TDL.ORG TEXAS DIGITAL LIBRARY

Journal of Regulatory Science

http:\\journalofregulatoryscience.org

Journal of Regulatory Science 04 (2016) 18–20

Regulatory Science

Regulation of Pharmaceuticals in Developing Nations: A Case from Nepal

Bhupendra Kumar Poudel[a,b*], Itsuko Ishii[a,c]

[a]*Graduate School of Pharmaceutical Sciences, Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba 260-8675, Japan*
[b]*Department of Drug Administration (DDA), Kathmandu, Nepal*
[c]*Division of Pharmacy, Chiba University Hospital, 1-8-1 Inohana, Chuo-ku, Chiba 260-8677, Japan*

Abstract

Department of Drug Administration (DDA), medicine regulatory authority of Nepal, is aligned towards achieving Universal Health Coverage through the regulation of medicines, pharmacies, manufacturing facilities and medicine testing laboratories from its offices located in Kathmandu, Birgunj, Biratnagar and Nepalgunj and takes legal or administrative actions as appropriate. It has its own regulatory laboratory, National Medicines Laboratory for testing and analysis of medicines. Besides, DDA reports suspected ADR to Upshala Monitoring Centre, Sweden provides information on medicines and conducts regulatory trainings. Unlike medicine regulatory authorities of the developed world, DDA has not been able to fulfill many of the objectives. Even then, a mechanism of regulation of pharmaceuticals is functional and is dynamic as per national need.

Keywords: Medicine Regulatory Agency, Developing country, GMP

1. Introduction

Medicine regulatory agencies around the world bear the responsibility of evaluating whether the research data support the safety, efficacy and quality of a new product. Standards for filing and regulatory approval for medicines differ across them. For instance, US Food and Drug Administration (USFDA) regulates food and medicines in US while European Medicines Agency (EMA) regulates medicines through its decentralized body in EU. USFDA involves submission of Investigational New Drug Application, followed by submission of New Drug Application. The applications are then reviewed and approved only after the medicine's safety and efficacy data are found satisfactory. EU however establishes 4 different approval processes: Centralized, Decentralized, National and Mutual recognition procedures [1].

Unlike that of developed nations, in Nepal manufacturers and importers don't need to go through a rigorous clinical trial approval or preapproval screening as because the molecules that are registered will be with already established safety and efficacy data. Sometimes ago, Nepal was largely dependent on imported medicines, regulation of which was poor; therefore, Drugs Act was enacted in 1978, and subsequently Department of Drug Administration (DDA), its branch offices and medicine testing laboratories were established.

Ministry of Health and Population (MOHP) is responsible for national planning and coordination in the health sector and DDA, a wing of MOHP, is assigned responsibility to ensure pharmaceutical sector related objectives of Nepal Government [2]. DDA has three divisions, Inspection Division, Registration Division and Management Division, four offices in Kathmandu, Birgunj, Biratnagar, Nepalgunj and one medicine testing laboratory, National Medicines Laboratory (NML) [2]. Inspection Division inspects manufacturing facilities, pharmacies and private medicine testing laboratories; Registration Division provides licenses to manufacturing facilities, pharmacies and private medicine testing laboratories and NML tests the quality of medicines available in Nepalese market.

These days market share of domestic products is escalating (e.g. from 42% in July 2014 to 43% in July 2015) but then certain products like injectables, biotechnology products, vaccines, contraceptives are still imported [3, 4]. Unlike in the USFDA or EMA, the registration of these products is done only on the basis of submitted documents. However, DDA conducts risk and evidence based regulation through Good Regulatory Practice, online regulatory process and aims to achieve Universal Health Coverage by controlling risks to products and patients and promotes safety, rational use, access and legislative compliance.

As of July 2015, among the registered domestic pharmaceu-

*Corresponding author: Bhupendra Kumar Poudel, Tel: +9779841380139. E-mail address: poudel.bhupen@gmail.com, Address: Department of Drug Administration (DDA), Kathmandu, Nepal

tical manufacturers, 15.04% are domestic allopathic, 22.85% domestic veterinary and 68.86% are domestic ayurvedic manufacturers; of which, 68.62% of the allopathic, 1.37% of ayurvedic and 0.00% of veterinary manufacturers are found to comply with GMP requirements [4]. While among the registered foreign manufacturing facility, 48.21% of the allopathic, 78.78% of the Ayurvedic/Homeopathic/Unani and 91.67% of the Veterinary Companies are not Stringent Regulatory Authority (SRA) approved and hence require inspections of manufacturing facilities for GMP approval [4].

2. Legislative provisions

Regulatory authorities of different nations have different legislative provisions for regulation of pharmaceuticals. In Nepal, those provisions are Drugs Act 1978, Drugs Registration Rules 1981 (DRR), Drug Investigation and Inspection Rules 1983, Codes on Good Manufacturing Practice 2016 and Drug Standards Regulation 1986. Other provisions are Codes on Sales and Distribution of Drugs 2014, Drug Advisory Committee (DAC) Regulation 1980, National Drug Policy 1995, WHO Good Manufacturing Practice (GMP) Guidelines, and WHO Guidelines on Quality Control and Microbiology Laboratories [5–7]. All pharmaceutical registrations as per these legislative provisions are validated by DDA for two years initially and renewed annually based on analytical or inspection report, where applicable [8].

2.1. Regulatory Provision for Domestic and Foreign manufacturing facilities

An applicant of a domestic manufacturing site should submit detailed documents as per DRR, should get recommendation letter for establishment of layout and facility, then only should apply for marketing license along with documents as mentioned in DRR [7, 8].

For registration of foreign manufacturing facility, WHO-GMP certification and registration of wholesale is needed. If the manufacturer is neither approved by FDA nor by Stringent Regulatory Authority (SRA), on-site inspection for GMP compliance is necessary regulatory provision [7].

2.2. Regulatory Provision for allopathic and traditional medicines

For the registration of allopathic medicines, a notarized copy of Certificate of Pharmaceutical Products (CPP) as prescribed by WHO (in the case of import), BA/BE report of modified release dosage forms, clinical study report on safety and efficacy of new product, specification with quality control parameters, analytical reports, Summary of Product Characteristics (SPC) along with the application documents as mentioned in DRR is to be submitted. BA/BE studies for domestic manufacturers are not mandatory and as such, comparative dissolution profile with innovator product is also sufficient for product registration. For the traditional medicines, the registration process is not strict but then scientific study of safety and quality of those medicines is assessed prior to registration [7].

Medicines on special permit are also recommended for import by DDA in two cases: for specific patients (only against prescription) and for hospitals (only on recommendation by Medicines & Therapeutic Committee of hospitals). All donated medicines should fulfill Drug Donation Guidelines 2003. Such donation is accepted only on expressed need, should be relevant to disease pattern, labeled in English and should have shelf life of at least 1 year. Medicines banned and of inferior quality are not accepted as donation [9].

2.3. Regulatory provision for Pharmacies

The registration of pharmacies is done based on the submitted documents as prescribed in DRR. Provision of more than one pharmacist or pharmacy assistant or professional is mandatory in pharmacies operating 24 hours in hospitals or in vicinity of hospitals [7]. Pharmacies are required to follow Codes on Sales and Distribution of Drugs 2014 but unlike for pharmaceutical manufacturers and laboratories, no prior inspection of wholesales/retails is done for compliance to provisions.

3. Other Regulatory Activities

DDA, via VigiFlow, reports suspected Adverse Drug Reactions (ADRs) obtained from various hospitals to Upshala Monitoring Centre, Sweden. DDA, however, lacks pharmacovigilance assessment, unlike in medicine regulatory authority of developed world (eg USFDA's Adverse Event Reporting System, EMA's Pharmacovigilance and Risk Assessment Committee). It also provides training and medicine information, issues Certificate of Pharmaceutical Products (CPP) for export, issues advertisement permission for medicines, approves new analytical methods, scrutinizes scientific/clinical basis for registration of new combinations and provides clinical trial approval for medicines recommended by Nepal Health Research Council (NHRC) or other government agencies.

4. Discussion

Unlike competent regulatory authorities of developed world (e.g USFDA) that regulate food safety, dietary supplements, medical devices, blood transfusions, electromagnetic radiation emitting devices, cosmetics, animal food and feed, DDA only regulates medicines for human and veterinary use. The regulatory activity is also not stringent as in developed countries.

Many pharmaceutical manufacturers are not GMP compliant, but are given flexibility for registration. But then, they cannot bid government tenders and from 2016 onwards new manufacturers are required to follow GMP.

Further to improve compliance, manufacturers should develop laboratory information management system and provide regulatory documents to include laboratory data. For example, HPLC chromatograms should be included in the laboratory documentation from manufacturers prior to renewal of license. In the regulation of pharmaceuticals, contextual interventions like scrutinizing quality of active pharmaceutical ingredients

and excipients will help strengthening the pharmaceutical products quality from the very beginning. Besides, issues on drug-excipients compatibility, bioequivalence studies, process and analytical method validations are also important for ensuring the quality of medicines.

Since the registration of pharmacies is done only on the basis of submitted documents, the inspection of facilities prior to registration could be an alternative to ensure compliance. Further, issues of non-compliance to regulatory provisions and poor physical premises is to be addressed for improving the standards and quality of services by pharmacies distributed throughout the country[2, 10].

Stringent follow up inspections and testing of post marketed samples will help in ensuring quality of medicines available in Nepalese market.

In contrast to USFDA and EMA, unethical marketing practices like provision of incentives to prescribers, wholesalers or distributors, false and misleading advertisements of medicines, ignorance on clinical trial regulatory requirements, ineffective ADR reporting, availability of unregistered medicines and nutraceuticals, lack of proper mechanism of detecting SSFFCs among others are still issues that need to be addressed by DDA. Therefore, the legislative provisions for pharmaceuticals including developing hospital pharmacy services should be prioritized to improve quality of care[2, 11].

Besides, issues of misbranding and adulteration, post marketing safety surveillance, regulation of orphan drugs, registration and scrutiny of patents, warning letters, risk minimization action plans are prevalent in USFDA and EMA which are not given much attention by DDA.

Therefore, technology transfer, development of highly skilled human resources, enhancement of quality, traceability, transparency, curbing unhealthy marketing, prompt public hearing, and indicator based surveillance and reporting are factors that can enhance good governance in pharmaceutical regulation of developing nations like Nepal.

5. Conclusion

DDA is regulating pharmaceuticals available in Nepalese market. Stringent registration, improved regulation and follow up inspections as in developed nations are advisable for enhancing the regulation of pharmaceuticals.

6. Article Information

The article was received May the 30th, 2016, in revised form July the 30th, 2016 and available on-line September the 15th, 2016.

References

[1] N. U. Kashyap, V. Gupta, H. P. Raghunandan, Comparision of Drug Approval Process in United States and Europe, Journal of Pharmaceutical Sciences and Research 5(6) (2013) 131–136.

[2] B. K. Poudel, I. Ishii, B. Khakurel, Assesment of Regulatory Compliance in Selected Pharmacy Outlets of Nepal, Journal of Pharmaceutical Health Services Research 7 (2016) 31–36.

[3] Department of Drug Administration. Regulatory News Drug Bull Nepal, 2014; 26(1) 18-19.

[4] Department of Drug Administration. Regulatory News Drug Bull Nepal, 2015; 27(1) 8-9.

[5] Drugs Registration Rules 1981. Available online (Accessed 3 May 2016). URL http://apps.who.int/medicinedocs/documents/s18830en/s18830en.pdf

[6] Drugs Investigation and Inspection Rules 1983. Available online (Accessed 4 May 2016). URL http://www.lawcommission.gov.np/en/documents/2015/08/drug-investigation-and-inspection-rules-2040-1983.pdf

[7] Medicines Registration Guidance 2016. Available online (Accessed 7 May 2016). URL http://www.dda.gov.np/files/attachment1.pdf

[8] Drugs Act 1978. Available online (Accessed 27 April 2016). URL http://apps.who.int/medicinedocs/documents/s18829en/s18829en.pdf

[9] Department of Drug Administration. Guidelines for Drug Donation to Nepal, 2003.

[10] B. K. Poudel, I. Ishii, Assesment of Physical Premises of Selected Pharmacies of Nepal, Sage Open Medine 4 (2016) 1–5.

[11] B. K. Poudel, I. Ishii, Hospital Pharmacy Service in Developing Nations: The Case of Nepal, 2016. URL http://dx.doi.org/10.1016/j.sapharm.2016.05.046