional materials for amoxicillin and their adherence to ethical guidelines on promotions-

MI	BN	P	NAI	RSL	NAMD	DFR	SC	PKP	ATU	SE/ADR	PCW	MI	MODT	UPL
UNICHEM LABORATORIES LIMITED	Maxifect	29.16	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
MEDREICH STERILAB LTD., INDIA	Wymox	12.36	Y	Y	Y	Y	N	N	Y	Y	N	N	N	N
MICRO LABS LIMITED	Erox	10.40	Y	Y	Y	Y	N	N	Y	N	N	N	N	N
DINGLA PHARMACEUTICALS (P) LTD	Amoxydin	10.00	Y	Y	Y	Y	N	N	Y	N	N	N	N	Y
SQUARE PHARMACEUTICALS LIMITED	Moxacil	9.85	Y	N	Y	Y	N	N	Y	N	N	N	N	N
DCI PHARMACEUTICAL	Dicimox forte	9.35	Y	Y	Y	Y	N	N	Y	N	N	N	N	N

P.LTD.	capsules													
HUKUM PHARMACEUTICALS PVT. LTD.	Humoxyl	9.20	Y	N	Y	Y	N	N	N	N	N	N	N	N
SIDDHARTHA PHARMACEUTICALS PVT. LTD.	Rumex	9.00	Y	N	Y	Y	Y	Y	Y	N	N	N	N	Y
LOMUS PHARMACEUTICALS PVT. LTD.	Curemox	9.00	Y	N	Y	Y	N	N	Y	Y	Y	N	N	N
ARYA PHARMALAB PVT.LTD	Supramox	9.00	Y	Y	Y	Y	N	N	Y	N	N	N	N	N
data available for each category of information i.e. mandatory information as per the WHO guidelines			10/10	4/10	10/10	10/10	2/10	2/10	9/10	3/10	2/10	0/10	0/10	3/10

Table-5.3- Promotional materials for Ciprofloxacin and their adherence to ethical guidelines on promotions

MI	GN	P	NAI	RSL	NAMD	DFR	SC	PKP	ATU	SE/ ADR	PCW	MI	MODT	UPL
XL LABORATORIES PVT. LTD	Cipfast	71.00	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y
RANBAXY LABORATORIES LIMITED	Cifran	14.33	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	Y
VIJAYADEEP LABORATORIES LTD.	CIPRODEEP 500 FILM TAB	12.00	Y	N	Y	Y	N	N	Y	N	N	N	N	N
PHARMACE	Placin	12.	Y	N	Y	Y	N	N	Y	N	N	N	N	N

UTICAL COMPANY OF NEPAL		00												
SIMCA LABORATORIES PVT. LTD.	CIFLON	11.99	Y	N	Y	Y	N	N	Y	N	N	N	N	N
HUKUM PHARMACEUTICALS PVT. LTD.	BACTOCIP	11.77	Y	N	Y	Y	N	N	N	N	N	N	N	N
TIME PHARMACEUTICALS PVT. LTD	CIFROX	11.48	Y	N	Y	Y	N	N	Y	N	N	N	N	N
BAYER PHARMACEUTICALS LTD.	BAYCIP	11.03	Y	Y	Y	Y	N	N	Y	N	N	N	N	Y
CADILA HEALTH CARE LIMITED.	CIPROBID-	11.00	Y	N	Y	Y	Y	N	Y	Y	N	N	N	Y
CONCEPT PHARMACEUTICALS (N) PVT. LTD	CONFLOX	10.73	Y	N	Y	Y	N	N	Y	N	N	N	N	N
data available for each category of information i.e. mandatory information as per the WHO guidelines			10/10	3/10	10/10	10/10	3/10	1/10	9/10	2/10	1/10	0/10	0/10	4/10

Table- 5.4- Promotional materials for Cefadroxil and their adherence to ethical guidelines on promotions

MI	GN	P	NAI	RSL	NAMD	DFR	SC	PKP	ATU	SE/ADR	PCW	MI	MODT	UPL
CHEMI DRUG INDUSTRIES PVT LTD.	DOXIL	16.50	Y	Y	Y	Y	N	Y	Y	N	N	N	N	Y
G.D.PHARMACEUTICALS PVT.LTD.	BIDROXIL	15.25	Y	N	Y	Y	N	Y	Y	Y	N	N	N	N
ALIVE PHARMACEU	ALDROXIL	15.00	Y	N	Y	Y	N	N	Y	N	N	N	N	N

TICALS PVT. LTD														
CUREX PHARMACEUTICALS PVT.LTD.	TWICEF	14.00	Y	Y	Y	Y	N	N	Y	N	N	N	N	Y
TIME PHARMACEUTICALS PVT. LTD.	FEDROX	14.00	Y	N	Y	Y	N	N	Y	N	N	N	N	N
HUKUM PHARMACEUTICALS PVT. LTD.	CEDROXIL	13.50	Y	N	Y	Y	N	N	N	N	N	N	N	N
APEX PHARMACEUTICALS PVT.LTD.	CEDROX	12.50	Y	N	Y	Y	N	N	Y	N	N	N	N	N
NEPAL PHARMACEUTICALS LAB. PVT. LTD.	CIDOXIL	12.50	Y	N	Y	Y	N	N	Y	N	N	N	N	Y
NATIONAL HEALTH CARE PVT.LTD.	NEDROXYL	12.00	Y	N	Y	Y	N	N	Y	N	N	N	N	N
DEURALI-JANTA PHARMACEUTICALS PVT. LTD.	XILCEF	12.00	Y	N	Y	Y	N	Y	Y	N	N	N	N	Y
data available for each category of information i.e. mandatory information as per the WHO guidelines			10/10	2/10	10/10	10/10	0/10	3/10	9/10	1/10	0/10	0/10	0/10	4/10

5.5- Discussion-

The cost of the oldest and most frequently used antibiotics is (probably) mainly in the packaging (Davies 2010, Sep). Still then none of the promotional brochures had all the information as per the, 'WHO Ethical Criteria for Medicinal Drug Promotion'. None of the promotional brochures had information about, MI- Major interactions, MODT- Management in case of over dose/toxicity. Side effects/ adverse drug reactions were mentioned in 3 of the promotional materials in the case of amoxcillin. Both MI, MODT, were not mentioned in any of the promotional brochures. NAI- Name of active ingredient(s) NAMD- Name and address of manufacturers or distributor were found in all the promotional brochures. ATU- Approved therapeutic use was mentioned in all the promotional brochures except for one company's product (Hukum). Hukum pharmaceuticals sold all the 3 antibiotics and was the only company to do so as per the tables below RSL- Reference to scientific literature, SC- Storage conditions and PKP- Pharmacokinetic profile were also missing in the majority of the promotional brochures. The DDA issues notices, warning letters and publishes The Drug Bulletin of Nepal. Regarding the issue of providing promotion as per the prescribed guidelines the DDA has not paid any attention towards it.

Chapter- 6

Conclusion and Discussion-

This study looks at medicinal drug promotion and adherence to ethical guidelines in Nepal. The public health consequences of, and ethical responsibilities associated with, drug promotion are substantially larger when viewed through the prism of the realities faced by persons living in developing countries. The present study was carried out with the aim of analysing the medicinal drug promotion in Nepal. Medicinal drug promotion has been a subject of debate and controversy. Some argue for self regulation by the pharmaceutical industry and others argue for more government control. There have also been discussions on independent bodies regulating drug promotion. The issues dealt in this study are those that are available for public scrutiny. But, pharmaceutical industry is a highly secretive industry where not all issues are overt in nature. The practice of double standards is obvious in the present era of laissez fairer economy. Medicinal drugs that have been banned in the developed countries are available in many developing countries. Studies indicate that poorer the country the higher percentage of expenditure on pharmaceuticals is from out of pocket The public health consequences of, and ethical responsibilities associated with, drug promotion are substantially larger when viewed through the prism of the realities faced by persons living in developing countries.

The study begins with an inquiry in to the various issues in medicinal drug promotion. Within medicinal drug promotion various issues exist and which is known like that of inaccurate and selective information is effective for drug promotion (Rane, 1998). It is also known that the quality of the drug information given to Indian doctors is poorer than that given to our western counterparts (Gitanjali, 1997). In Nepal, there is, at present, no legal requirement of continuing medical education or periodic recertification. Medical representatives are often the doctor's only source of information on the latest developments in therapeutics. Findings from chapter 5 confirms studies done earlier that promotional materials do not confirm as per the prescribed guidelines. The medicinal drugs chosen for the study were the top 3 selling antibiotics in Nepal. Amongst these top 3 antibiotics there exists hundreds of manufacturers whose products exist in the

market. Hence forth I decided to select the 10 most expensive medicinal drugs in each category. The negligence in the promotional materials was high and this was the case in medicinal drugs that were costlier then others. Information on Major interactions, Management in case of over dose/toxicity, - Reference to scientific literature, Approved therapeutic use , storage conditions and use during pregnancy lactation were not available. Going through the tables 4, 5 and 6 it seems that the prescribed guidelines was not followed. What contains inside the products of these companies selling the anti-biotics is an issue which should be investigated? These antibiotics selected for each category belonged to the top 10 based on their prices. There are domestic and international companies whose promotional materials were analysed. Self-regulation has been a major policy by the pharmaceutical companies. Medicinal Drug promotional materials are just the mask behind which the real value of the product lies. They are important because they provide information to prescribers and in developing nations are the sole providers of information for many prescribers. Seeing such gross negligence in the providing of information, I think it is important to consider the concept of 'self-regulation'? The Government of Nepal has a different view as understood by the following,

"The editorial in the Drug Bulletin of Nepal Volume 18 No. 2 expresses its opinion on medicinal drug promotion as follows, "The commonly talked unethical practice is to provide expensive gift, either in form of cash or kind to the prescriber, sponsoring pleasure trip abroad and in form of free medicine to the retailers. However, any such activities should be transparent, and only ethical practices can be transparent. Hence it is extremely necessary for every manufacturer to draw their own code of ethics or adapt already established ethical practices. It is a matter of immense pleasure that stakeholders have identified the unethical practice, and should get rid of it". (DDA 2007)

WHO ethical criteria for medicinal drug promotion, mentions that the criteria does not constitute legal obligations; governments may adopt legislation or other measures based on them as they deem fit. From this study it indicates that the regulation/code of conduct of advertising in the WHO prescribed style is not a panacea. There has to be independent authorities to regulate or regulation by the government. But, under the characteristic nature of a 'Laissez Fairer' economy it

sees regulation as an obstacle to the market. A 'Laissez Fairer' economic approach assumes that in a free market, information flows smoothly; property rights are protected; people can be trusted to live up to their promises; side effects on third parties are curtailed; and competition is fostered. By following the transactions of pharmaceuticals one may discern a biographical order in their "social life" (kopytoff, 1986). Firstly they are prepared usually in a technologically advanced settings, and marketed to wholesalers suppliers such as ministries of health, private firms, whole sellers, retailers, hospitals etc. Next these medicinal drugs distributed to consumers either by prescription or direct sale. The prescription is an intermediate phase. The medicinal drug's efficacy is its ultimate and decisive life stage. In the primary stage the scientists and businesspersons are the primary decision makers. The second stage involves the drugs/medicines prescribers and this is where medicinal drugs promotion plays a crucial role. Since the Direct to Consumer advertisement is restricted in Nepal, promotional activities are directed towards the prescribers.

This study also looks at the prevalence of medicinal drugs that are banned as per the "Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted or not Approved by Governments" . A total of 12 different medicines under their generic names were found to be existing in the market. These 12 different medicines are sold under different brand names. Phenylpropanolamine according to the DBN 2007 was stopped considering the adverse drug reaction, use . It further goes on to state that Pseudoephedrine has become a popular ingredient in cough and cold preparations, once use of Phenylpropanolamine had stopped. Currently 18 different manufacturing companies are still marketing these medicinal drugs. Similarly, according to the DBN 2006, iodochlorhydroxyquinoline was banned in Nepal long ago because serious adverse effect was observed in Japanese population. Products containing Iodochlorhydroxyquinoline were available in ointment form from two companies . Here the role and authority of the DDA has been undermined. Medicinal drugs that have been banned in other South Asian nations like Sri-Lanka and Bangladesh are available in Nepal, the most common example is the existence of Nimesulide in the market.

Regarding the presence of harmful, irrational and banned medicinal drugs the National Good Pharmacy Practice Guidelines, developed by Nepal

Pharmacy Council in the year 2005 requires that, the pharmacy should have the latest version of Essential Drug List and Nepalese National Formulary and other relevant documents about the banned and DDA registered Drugs. The medicinal drug retail shops did not have these documents. Isues of sale in the Third World of drugs banned in the West are crimes in the countries where they occur, at least on English jurisdictional principles. According to Braithwaite, "it remains the case that in taking a purely legalistic view of their responsibilities, corporations show a callous disregard for the ethical principles upon which drugs have been banned in the West. The hydrogenated hydroxyquinolines such as clioquinol responsible for SMON defectare a case in point. CIBA/GEIGY paid out £300 million in compensation to about 9,000 victims and apologised to the Japanese in court, they continue to market this drug which has doubtful benefits for diarrhoea control abroad, arguing that other countries do not use it so regularly as did the Japanese. (Braithwaite 1984). The discovery of infectious agents (bacteria) in the late 19th century stimulated the search for appropriate preventative and therapeutic regimens; however, successful treatment came only with the discovery and introduction of antibiotics half a century later. Antibiotics have revolutionized medicine in many respects, and countless lives have been saved; their discovery was a turning point in human history. Regrettably, the use of these wonder drugs has been accompanied by the rapid appearance of resistant strains.

The use of antibiotics has been a cause for worry due to the development of the drug resistance which has been been prevalent for many years. Failure to appreciate the evolutionary change that occurs in disease organisms as a direct consequences of the attempts to deal with them was not appreciated though 'Drug resistance' has been reported since the 1950's and 'pesticide resistance' even earlier. The 'magic-bullet' approach to disease jargoned with militarised metaphors like, 'weapons in the war on(Tuberculosis, HIV/Aids etc)', 'attack', 'come in for the kill', 'fight these invading diseases', unvalued that nature is also active and that treatments necessarily evoke some responses.

Unfortunately, the stupendous need for these valuable drugs has had a crucial environmental downside. In the 60 years since their introduction, millions of metric tons of antibiotics have been produced and employed for a wide variety of purposes. Improvements in production have provided increasingly less expensive

compounds that encourage non prescription and off-label uses. The cost of the oldest and most frequently used antibiotics is (probably) mainly in the packaging (Davies 2010, Sep). The development of generations of antibiotic-resistant microbes and their distribution in microbial populations throughout the biosphere are the results of many years of unremitting selection pressure from human applications of antibiotics, via underuse, overuse, and misuse. This is not a natural process, but a manmade situation superimposed on nature; there is perhaps no better example of the Darwinian notions of selection and survival (Davies 2010, Sep).

Recommendations-

Medicinal drugs are an important product consumed by us. The pharmaceutical sector has been a very secretive industry. The more advanced a company gets the more secret becomes its activities which are also protected by law regarding patents ad copy rights. Patents and copy right laws have been strongly pursued by the pharmaceutical companies exclusively from the developed countries.

Nepal which comes under the least developed country and out of pocket expenditure is high. Allopathic medicinal drugs has been strongly promoted by the companies. The major findings of the study are nothing new unethical issues that were addressed decades ago still exist in the pharmaceutical sector. Nationalists will argue that the share of the domestic sector is rising, but the issue is at what cost? And for whose benefits? The domestic pharmaceutical sector is restricted to Secondary manufacture, or formulation into tablets, capsules or injection, for products, involving long-established technologies. The domestic pharmaceutical companies and foreign pharmaceutical companies both are involved in selling of banned medicinal drugs. Some of the banned products were available only from foreign companies. The existence of incomplete medicinal drug promotional materials can be seen as a very callous attitude by the pharmaceutical companies.

The major recommendation of the study is that, medicinal drugs should be treated differently (economically) than other consumer products in the market.

These products should be monitored by regulatory bodies that are independent from the control of the pharmaceutical companies.

The pharmaceutical sector is an important sector and not only the overt information available but also the covert issues should be studied. From the clinical trials to the consumption pattern (irrational use) of medicinal drugs should be monitored. This study has dealt with issues of medicinal drug promotion and a study on the availability of banned medicinal drugs available in Nepal.

Annexure-

Guidelines for ethical promotion of medicinal drugs-

औषधि बिक्री प्रवर्द्धन निर्देशिका २०६४

उद्देश्य र कारण

विरामीलाई स्तरिय स्वास्थ्य सेवा उपलब्ध गराउने औषधि उद्योगको लक्ष्य परिपूर्तिमा औषधिको समुचित प्रवर्द्धनको महत्वपूर्ण भूमिका रहेको हुन्छ । औषधिको समुचित प्रवर्द्धनले चिकित्सक र स्वास्थ्यकर्मीलाई आवश्यक जानकारी सही किसिमले प्राप्त हुन सहयोग पुऱ्याउँछ जसका कारण स्वास्थ्य प्रवर्द्धनमा अत्यधिक फाइदा हुने गरी विरामीलाई औषधि सिफारिस गर्न र विरामीले औषधि प्रयोग गर्न सक्षम हुन्छन् । औषधिको समुचित प्रयोग राष्ट्रिय औषधि नीति, २०५१ मा समेत व्यवस्था रहेको देखिन्छ ।

चिकित्सक तथा स्वास्थ्यकर्मीबाट औषधिको समुचित प्रयोग प्रवर्द्धनका लागि औषधिका बारेमा सही जानकारी प्रदान गर्नु औषधि उद्योगको दायित्व तथा कर्तव्य हो । यो निर्देशिकाको प्रभावकारी कार्यान्वयनबाट देशभरि औषधिको बिक्री प्रवर्द्धन कार्य अन्तर्राष्ट्रिय व्यवहार र संहिता अनुरुप भई नैतिकताको पालना सहित संचालन हुने विस्वास लिइएको छ ।

औषधिको बिक्री प्रवर्द्धनमा देखिएका अनैतिक कृयाकलापका कारण धेरै विकासोन्मुख देशहरुमा औषधिको समुचित प्रयोगमा समस्याहरु वृद्धि भएका तथ्यहरु छन् । यस सम्बन्धमा औषधि व्यवस्था विभाग र विश्व स्वास्थ्य संगठनको सहयोगमा ग्राजुएट फर्मासिष्ट एसोसिएसन नेपालले एक सर्भेक्षण अध्ययन गरेको थियो । सो अध्ययनको नतिजा माघ २०, २०६३ मा एक गोष्ठीमा प्रस्तुत गरिएको थियो । सो नतिजा प्रस्तुतिकरणका बेला औषधिको बिक्री प्रवर्द्धन निर्देशिका लागु गर्नु पर्ने आवश्यकताको पहिचान गरियो । सो एसोशएसनले विश्व स्वास्थ्य संगठनको Ethical Criteria for Medicinal Drug Promotion, 1988 र International Federation of Pharmaceutical Manufacturers and Associations को Code of Pharmaceutical Marketing Practices, 2006 का आधारमा औषधि बिक्री प्रवर्द्धन निर्देशिका तर्जुमा गऱ्यो । सरोकारवालाहरुले त्यस मस्यौदामा छलफल गरी सुझाव पेश गर्नुका साथै मस्यौदालाई परिमार्जन गर्न औषधि व्यवस्था विभागको संयोजकत्वमा एक समिति गठन गऱ्यो ।

औषधि बिक्री प्रवर्द्धन निर्देशिका तर्जुमा समितिले परिमार्जन गरेको मस्यौदालाई विभागले सम्पादन गरी प्रतिकृयाकालागि पुन: सरोकारवालालाई पठाइयो । प्राप्त सुझावहरुका महत्वपूर्ण कुरा समेटी २०६४ आषाढ ३२ मा औषधि बिक्री प्रवर्द्धन निर्देशिका जारी गरियो । यो निर्देशिकाको कार्यान्वयन पक्षको अनुभव पछि परिमार्जन गरी औषधि ऐन २०३५ को दफा ४० र औषधि दर्ता नियमावली २०३८ को नियम ११ अन्तर्गत औषधि बिक्री प्रवर्द्धन संहिता जारी गरिनेछ ।

औषधि बिक्री प्रवर्द्धन निर्देशिका, २०६४

औषधिको समुचित प्रयोगबाट जनताको स्वास्थ्यस्तरमा सुधार ल्याउनका लागि औषधिको नैतिक बिक्री प्रवर्द्धन गर्न र अनैतिक बिक्री प्रवर्द्धनलाई दुरुत्साहित गर्न औषधि व्यवस्था विभागले यो निर्देशिका बनाई जारी गरेकोछ।

परिच्छेद-१
प्रारम्भिक

१. **संक्षिप्त नाम र प्रारम्भ:** (१) यस निर्देशिकाको नाम औषधि बिक्री प्रवर्द्धन निर्देशिका, २०६४ रहेको छ।

(२) यो निर्देशिका तत्काल प्रारम्भ हुनेछ।

२. **परिभाषा:** विषय वा प्रसंगले अर्को अर्थ नलागेमा यस निर्देशिकामा :-

(१) मन्त्रालय भन्नाले स्वास्थ्य तथा जनसंख्या मन्त्रालय सम्झनु पर्छ।

(२) विभाग भन्नाले औषधि व्यवस्था विभागलाई सम्झनु पर्छ।

(३) चिकित्सक भन्नाले चिकित्साशास्त्रमा कम्तीमा स्नातक भई सम्बन्धित परिषद्मा दर्ता भएको व्यक्ति सम्झनु पर्छ।

(४) स्वास्थ्यकर्मी भन्नाले स्वास्थ्य सेवा प्रदान गर्ने र सम्बन्धित परिषद्मा दर्ता भएको विभिन्न तहको व्यक्ति सम्झनु पर्छ। यस शब्दले चिकित्सक समेतलाई जनाउने छ।

परिच्छेद-२
निर्देशिकाको कार्यान्वयन

२.१ यो निर्देशिका नेपालमा बिक्री वितरण हुने सबै प्रणालीका सम्पूर्ण औषधि र औषधिका रुपमा प्रवर्द्धन गरिने स्वास्थ्यवर्धक वस्तुमा लागु हुनेछ। यो निर्देशिका औषधि उत्तोग (उत्पादक, थोक विक्रेता र खुद्रा विक्रेता समेत), प्रवर्द्धन उद्योग (विज्ञापन एजेन्सी, बजार अनुसन्धान संस्था आदि), औषधि प्रेस्काइब, डिस्पेन्स, आपूर्ति र वितरण गर्ने स्वास्थ्यकर्मी, विश्वविद्यालय र शैक्षिक संस्था, व्यवसायिक संघ संस्था, विरामी तथा उपभोक्ता समुह, व्यवसायिक र संचार क्षेत्र (चिकित्सा विज्ञानसित सम्बन्धित विषयका प्रकाशक, सम्पादक समेत) लाई लागु हुनेछ। यी सबै क्षेत्रले आ-आफ्ना दक्षता, कार्यक्षेत्र र दायित्वको परिधिभित्रका व्यवस्थाहरु अपनाउन प्रोत्साहित गरिनेछ। यो निर्देशिकामा आधारित भएर आफ्नो क्षेत्रसित सम्बन्धित औषधि बिक्री प्रवर्द्धन कार्यकालागि स्तर निर्धारण गरी लागु गर्न सकिनेछ। सबै सरोकारवालाले आ-आफ्नो क्षेत्रमा प्रभावकारी रुपमा लागु गरी अनुगमन समेत गर्नुपर्नेछ।

परिच्छेद-३
बिक्री प्रवर्द्धन

३.१ यस निर्देशिकामा प्रवर्द्धन या बिक्री प्रवर्द्धन भन्नाले औषधि उत्पादक वा वितरकबाट गरिने औषधिको प्रेस्क्रीप्सन, आपूर्ति, खरिद वा प्रयोगमा वृद्धि गराउन प्रभावित गर्ने वा सूचनामूलक गतिविधिलाई जनाउँछ ।

३.२ कानूनी रुपमा उपलब्ध औषधिको मात्र बिक्री प्रवर्द्धन गर्न सकिने छ । प्रवर्द्धन गर्दा राष्ट्रिय औषधि नीति, औषधि ऐन र अन्तर्गतका नियमावलीहरु साथै आफ्नै स्वैच्छीक स्तर भएमा सो समेत पालना गर्नु पर्नेछ । प्रवर्द्धनका सन्दर्भमा उल्लेख गरिएका कुराहरु भरपर्दो, सहि, तथ्यमा आधारित, जानकारीमुलक, व्यवस्थित, अध्यावधिक, प्रमाणित गर्न सकिने र चित्त बुझ्दो भाषामा हुनुपर्दछ । भ्रम सिर्जना गर्ने वा प्रमाणित गर्न नसकिने कुरा वा जनस्वास्थ्यमा प्रतिकुल असर हुने किसिमले तथ्य लुकाइएको हुनु हुदैन । औषधिको उपयोगिता, नराम्रा असर, प्रयोग गर्न नहुने अवस्था र अपनाउनु पर्ने सावधानी आदि प्रष्ट र वैज्ञानिक तथ्यमा आधारित हुनुपर्दछ । सुरक्षित भन्ने शब्द प्रमाणित गर्न सकिने अवस्थामा मात्र प्रयोग गर्नुपर्दछ र तुलनात्मक प्रस्तुती पनि प्रमाण भएमा मात्र प्रस्तुत गर्नुपर्दछ । सहि कुरा लुकाउने अभिप्रायले प्रवर्द्धन सामग्री तयार गर्नुहुदैन ।

३.३ सार्वजनिक भइसकेका वैज्ञानिक तथ्यहरु चिकित्सक तथा सम्बन्धित व्यक्तिलाई माग अनुसार उपलब्ध गराउनु पर्दछ । चिकित्सक वा स्वास्थ्यकर्मी वा सेवा प्रदायक तथा विक्रेतालाई आर्थिक वा भौतिक प्रलोभन (बोनस, थप औषधि वा आर्थिक वा भौतिक उपहार सहितको प्रवर्द्धन कार्यक्रम समेत) दिई बिक्री प्रवर्द्धन गर्नुहुदैन र चिकित्सक, स्वास्थ्यकर्मी र विक्रेताले पनि यस्ता प्रलोभन स्वीकार गर्नुहुदैन ।

३.४ वैज्ञानिक वा शैक्षिक कृयाकलापलाई जानी जानी प्रवर्द्धन प्रयोजनकालागि प्रयोग गर्नु हुदैन ।

परिच्छेद-४
चिकित्सक तथा स्वास्थ्यकर्मीकालागि जानकारी

४.१ चिकित्सक तथा स्वास्थ्यकर्मीकालागि तयार गरिएको जानकारीको शब्द तथा चित्रहरु आधिकारिक वैज्ञानिक तथ्यहरुसित मेल खाने हुनुपर्दछ । यस्तो जानकारी प्रष्टसित पढ्न सकिने हुनुपर्दछ ।

४.२ बिक्री प्रवर्द्धनकालागि प्रयोग गरिने जानकारीमा वैज्ञानिक तथ्यमा आधारित सारांश हुनु आवश्यक छ । यस्ता जानकारीमा सामान्यत: अन्य आवश्यक जानकारीका साथ निम्न कुराहरु हुनुपर्दछ :

- सकृय तत्वको जेनेरिक नाम र व्यापारिक नाम
- सकृय तत्वको परिमाण
- सबै साधक पदार्थको नाम र प्रयोग गर्नुको प्रयोजन
- कुन रोगमा प्रयोग गर्न प्रमाणित भएको हो सो रोगको नाम
- औषधिको स्वरुप (डोसेज फर्म)
- अवांछीत असर र मुख्य नराम्रा असरहरु

- सावधानी, प्रयोग गर्न नहुने अवस्था र सतर्कता
- अन्य औषधि वा खाद्य पदार्थसित हुनसक्ने प्रमुख प्रतिकृया
- उत्पादक तथा आवश्यक भए वितरकको नाम
- वैज्ञानिक सन्दर्भ ग्रन्थहरुको नाम
- जानकारी तयार गरेको मिति

परिच्छेद-५
सर्वसाधारणकालागि जानकारी

५.१. सर्वसाधारणकालागि आवश्यक जानकारी औषधिको वट्टाभित्र राख्ने या छुट्टै दिने पुर्जाका रुपमा तयार गर्नु पर्दछ । यस्तो जानकारी फार्मेसीबाट प्रेस्कीप्सन विना वेच्न हुने औषधिकालागि उपलव्ध भएमा उपभोक्ताबाई औषधि प्रयोगका सम्वन्धमा समुचीत निर्णय गर्न महत मिल्दछ । यस्ता पुर्जाले उपभोक्ताको जानकारी प्राप्त गर्न चाहने जिज्ञासा पूर्ति गर्ने भएता पनि उपभोक्ताको स्वास्थ्य प्रतिको चासोको गलत फाइदा लिने गरी तयार गरेको हुनुहुदैन । वालवालिकाको लागि लक्षित स्वास्थ्य शिक्षाको उपयोगिता भएता पनि औषधि सम्वन्धि जानकारी तिनीहरु प्रति लक्षित हुनुहुदैन । प्रमाणित गर्न सकिने हदसम्म मात्र औषधिले रोग निको पर्ने, रोग लाग्नबाट वचाउन सक्ने, रोक थाम गर्न सक्ने वा साम्य पार्न सक्ने कुरा उल्लेख गर्नुपर्दछ । औषधि प्रयोग हुन सक्ने वा नसक्ने निस्चित अवस्था भएमा सो समेतको जानकारी दिनुपर्दछ ।

५.२. जानकारी सामान्यतया वोलचालको भाषामा तयार गरिएता पनि दिइएका जानकारी वैज्ञानिक तथ्यमा आधारित हुनु पर्दछ । डर या त्रास पैदा गर्ने भाषा प्रयोग गर्नु हुदैन ।

५.३ सर्वसाधारणलाई जानकारी दिंदा संचार माध्यमको छनोटप्रति पनि ध्यान दिनु पर्दछ । सर्वसाधारणलाई दिइने जानकारीमा हुनु पर्ने कुराको उदाहरण निम्न वमोजिम छ
- औषधिको जेनेरिक नाम
- औषधिको व्यापारिक नाम
- सो औषधि प्रयोग गर्न सकिने प्रमुख रोगहरु
- अपनाउनु पर्ने मुख्य सावधानी, प्रयोग गर्न नहुने अवस्था र चेतावनी
- औषधिको समुचित प्रयोगमा सहयोग पुग्ने अन्य जानकारी, जस्तै आयुर्वेदीक औषधिका हकमा अनुपान तथा सहपान ।
- औषधि उत्पादक (आवश्यक भए वितरक) को नाम र ठेगाना

५.४. औषधिको मुल्य र मुल्य परिवर्तन भएको अवस्थामा परिवर्तित मुल्यको जानकारी विभागलाई दिनुपर्दछ ।

परिच्छेद-६
विज्ञापन

६.१. प्रेस्कीप्सनमा मात्र बेच्न हुने औषधिको विज्ञापन छापा वा विद्युतिय माध्यमबाट सर्वसाधारणलाई लक्षित गरी गर्न पाइने छैन । वैज्ञानिक वा व्यवसायिक पत्रिकाको माध्यमबाट बजारमा उपलब्ध हुने औषधि, सोको स्वरुप (डोसेज फर्म) र मात्रा आदि बारे चिकित्सक तथा स्वास्थ्यकर्मीलाई जानकारी गराउन सकिनेछ ।

६.२. प्रेस्कीप्सन विना बेच्न सकिने औषधिको हकमा विज्ञापन गर्न अनुमति दिन सकिनेछ तर परिच्छेद ५ को परिधिमा रही विभागको अनुमति लिएर मात्र विज्ञापन गर्नुपर्नेछ ।

परिच्छेद-७
कम्पनीको प्रक्रिया र उत्तरदायित्व

७.१. औषधि उद्योगले यो निर्देशिकाको पूर्ण पालना गरी बिक्री प्रवर्द्धन गर्न र बिक्री प्रवर्द्धन सम्बन्धि गतिविधिको अनुगमन गर्न औषधि बिक्री प्रवर्द्धन सम्बन्धि संहिता र कार्यविधि तयार गर्नु पर्नेछ । विज्ञान तथा स्वास्थ्य सेवा सम्बन्धी शैक्षिक योग्यता र ज्ञान भएको कर्मचारीलाई बिक्री प्रवर्द्धन सम्बन्धी जानकारीलाई मान्यता दिन तोक्नुपर्दछ ।

७.२. सिलैमा औषधि दिने जगायत नगद वा जिन्सी उपहारको माध्यमबाट चिकित्सक वा स्वास्थ्यकर्मी वा औषधि विक्रेतालाई न लोभ्याउने नीति औषधि उद्योग तथा वितरकको हुनुपर्दछ ।

परिच्छेद-८
औषधि बिक्री प्रतिनिधि (मेडिकल रिप्रेजेन्टेटिभ)

८.१. मेडिकल रिप्रेजेन्टेटिभले स्वास्थ्यकर्मीको आंखामा आफ्नो कम्पनीकासाथै समस्टीगत रुपमा औषधि उद्योगको प्रतिनिधित्व गरेको हुन्छ । उद्योग र स्वाथ्य क्षेत्रका अन्य सरोकारवालाको बिचको प्रमुख सम्पर्क व्यक्तिका रुपमा मेडिकल रिप्रेजेन्टेटिभ रहेको हुन्छ । अत: मेडिकल रिप्रेजेन्टेटिभमा योग्य व्यक्ति मात्र छानिउन् र भर्ना होउन् भन्ने कुरामा आस्वस्त हुन उच्च स्तरियता अवलम्बन गर्नु पर्दछ । मेडिकल रिप्रेजेन्टेटिभ विज्ञान वा प्रविधिमा कम्तीमा स्नातक हुनु पर्दछ ।

८.२. आफ्नो जिम्मेवारीको बोध हुन र जिम्मेवारी अनुसार काम गर्न सक्षम हुनकालागि पूर्व निर्धारित पाठ्यक्रम र म्यानुअल अनुसार तालिम प्रदान गर्नु पर्दछ । नयां कर्मचारीका हकमा यस्तो

परिच्छेद-६
विज्ञापन

६.१. प्रेस्क्रीप्सनमा मात्र बेच्न हुने औषधिको विज्ञापन छापा वा विद्युतिय माध्यमबाट सर्वसाधारणलाई लक्षित गरी गर्न पाइने छैन । वैज्ञानिक वा व्यवसायिक पत्रिकाको माध्यमबाट बजारमा उपलब्ध हुने औषधि, सोको स्वरुप (डोसेज फर्म) र मात्रा आदि बारे चिकित्सक तथा स्वास्थ्यकर्मीलाई जानकारी गराउन सकिनेछ ।

६.२. प्रेस्क्रीप्सन विना बेच्न सकिने औषधिको हकमा विज्ञापन गर्न अनुमति दिन सकिनेछ तर परिच्छेद ५ को परिधिमा रही विभागको अनुमति लिएर मात्र विज्ञापन गर्नुपर्नेछ ।

परिच्छेद-७
कम्पनीको प्रकृया र उत्तरदायित्व

७.१. औषधि उद्योगले यो निर्देशिकाको पूर्ण पालना गरी बिक्री प्रवर्द्धन गर्न र बिक्री प्रवर्द्धन सम्बन्धि गतिविधिको अनुगमन गर्न औषधि बिक्री प्रवर्द्धन सम्बन्धि संहिता र कार्यविधि तयार गर्नु पर्नेछ । विज्ञान तथा स्वास्थ्य सेवा सम्बन्धी शैक्षिक योग्यता र ज्ञान भएको कर्मचारीलाई बिक्री प्रवर्द्धन सम्बन्धी जानकारीलाई मान्यता दिन तोक्नुपर्दछ ।

७.२. सिलैमा औषधि दिने जगायत नगद वा जिन्सी उपहारको माध्यमबाट चिकित्सक वा स्वास्थ्यकर्मी वा औषधि विक्रेतालाई न लोभ्याउने नीति औषधि उद्योग तथा वितरकको हुनुपर्दछ ।

परिच्छेद-८
औषधि बिक्री प्रतिनिधि (मेडिकल रिप्रेजेन्टेटिभ)

८.१. मेडिकल रिप्रेजेन्टेटिभले स्वास्थ्यकर्मीको आंखामा आफ्नो कम्पनीकासाथै समस्टीगत रुपमा औषधि उद्योगको प्रतिनिधित्व गरेको हुन्छ । उद्योग र स्वाथ्य क्षेत्रका अन्य सरोकारवालाको बिचको प्रमुख सम्पर्क व्यक्तिका रुपमा मेडिकल रिप्रेजेन्टेटिभ रहेको हुन्छ । अतः मेडिकल रिप्रेजेन्टेटिभमा योग्य व्यक्ति मात्र छानिउन् र भर्ना होउन् भन्ने कुरामा आश्वस्त हुन उच्च स्तरियता अवलम्बन गर्नु पर्दछ । मेडिकल रिप्रेजेन्टेटिभ विज्ञान वा प्रविधिमा कम्तीमा स्नातक हुनु पर्दछ ।

८.२. आफ्नो जिम्मेवारीको बोध हुन र जिम्मेवारी अनुसार काम गर्न सक्षम हुनकालागि पूर्व निर्धारित पाठ्यक्रम र म्यानुअल अनुसार तालिम प्रदान गर्नु पर्दछ । नयां कर्मचारीका हकमा यस्तो

तालिमले कम्पनीको उत्पादनका बारेमा वैज्ञानिक तथा प्राविधिक जानकारी दिनुका साथै यस निर्देशिकाले प्रतिपादित गरेको नैतिक सिद्धान्त र स्तरिय व्यवहारको ज्ञान प्राप्त गरेको बारे आस्वस्त गर्न सक्नु पर्दछ ।

८.३. कम्पनीले मेडिकल रिप्रेजेन्टेटिभकालागि पटक पटक पुनर्तजगी तालिमको आयोजना गर्नु पर्दछ । कम्पनीले मेडिकल रिप्रेजेन्टेटिभलाई अध्ययन तथा स्व-उन्नती सम्बन्धी कार्यक्रममा सहभागी हुन प्रेरित गर्नु पर्दछ ।

८.४. मेडिकल रिप्रेजेन्टेटिभले व्यवसायिक र नैतिक क्षेत्रमा उच्चतम स्तर प्रदर्शन गर्न सक्नु पर्दछ । मेडिकल रिप्रेजेन्टेटिभबाट आचार संहिताको ज्ञान र पूर्ण पालनाको अपेक्षा गरिन्छ ।

८.५. मेडिकल रिप्रेजेन्टेटिभले उत्पादनका बारेमा तथ्य र जानकारी बढाइ चढाइ नगरी प्रदान गर्नु पर्दछ । मेडिकल रिप्रेजेन्टेटिभले प्रदान गर्ने जानकारी सहि र पूर्ण हुनुका साथै सोझै या बुझाईबाट भ्रम सिर्जना गर्ने खालको हुनु हुदैन । यस्ता जानकारी वैज्ञानिक तथ्यमा आधारित हुनुका साथै कम्पनीको आधिकारिक जानकारी भन्दा फरक हुनु हुदैन ।

८.६. आचार संहिताको पालना र उत्पादनबारे जानकारी आदान प्रदान गर्ने काम सही रुपमा भईरहेको बारे आस्वस्त हुन कम्पनीको व्यवस्थापन पक्ष र मेडिकल रिप्रेजेन्टेटिभका बिच नियमित सहकार्य हुनुपर्दछ ।

८.७. मेडिकल रिप्रेजेन्टेटिभलाई आधारभूत तथा नियमित तालिम दिने अभिभारा कम्पनीले बहन गर्नु पर्दछ । साथै मेडिकल रिप्रेजेन्टेटिभको प्रस्तुती तथा गतिविधिकालागि समेत कम्पनीले उत्तरदायित्व बहन गर्नु पर्दछ ।

८.८. कुनै पनि अवस्थामा मेडिकल रिप्रेजेन्टेटिभले चिकित्सक वा स्वास्थ्यकर्मीलाई भेट्नकालागि शुल्क दिनुहुदैन । त्यस्तै चिकित्सक वा स्वास्थ्यकर्मी वा औषधि विक्रेतालाई प्रलोभन दिनुहुदैन । चिकित्सक वा स्वास्थ्यकर्मी वा औषधि विक्रेताले पनि मेडिकल रिप्रेजेन्टेटिभबाट यस्तो अपेक्षा गर्नुहुदैन । अनावश्यक बिक्री प्रवर्द्धनलाई प्रोत्साहन नगर्नकालागि मेडिकल रिप्रेजेन्टेटिभको पारिश्रमिकको मुख्य भाग औषधिको बिक्रीसित सोझै आवद्ध हुनुहुदैन ।

८.९ नेपालमा आफ्नो उत्पादन बिक्री वितरण गर्ने विदेशी कम्पनीले नेपालमा आफ्नै कार्यालय स्थापना गर्नु पर्नेछ अथवा बिक्री प्रवर्द्धन र मेडिकल रिप्रेजेन्टेटिभको जिम्मेवारी नेपाली पैठारीकर्तालाई दिनु पर्दछ । बिक्री प्रवर्द्धन प्रमुखको नाम विभागलाई दिनु पर्दछ र प्रमुख परिवर्तन भएमा पनि विभागलाई जानकारी दिनु पर्दछ ।

परिच्छेद-९
बिक्री प्रवर्द्धनकालागि निःशुल्क औषधिको नमूना

९.१ चिकित्सकबाट माग भएमा दर्तामा रहेका औषधिको नुमना सामान्य परिमाणमा चिकित्सकलाई उपलब्ध गराउन सकिनेछ । यस्ता औषधिमा "Physician's sample" भनी उल्लेख हुनुकासाथै मुल्य अंकित हुनु हुँदैन । यस्ता औषधिको वितरणको अभिलेख राख्नुपर्दछ ।

परिच्छेद-१०
सम्मेलन तथा अन्य वैज्ञानिक बैठकहरु

१०.१. औषधि उद्योगले आयोजना गरेको वा प्रायोजन गरेको सभा, सम्मेलन र अन्य प्रवर्द्धनात्मक वैज्ञानिक तथा व्यवसायीक सम्मेलनहरुको उद्देश्य स्वास्थ्यकर्मीलाई उत्पादनकाबारेमा जानकारी दिनु वा वैज्ञानिक र शैक्षिक जानकारी दिनकालागि हुनु पर्दछ । वैज्ञानिक या व्यवसायीक संघ संस्थाले आयोजना गर्नाले यस्ता सभा, सम्मेलनको शैक्षिक महत्व अभिवृद्धि हुने गर्दछ ।

१०.२. औषधि उत्पादक वा वितरकले प्रायोजन गर्ने गोष्ठीका बारेमा गोष्ठी आयोजना गर्न भन्दा पहिले नै, साथै गोष्ठी सम्बन्धि प्रकाशनमा समेत उल्लेख हुनु पर्नेछ । प्रकाशनमा गोष्ठीमा भएको प्रस्तुती र छलफल बारे सही जानकारी दिनु पर्दछ । यस्ता गोष्ठीमा स्वास्थ्य क्षेत्रका सहभागीहरुकालागि मनोरंजन, स्वागत सत्कार र उपहारहरु खर्चिलो हुनुहुदैन ।

१०.३. कम्पनीले स्वास्थ्यकर्मीकोलागि मनोरंजन गर्ने, विदा मनाउने वा सामाजिक गतिविधि अयोजना गर्ने या यस्तो कार्यक्रमको खर्च बेहोर्ने गर्नुहुदैन ।

परिच्छेद-११
प्रायोजन

११.१. औषधि उद्योगले स्वास्थ्यकर्मीलाई सभा सम्मेलन तथा वैज्ञानिक बैठकमा भाग लिनकालागि निम्न सर्तको अधिनमा रही प्रायोजन गर्न सक्नेछ :

- प्रायोजन केवल भ्रमण, बस्न, खान र दर्ता शुल्कको भूक्तानी गर्नमा मात्र सिमित हुनु पर्दछ ।
- स्वास्थ्यकर्मीको सम्मेलनमा भाग लिन खर्च भएको समयको पारिश्रमिक दिन हुने छैन । र
- यसरी गरेका प्रायोजन वापत कम्पनीको औषधि प्रेस्काइब गर्ने, प्रवर्द्धन गर्ने या प्रयोगकालागि सिफारिस गर्ने सर्त राख्न पाइने छैन ।

११.२. स्वस्थ्यकर्मीका साथ सभा सम्मेलनमा भाग लिन जाने अन्य व्यक्तिको कुनै खर्च कम्पनीले बेहोर्नु हुँदैन ।

११.३. सभा वा सम्मेलनमा कम्पनीकालागि श्रोत व्यक्ति वा वक्ताका रुपमा भाग लिंदा भ्रमण, बास र पकेट खर्च बाहेक लिखित करारका अधिनमा कम्पनीले उचित पारिश्रमिक दिन सक्नेछ।

११.४. नगद वा नगद सरह मुल्यवान वस्तु स्वास्थ्यकर्मीलाई दिन पाइने छैन । व्यक्तिगत प्रयोगका वस्तुहरु पनि स्वास्थ्यकर्मीलाई उपहारका रुपमा दिन हुने छैन ।

११.५. कम्पनीले स्वास्थ्यकर्मी वा संस्थालाई गर्ने व्यक्तिगत सहयोग पारदर्शी हुनु पर्दछ।

११.६. स्वास्थ्यकर्मी तथा सम्बन्धित प्रशासनिक कर्मचारीलाई स्वास्थ्य सेवा प्रदान गर्ने क्रममा प्रयोग हुने वस्तुहरु मुल्यवान नभएमा प्रवर्द्धन या सम्झनालागि दिन सकिनेछ।

११.७. स्वास्थ्य सेवा तथा विरामीको सेवाकालागि फाइदा जनक हुने भएमा चिकित्सासित सम्बन्धित वस्तु स्वास्थ्यकर्मीलाई निःशुल्क दिन सकिनेछ ।

परिच्छेद-१२
बिक्री वितरण भएका औषधिका बारेमा वैज्ञानिक अध्ययन, अनुगमन तथा जानकारी सार्वजनिक गर्ने प्रक्रिया

१२.१. औषधिको समुचित प्रयोगकालागि बिक्री वितरणमा रहेका औषधिको वैज्ञानिक अध्ययन महत्वपूर्ण हुन्छ । यस्ता अनुसन्धान गर्न आवश्यकता अनुसार विभाग वा / र नेपाल स्वास्थ्य अनुसन्धान परिषद्बाट अनुमति लिनु पर्दछ र यस्तो अनुसन्धान गर्न सम्बन्धित वैज्ञानिक वा नैतिक समितिबाट स्वीकृत भएको हुनु पर्दछ । यस्ता अनुसन्धानमा अन्तर्राष्ट्रिय वा क्षेत्रिय स्तरमा सहकार्य उपयोगी हुन सक्दछ । यस्तो अनुसन्धानको नतिजाको सारांश सम्बन्धित स्वास्थ्य अधिकारीलाई उपलब्ध गराउनु पर्दछ।

१२.२. बिक्री वितरण भएका औषधिको वैज्ञानिक अनुसन्धानबाई गलत तरिकाले बिक्री प्रवर्द्धनकालागि प्रयोग गर्न पाइने छैन ।

१२.३. औषधिबाट भएका हानी नोक्सानी तथा औषधिको नराम्रा असरहरु प्राथमिकताका साथ विभागका जानकारी गराउनु पर्नेछ।

परिच्छेद-१३
औषधिको प्याकिङ्ग र लेवल

१३.१. औषधिको समुचित प्रयोगकालागि उपयुक्त जानकारीको महत्व भएकोले प्याकीङ्ग र लेवलमा उल्लेख हुने जानकारी औषधि ऐन र नियमावली तथा विभागले तोके अनुसार हुनु पर्दछ । प्याकिङ्ग र लेवलमा भएका शब्द र चित्रहरु यस निर्देशिकामा उल्लेख भएका नैतिक पक्षसित मेल खाने हुनुपर्दछ ।

परिच्छेद-१४
विरामीकालागि जानकारी : (चट्टा भित्र राखे पुर्जा तथा पुस्तिका)

१४.१. औषधिको समुचित प्रयोगकालागि चाहिने जानकारी विरामीलाई पूर्जाका रुपमा उपलब्ध गराउनु पर्नेछ । यस्तो जानकारी सम्भव भएसम्म चिकित्सक वा स्वास्थ्यकर्मी तथा फर्मासिष्टबाट उपलब्ध गराउनु उपयुक्त हुन्छ । यदि यस्तो पूर्जा कानूनी रुपमा आवश्यक भएमा नियमानुसार विभागबाट स्वीकृत जानकारीमात्र राखिएको छ भन्नेबारे उत्पादक र पैठारीकर्ताले सुनिश्चित गर्नुपर्दछ । यस्तो पुर्जा बिक्री प्रवर्द्धनकालागि प्रयोग गरिएमा यस निर्देशिकामा भएका व्यवस्थाको पालना गरी गर्नुपर्दछ । विरामीकालागि लक्षित गरी तयार गरिएको जानकारी सरल भाषामा हुनुपर्दछ तर वैज्ञानिक तथ्यलाई सहि प्रकारले प्रस्तुत गर्नुपर्दछ ।

१४.२. प्याकिङ्ग भित्रको पूर्जा बाहेक पनि विरामी र उपभोक्ताकालागि जानकारीमुलक वस्तुहरु उपलब्ध गराउन उपयुक्त हुन्छ । तर यस्ता वस्तु पनि यो निर्देशिकाको परिधिभित्र रही तयार गर्नुपर्दछ ।

परिच्छेद-१५
अस्पतालको फार्मेसीमा औषधिको प्रवर्द्धन

१५.१ अस्पतालको ड्रग एन्ड थेराप्युटिक्स कमिटी वा यस्तै प्रकारको अन्य समितिले अस्पतालमा औषधि उद्योगले औषधिको प्रवर्द्धन गर्न संहिता तयार गर्नुपर्नेछ । औषधि उद्योग तथा मेडिकल रिप्रेजेन्टेटिभले यस्तो संहिताको पालना गर्नुपर्नेछ ।

परिच्छेद-१६
निर्देशिकाको कार्यान्वयन

यो निर्देशिका श्रावण १, २०६४ देखि कार्यान्वयन गरिनेछ । निर्देशिका कार्यान्वयनका क्रममा विभागले अनुगमन गर्नेछ । विभागले कार्यान्वयनकालागि प्रकृया, विधि र कार्यविधिहरु तयार गर्न सक्नेछ ।

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Guidelines on Ethical Promotion of Medicine, 2007

(Unofficial document; official in Nepali Version)

Introduction

The ethical promotion of medicine is vital to the pharmaceutical industry's mission of helping patients for better healthcare. Ethical promotion helps to ensure that healthcare professionals have access to information they need and that medicines are prescribed and used in a manner that provides the maximum healthcare benefit to patients. The pharmaceutical industry has an obligation and responsibility to provide accurate information about its products to healthcare professionals in order to establish a clear understanding of the appropriate use of medicines. Through the effective implementation of this guideline, it is expected to establish ethical promotional practices throughout the country in alignment with acceptable international norms and codes. There is evidence that drug utilisation problems are increasingly encountered in many developing countries due to unethical practices of medicine promotion. Recently Graduate Pharmacists' Association -Nepal (GPAN) has conducted a study on promotional practices in Nepalese pharmaceutical market in collaboration with DDA and World Health Organization (WHO). The findings were presented in a seminar on 20 Magh, 2063 (3 February, 2007). The study results indicated the need for implementation of guidelines on ethical promotion. GPAN developed the guideline, based on Ethical Criteria for Medicinal Drug Promotion (World Health Organization, Geneva 1988) and Code of Pharmaceutical Marketing Practices, (2006 Revision) (International Federation of Pharmaceutical Manufacturers Associations (IFPMA)). The stakeholders discussed on the guidelines and formed a committee to revise the
draft on the basis of the comments provided during discussion. Draft thus modified, with some editing from DDA, was sent again to stakeholders on 23 Jestha 2064 (6 June 2007) for further comment. The guideline is finalised after incorporating relevant comments received and has been issued from the department for implementation on 32 Asadh 2064 (16 July 2007). With some experience on implementation of the guideline, it will be approved as "Code on Sales Promotion of Medicine within Drug Registration Regulation, as per Clause 40 of the Drug Act 1978.

1. Objective

1.1 The objective of this guideline is to promote ethical promotion of medicine to support and encourage the improvement of healthcare through the rational use of medicine and discourage unethical practices.

2. Implementation of the Guideline

2.1 This guideline is applicable to all medicines sold in Nepalese market. It applies prescription and non-prescription medicines (over-the-counter drugs). They apply to all systems of medicine available in the country, and to any other product promoted as a medicine. The guideline is applicable to the pharmaceutical industry (manufacturers, distributors and retailers); the promotion industry (advertising agencies, market research organizations etc.); healthcare personnel involved in the prescription, dispensing, supply and distribution of medicines; universities and other teaching institutions; professional associations; patients and consumer groups; and the professional and general media (including publishers and editors of medical journals and related publications). All these are encouraged to use this Guideline as appropriate to their spheres of competence, activity and responsibility. They are also encouraged to take the Guideline into account in developing their own sets of ethical standards in their own field relating to ethical promotion of medicine. All these bodies should monitor and enforce their standards.

3. Promotion

3.1 In this guideline, "promotion" refers to all informational and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply, purchase and/or use of medicine.

3.2 Active promotion should take place only with respect to medicine legally available in the country. Promotion should be in keeping with National Drug Policy and in compliance with Drug Act and regulations, as well as with voluntary standards where they exist. All promotion-making claims concerning medicine should be reliable, accurate, truthful, informative, balanced, up-to-date, capable of substantiation and in good taste. They should not contain misleading or unverifiable statements or omissions likely to induce medically unjustifiable medicine use or to give rise to undue risks. Claims for therapeutic indications and conditions of use must be based on valid scientific evidence and include clear statements with respect to side effects, contraindications, and precautions. The word "safe" should only be used if properly qualified. Comparison of products should be factual, fair and capable of substantiation.
Promotional material should not be designed so as to disguise its real nature.
3.3 Scientific data in the public domain should be made available to prescribers and any other person entitled to receive it, on request, as appropriate to their requirements. Promotion in the form of financial or material benefits (including the deal, bonus and promotional schemes) should not be offered to or sought by health care practitioners and retailers to influence in the prescription or sale of medicine. Scientific and educational activities should not be deliberately used for promotional purposes.

3.5 Information to physicians and health-related professionals

3.5.1. The wording and illustrations in information to physicians and related health professionals should be fully consistent with the approved scientific data sheet for the medicine concerned or other source of information with similar content. The text should be fully legible.

3.5.1. Information that make a promotional claim should at least contain summary scientific information. Information should usually contain, among others:

The name(s) of the active ingredient(s) using either international non-proprietary names (INN) or the approved generic name of the drug; The brand name; Content of active ingredient(s) per dosage form or regimen; Name of all the excipients and their role in the dosage form; Approved therapeutic uses; Dosage form or regimen; Side-effects and major adverse drug reactions; Precautions, contra-indications and warnings; Major interactions; Name and address of manufacturer, and distributor, where applicable; Reference to scientific literature as appropriate. Date of production of the information;

3.6. Information to the general public

3.6.1. Information to the general public should be available as information leaflet or insert. Such information leaflet made available from the pharmacy should help people to make rational decisions on the use of over- the-counter medicines. While they should take account of people's legitimate desire for information regarding their health, they should not take undue advantage of people's concern for their health. While health education aimed at children is highly desirable, medicine information should not be directed at children. The information may claim that a drug can cure, prevent, or relieve an ailment only if this can be substantiated. They should also indicate, where applicable, appropriate limitations to the use of the medicine.

3.6.2. When lay language is used, the information should be consistent with the approved scientific data sheet or other legally determined scientific basis for approval. Language, which brings about fear or distress, should not be used. 3.6.3. The media employed should be considered when providing information to the general public. The following list serves as an illustration of the type of information:

The name(s) of the active ingredients(s) using either international non proprietary names (INN) or the approved generic name of the drug; The brand name; Major indication(s) for use; Major precautions, contra-indications and warnings; Other relevant information supporting rational use of medicine, including Anupana and Sahapana in case of Ayurvedic medicine;

3.6.4. Information on price to the consumer and change of price should be informed to DDA.

4. Advertisement

4.1. Prescriptive drugs should never be advertised in any form of printing or electronic media targeting the general public. However, the company can inform the prescribers about the introduction of their brand (including its strength and dosage forms) in the market in allied professional bulletins or technical publications.

4.2. The provision of advertisement could be relaxed for OTC drugs but the information to be given in the advertisement should follow the instructions given in clause 4.6 and the text of the advertisement to be approved from DDA before going to the media.

5. Company Procedures and Responsibilities

5.1 Pharmaceutical industries should develop a manual on promotion of medicine to ensure full compliance with this guideline and to review and monitor all of their promotional activities and materials. A designated company employee, with sufficient knowledge and appropriate scientific or healthcare qualifications should be responsible for approving all promotional communications.

5.2 Manufacturer and distributors should have policy not to provide any kind of inducement in cash or kind, including but not limited to, free medicines to prescribers or dispensers or retail pharmacy as a promotional practice.

6. Medical Representatives

6.1. Medical representatives of pharmaceutical industry represent both their company and the pharmaceutical industry as a whole in the eyes of healthcare practitioners. They are the main point of contact between the pharmaceutical industry and other partners in healthcare sector. For this reason, the industry should establish and maintain high standards in the recruitment and selection of medical representatives, to ensure that well-qualified people are hired. Medical representatives should be science or applied science graduates.

6.2. Supervised training must be provided as per company's training manual developed prior to the recruitment to enable the persons to become familiar with and carry out their responsibilities. This training will require new employees to acquire both technical and scientific information on company products, as well as knowledge of the ethical principles and standards of conduct set out in this guideline.

6.3. From time to time, the companies shall conduct refresher courses for medical representatives. Companies should also encourage all medical representatives to take courses of study and self-improvement.

6.4. Medical representatives must display the highest professional and ethical standards at all times. Medical representatives are expected to understand and abide by established codes of conduct.

Medical representatives must provide full and factual information on products, without misrepresentation or exaggeration. Medical representatives' statements must be accurate and complete; they should not be misleading, either directly or by implication. Their assertions must be scientific and should not vary in any way from the official product monograph.

6.6. Company management shall work with representatives on a regular basis to ensure appropriate information exchange occurs regarding code of conduct and information on products.

6.7. Employers are responsible for the basic and continuing training of their representatives. Employers should also be responsible for the statements and activities of their medical representatives.

6.8. Under no circumstances shall medical representatives pay a fee in order to gain access to a healthcare practitioner. They should not offer inducements to prescribers and dispensers. Prescribers and dispensers should not solicit such inducements. In order to avoid over-promotion, the main part of the remuneration of medical representatives should not be directly related to the volume of sales they generate.

6.9. The foreign companies exporting their products to Nepal should either open their office in Nepal or the importer is made responsible on their behalf. Name of the chief of the marketing of domestic as well as foreign companies must be provided to the DDA and any change of person should be notified as soon as possible.

7. Free Samples of Medicine for Promotional Purposes 7.1 Free samples of legally available medicine may be provided in modest quantities to prescribers, generally on request. Free samples normally should be labelled as "Physician's Sample" and price should not be printed on it. Record of distribution of such samples should be maintained.

8. Symposia and Other Scientific Meetings

8.1. The purpose and focus of all symposia, congresses and other promotional, scientific or professional meetings for healthcare professionals organised or sponsored by a pharmaceutical industry should be to inform healthcare professionals about products and/or to provide scientific or educational information. Their educational value may be enhanced if they are organized by scientific or professional bodies.

8.2. The fact of sponsorship by a pharmaceutical manufacturer or distributor should clearly be stated in advance, at the meeting and in any proceedings of the meeting. The proceedings should accurately reflect the presentations and discussions. Entertainment or other hospitality, and any gifts offered to members of the medical and allied professions, should be secondary to the main purpose of the meeting and should be kept to a modest level.

8.3. No stand-alone entertainment or other leisure or social activities should be provided or paid for by the industry or distributor.

Sponsorship

9.1 The pharmaceutical industry may sponsor healthcare professionals to attend symposia and other scientific meetings provided such sponsorship is in accordance with the following requirements:

• Sponsorship to healthcare professionals is limited to the payment of travel, meals, accommodation and registration fees; No payments are made to compensate healthcare professionals for time spent in attending the symposium; and Any sponsorship provided to individual healthcare professionals must not be conditional upon an obligation to prescribe, recommend or promote any pharmaceutical product.

9.2 Companies should not pay any costs associated with individuals accompanying invited healthcare professionals.

9.3 Payments of reasonable fees and reimbursement of out-of-pocket expenses, including travel and accommodation, may be provided to healthcare professionals who are providing genuine services as speakers or presenters on the basis of a written contract with the company at the symposium or meting.

9.4 Payments in cash or cash equivalents (such as gift certificate) must not be offered to healthcare professionals. Gifts for the personal benefit of healthcare professionals (including, but not limited to, music CDs, DVDs, electronic items etc) must not be provided or offered.

9.5 Any support provided to individual health practitioner or organization should be transparent.

9.6 Promotional aids or reminder items may be provided or offered to healthcare professionals and appropriate administrative staff, provided the gift is of minimal value and relevant to the practice of the healthcare professional.

9.7 Items of medical utility may be offered or provided free of charge provided that such items are beneficial to the provision of medical services and for patient care. 10. Post-Marketing Scientific Studies, Surveillance and Dissemination of Information 10.1 Post-marketing scientific studies for approved medicine are important to ensure their rational use. Approval for such research should be obtained from Nepal Health Research Council (NHRC) and/or Department of Drug Administration (DDA) where necessary and relevant scientific and ethical committees confirm the validity of the research. Inter-country and regional cooperation in such studies may be useful. Substantiated information on such studies should be reported to the appropriate national health authorities.

10.2 Post-marketing scientific studies and surveillance should not be misused as a disguised form of promotion.

10.3 Substantiated information on hazards associated with medicine or adverse drug reactions (ADR) should be reported to the DDA as a priority.

Packaging and Labelling

11.1 Appropriate information being important to ensure the rational use of medicine, all packaging and labelling material should provide information consistent with Drug Act and regulations and standards set by Department of Drug Administration. Any wording and illustration on the package and label should conform to the principles of ethical criteria enunciated in this guideline.

12. Information for Patients: Package Inserts, Leaflets and Booklets

12.1 Adequate information on the use of medicine should be made available to patients. Such information should be provided by physicians or pharmacists or health professionals whenever possible. When package inserts or leaflets are required by regulations, manufacturers or distributors should ensure that they reflect only the information that has been approved by DDA. If package inserts or leaflets are used for promotional purposes, they should comply with the ethical criteria enunciated in this guideline. The wording of the package inserts or leaflets, if prepared specifically for patients, should be in lay language on condition that the medical and scientific content is properly reflected.

12.2 In addition to approved package inserts and leaflets wherever available, the preparation and distribution of booklets and other informational material for patients and consumers should be encouraged as appropriate. Such material should also comply with the ethical criteria enunciated in this guideline.

13. Promotion at Hospital Pharmacies

13.1 Drug and Therapeutics Committee (DTC) or similar committee of the hospital should develop code for promotion of medicine by the pharmaceutical industries at the hospital. Pharmaceutical industries and medical representatives should abide by the code.

14. Implementation of the Guideline

This Guideline will be implemented from 1 Shravan, 2064 (17 July, 2007). DDA will monitor the implementation of this Guideline. DDA may develop procedures, processes and Standard Operating Procedures for monitoring the implementation.

Amoxicillin manufacturers in Nepal-

Aglowmed limited	Deurali-janta pharmaceuticals pvt. Ltd.
Alkem laboratories limited	Dingla pharmaceuticals (p) ltd
Apex pharmaceuticals pvt.ltd.	Eros pharma ltd
Asian pharmaceuticals pvt.ltd.	Florid laboratories pvt. Ltd.
Brown and burk pharmaceuticals p.ltd.	G.d.pharmaceuticals pvt.ltd.
Chemi drug industries pvt ltd	Hukum pharmaceuticals pvt. Ltd
Ctl pharmaceutical pvt. Ltd.	Indchemie health specialities p.ltd.
Everest pharmaceuticals pvt.ltd.	Lomus pharmaceuticals pvt. Ltd.
G.d.pharmaceuticals pvt.ltd	Mapra laboratories pvt. Ltd.
Hindustan medicine products	Medreich sterilab ltd., india
Lark laboratories (india) limited	Micro labs limited
Micro labs limited	National health care pvt.ltd.
National health care pvt.ltd	Nepal pharmaceuticals lab. Pvt. Ltd.
Pharmaceutical company of nepal	Pharmaceutical company of nepal
Royal drugs limited	Ranbaxy laboratories limited
Shiv pharmaceuticals laboratories pvt. Ltd.	Royal drugs limited
Alliance pharmaceutical pvt. Ltd.	S.r. drug laboratories pvt. Ltd.
Amie pharmaceuticals pvt ltd	Saga laboratories.
Aurobindo pharma ltd	Siddhartha pharmaceuticals pvt. Ltd.
Birat pharma lab pvt. Ltd	Simca laboratories pvt. Ltd.
Blue cross laboratories limited	Square pharmaceuticals limited
22.curex pharmaceuticals pvt.ltd	Unique pharmaceuticals (p) ltd.-
Dabur pharma limited	Unichem laboratories limited
Dci pharmaceutical p.ltd.	Time pharmaceuticals pvt. Ltd.
	The acme laboratories pvt. Ltd.
	Stallion laboratories pvt ltd

Ciprofloxacin manufacturers in Nepal-

Aglowmed limited
Albert david limited
Alembic limited, india
Alive pharmaceuticals pvt. Ltd

Alkem laboratories limited
Apex pharmaceuticals pvt.ltd.
Aristo pharmaceuticals ltd.
Asian pharmaceuticals pvt.ltd
Baxter (india) pvt. Ltd., alathur
Bayer pharmaceuticals ltd.
Birat pharma lab pvt. Ltd
Blue cross laboratories limited
Cadila health care limited
Centaur pharmaceuticals p.ltd.
Cipla limited
Concept pharmaceuticals (n) pvt. Ltd.
Ctl pharmaceutical pvt. Ltd.
Curex pharmaceuticals pvt.ltd
Dabur india limited
Deurali-janta pharmaceuticals pvt. Ltd.
Dingla pharmaceuticals (p) ltd
Dr. Reddy's laboratoris ltd
Emcure pharmaceuticals limited
Fdc limited
Fresenius kabi india ltd
G.d.pharmaceuticals pvt.ltd.
Hukum pharmaceuticals pvt. Ltd.
Indchemie health specialities p.ltd
Indoco remedies limited
Kamron laboratories limited
Lark laboratories (india) limited
Lincoln pharmaceuticls ltd.
Lomus pharmaceuticals pvt. Ltd.
Macleods pharmaceuticals ltd
Manoj pharmaceuticals works pvt.ltd.
Mapra laboratories pvt. Ltd.
Micro labs limited
National health care pvt.ltd.
Nepal pharmaceuticals lab. Pvt. Ltd.
Omnica laboratories pvt ltd
Ozone pharmaceuticals limited
Parenteral drugs (india) limited
Pharmaceutical company of nepal
Pharmaco industries pvt. Ltd
Quest pharmaceuticals pvt.ltd.
Ranbaxy laboratories limited.
Reliance formulation pvt. Ltd.
Royal drugs limited

. S.r. drug laboratories pvt. Ltd.
. Shiv pharmaceuticals laboratories pvt. Ltd.
. Simca laboratories pvt. Ltd.
. Square pharmaceuticals limited.
. Stallion laboratories pvt ltd
. The acme laboratories pvt. Ltd
. Time pharmaceuticals pvt. Ltd.
. Torrent pharmaceuticals limited
. Unique pharmaceuticals (p) ltd.
. Vijayadeep laboratories ltd.
. Xl laboratories pvt. Ltd.

Cefadroxil manufacturers in Nepal

Time pharmaceuticals pvt. Ltd
Stallion laboratories pvt ltd
Nepal pharmaceuticals lab. Pvt. Ltd.
National health care pvt.ltd.
Micro labs limited
Mapra laboratories pvt. Ltd.
Lupin limited
Hukum pharmaceuticals pvt. Ltd.
G.d.pharmaceuticals pvt.ltd.
Deurali-janta pharmaceuticals pvt. Ltd
Curex pharmaceuticals pvt.ltd.
Chemi drug industries pvt ltd.
Cadila pharmaceuticals limited
Blue cross laboratories limited
Birat pharma lab pvt. Ltd.
Aurobindo pharma ltd
Aristo pharmaceuticals ltd.
Apex pharmaceuticals pvt.ltd.
Alkem laboratories limited
Alive pharmaceuticals pvt. Ltd

Tables are based on the "List of List of Manufacture with product(s) including Ingredient" published by the DDA.

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