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Review Article



Regulation of Medicines in Bhutan: Current Status, Challenges and Opportunities

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ABSTRACT

Medicines Regulatory Agencies (MRAs) are responsible for evaluation of quality, safety and efficacy of medicinal products before it is approved for consumption. The regulatory procedures, however, differs from one country to another. Medical products including vaccines, blood and blood products, diagnostics and medical devices are essential for healthcare delivery across the world. The Drug Regulatory Authority (DRA) is an independent national agency for regulation of medicinal products in Bhutan and reports to Bhutan Medicines Board (BMB), the highest policy making body for regulation of medicinal products in the country.

Medicines Act of the Kingdom of Bhutan is the legal tool for regulation of medicines in Bhutan. Medicinal products are regulated through premarketing and post-marketing control systems. All medicinal products available in the Bhutanese market are registered. DRA regulates all the medicinal products including vaccines, blood products and traditional medicines used for human and veterinary.

DRA is fully financed by the Government of Bhutan. Bhutan's medicines regulatory system has evolved over the last one decade. However, as the regulatory mandate continues to increase, DRA is faced with several challenges in terms of human resource, infrastructure and testing laboratory among others. There are also opportunities for the DRA to improve its regulatory capacities to ensure availability of quality and safe medicines for the public.

Understanding the current practice of medicines regulation in Bhutan can help identify gaps and existing opportunities for improving the regulatory capacity. This article documents the existing practices, challenges and opportunities for regulation of medicinal products in Bhutan.

Keywords: Medicines, Regulation, DRA, Registration, Regulatory function, Bhutan.

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1. Introduction

MRAs around the world are responsible for evaluation of quality, safety and efficacy of medicinal products before it is approved for consumption. The regulatory procedures, however, differs from one country to another (1). These differences can be due to varying stringency of the regulatory tools and expertise involved in the evaluation process. For example, US Food and Drug Administration (US FDA) regulates food and medicines in the US and European Medicines Agency regulates medicines through its decentralized body in European Union. US FDA approves the applications for Investigational New Drug Application and New Drug Application only after the medicine's safety and efficacy

data are reviewed and found satisfactory. EU however establishes four different approval processes namely centralized, decentralized, national and mutual recognition procedures (2).

Medical products including vaccines, blood and blood products, diagnostics and medical devices are vital for healthcare delivery across the world (3). Countries around the world are striving to improve access to quality, safe, efficacious and affordable medicines for better public health and patient care. Medicinal products are highly regulated due to their complex nature, critical effect and sometimes due to controversies arising from assessing their quality, safety, efficacy (4). Strong and effective regulatory systems are critical in ensuring the quality,

safety and efficacy of medicinal products besides for promotion of trade and socioeconomic advancement (5). It is imperative for all countries to have their own MRAs mandated to regulate medicinal products.

The DRA is the national agency responsible for regulation of medicinal products in Bhutan. Medicinal products are regulated through premarketing and post marketing control mechanisms. As a non-producing country, Bhutan imports medicines from India, Bangladesh, Thailand and other countries. Unlike in the developed nations, importers in Bhutan do not need to go through rigorous clinical trial approvals as only the medicinal products with established safety and efficacy data are registered. Ministry of Health (MoH) is responsible for the selection, quantification and procurement of medicines for use in the public health facilities. The World Health Organization (WHO) (6) reported that lack of functional and well-resourced MRAs impacts access to life-saving medicines

Understanding the current practice of medicines regulation in Bhutan can help to identify gaps and existing opportunities for improving the regulatory capacity. This article documents the existing practices, challenges and opportunities for regulation of medicinal products in Bhutan in terms of policy and legal basis for regulation; organizational structure and management systems; human resources and core functions of the DRA.

2. Current State of Medicines Regulation in Bhutan

According to WHO (7) the core function of MRAs includes marketing authorization, licensing and inspection of manufacturing premises, control of import and export; inspection of sale and distribution channels, product quality control and monitoring, pharmacovigilance, control of drug promotion and advertisement, and oversight of clinical trials on drugs. A comprehensive legal basis with appropriate governance mechanisms, adequate technical expertise, sustainable funding and monitoring and evaluation system to assess the performance is a must requisite for any MRAs. The legal

basis gives MRAs the power to function while the level of autonomy in executing its mandate, the appropriate structure for proper coordination of various regulatory activities, availability of financial and adequate human resources with required competency to carry out their duties, are prerequisites for effective medicines regulation (8).

DRA regulates all medicinal products used for both veterinary and human including vaccines, traditional medicines (gSo-ba Rig-pa medicine in Bhutanese term), health supplements and blood and blood products. Blood and blood products are regulated as medicines in Bhutan in line with the Blood and Blood Products Regulation of Bhutan although much has to be done in terms of ensuring the quality and safety of blood and blood products in the country (9). The medicines regulatory provisions are implemented across private and public health facilities.

All medicinal products imported into the country are registered with DRA. It is illegal to import medicines without getting registered first. Import authorization is required for importing medicines. The DRA issues technical authorizations for manufacturing, storage, sale and distribution of medicinal products in the country. The licensed premises for manufacturing, sale, distribution and storage of medicines are inspected for their compliance. Medicinal products once placed in the Bhutanese market are monitored for adverse reactions and product defects to prevent or reduce harm resulting from quality issues. Pharmacovigilance activities, drug testing and control of product advertisement and dissemination of drug safety information for the healthcare professionals and the general public forms a part of post-marketing surveillance.

As of May 2018, a total of 1882 medicinal products are registered with the DRA. 86% of registered medicines are allopathic medicines as shown in Figure 1. The numbers of manufacturers, wholesalers and retail pharmacies registered with DRA is shown in Figure 2.

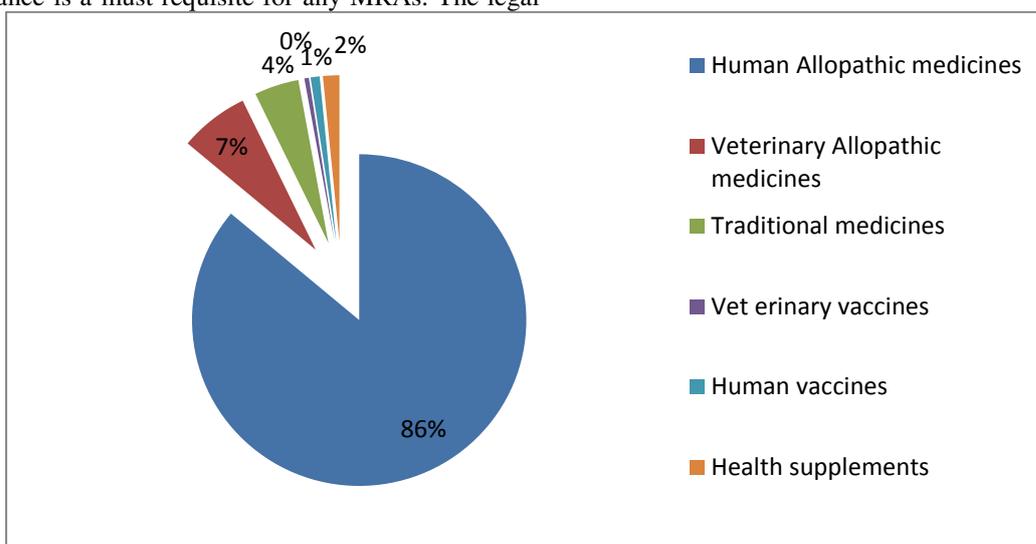


Figure 1. Different categories of medicinal products registered with DRA (10)

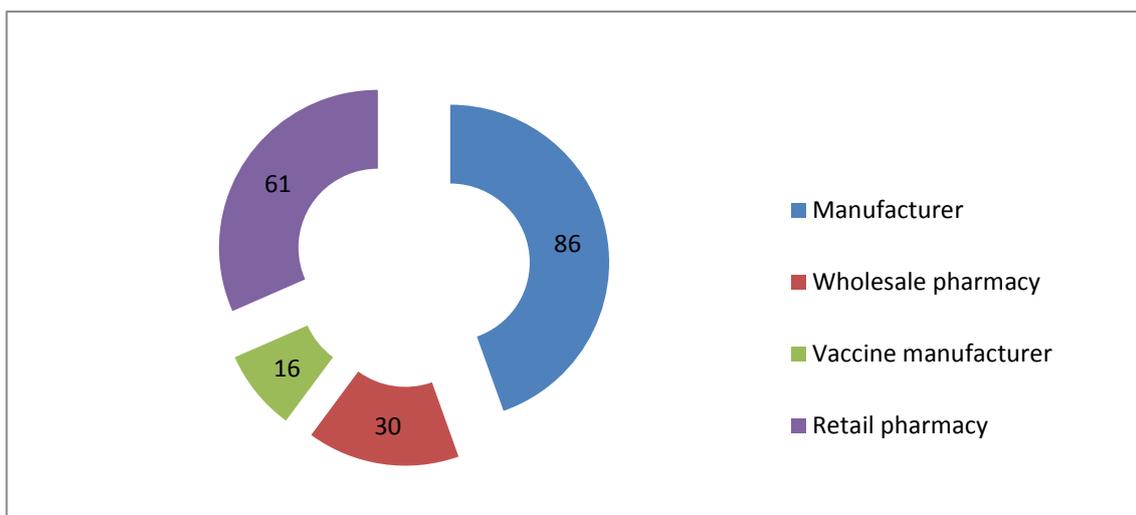


Figure 2. Number of manufacturers, retail and wholesale pharmacies registered with DRA (11)

2.1 Policies, Legislation and Management System

The DRA is an autonomous government agency governed by the BMB under the Chairmanship of the Minister for Health. BMB is the highest policy making body for the medicines regulation in the country and the DRA reports directly to BMB. The Drugs Technical Advisory Committee as a technical advisory body advises DRA on any technical matters related to regulation of medicinal products. Blood Technical Advisory Committee is another technical body that advises DRA on technical issues matters connected with regulation of blood and blood products in Bhutan.

DRA has three technical Divisions supported by a separate administration and finance section. Majority of the staffs working in the DRA are pharmacists. The DRA still lacks required number of technical staffs and the existing staffs are not adequately trained. A study conducted in Angola revealed critical understaffing in the Department of Pharmaceutical Inspection (12). Most of the developing countries are affected by lack of adequate human resource which is largely caused by low salaries, scarcity of pharmaceutical professionals and shortage of training institutions and lack of career structure and incentives.

The DRA is fully financed by the Royal Government of Bhutan. Similarly, MRAs in countries like Zanzibar, Rwanda, Burundi are also fully funded by their governments (13). Certain nominal fees are charged for the regulatory services provided by the DRA in Bhutan. However, the revenues generated from the regulatory fees are deposited into the government account. It is also not legal to use the money generated in the process of regulating medicinal products.

Bhutan's National Drug Policy (14) outlines ensuring quality, safety and efficacy of medicinal products as one of its objectives. Medicines Act of the Kingdom of Bhutan 2003 is the mother document for all the regulations, standards, guidelines and regulatory frameworks developed for regulation of medicinal products. Bhutan Medicines Rules and Regulation has been revised two times so far,

one in 2008 and another in 2012. Blood and Blood Products Regulation of Bhutan set rules of procedure for regulating blood and blood products in the country. Regulatory frameworks are timely revised and kept up-to-date to encourage customer compliance to provide quality and safer medicines for the public.

2.2 Regulatory Functions of DRA

Registration of medicines is the core function of the DRA. Medicinal products are evaluated for quality, safety and efficacy following the defined standards (15) before they are approved for consumption. Product category specific guidelines are developed for evaluation of vaccines, biotechnology products, health supplements, test kits and veterinary medicines. Bhutan has adopted abridge registration route from 2012 which is applicable for WHO prequalified products and the products registered in any of the DRA identified MRAs. (16)

Bhutan introduced the expedited registration process from 2017 to increase the availability of medicinal products for public health as per the approval of the Bhutan Medicines Board (17). The normal time required for evaluation of medicinal dossiers and issuance of registration certificate in Bhutan is 30 working days (16). Lengthy registration time is one of the reasons for companies refusing to supply medicines to African countries (18). Manufacturing firms and premises for sale, storage and distribution of medicines are licensed by DRA after satisfying all the requirements. These premises are monitored and inspected to verify their compliances. Inspection reports showed that the compliance shown by these facilities has improved over the years.

Pharmacovigilance and drug safety are central to post marketing surveillance. Bhutan became a member to WHO International Drug Monitoring Program in 2014 (19). Adverse drug reactions reported by healthcare professionals are received and assessed using the set guideline (20). Drug safety information is disseminated in the form of newsletters, notifications and control of drug advertisements. A study done in Africa reported a low rate

of withdrawal of medicinal products due to adverse drug reactions in many African countries is attributed to regulatory capacity limitation (21). According to the WHO rapid alert system, circulation of substandard and falsified medical products in the African Region are increasing and surveys reported quality failure rates of up to 28% in some cases (22).

Quality control of medicinal products is very crucial to verify the products compliance with the specifications of market authorization. It also serves to deter fraudulent manufacturing and trading practice of medicines (7). Medicinal products are sampled, prioritized and sent for testing to laboratories outside Bhutan as DRA do not have dug testing laboratory. National Drug Testing Laboratory under the Ministry of Health is still at a growing stage and hence not fully functional.

3. Challenges and Opportunities

MRAs need to balance diverse types of demands including timely entry of quality, safe and efficacious products into the market and public safety which is not so easy especially in the resource limited countries (8, 23). The DRA in Bhutan also faces several challenges such as lack of drug testing laboratory, inadequate infrastructure and human resource capacity as the scope of regulatory activities continues to expand.

Porous border provides an easy access for entry of unregistered medicines into the country and the risks of counterfeited medicines are high. This is evident from the prevalence of unregistered products in the market. Regulation of traditional medicine and health supplements is another issue for the DRA. Evidence based regulatory decisions are becoming highly important as many new medicines are put onto the market every day. The DRA has to invest in developing the research capacities of the officials and encourage research activities in the area of medicines regulation and control.

There are also many gateways of opportunities for the DRA to improve its regulatory capacity. The DRA need to leverage on the well established MRAs for their expertise and standards for regulation of medicines as financial resources are scarce and human expertise inadequate in Bhutan to carry out all the regulatory activities. This reliance practice is lately seen in the African countries in which all the countries are harmonizing their regulatory provisions to avoid unnecessary duplication of regulatory work that has been done in another country (3). Similarly, Bhutan DRA can take maximum benefits from South East Asia Regional Network (SEARN) which had its first annual meeting in March 2018. In this way, the DRA can prioritize its limited resources in other important and crucial areas of drug regulation.

Digitization of regulatory services will ease and enhance registration of medicinal products by the companies. Studies reported that digitization of drug regulatory services are effective (8). The DRA has already few services made online from 2018. However, these e-services must be improved to ensure efficient service delivery and prevent corruption. Abridged registration or expedited review process for registration of medicinal products must be reviewed timely to understand its impact

on the quality versus availability of medicinal products in the country.

The DRA can collaborate with other law enforcement agencies like Bhutan Narcotics Control Agency, Bhutan Agriculture and Food Regulatory Authority, Department of Customs and other relevant stakeholders. The DRA must collaborate and capitalize on the expertise and capacities of these agencies. Quality Management System (QMS) is essential for any MRAs for efficient regulatory services. QMS was instituted in DRA in 2016. Proper implementation of QMS will help to realize the organizational dream of becoming a model regulatory authority.

4. Conclusion

Bhutan's medicines regulatory system has evolved over the decade. The mandate to ensure the quality, safety and efficacy of medicinal products is achieved through premarketing and post-marketing control of medicines. Regulation of medicinal products in a resource limited setting is a challenge but leveraging on the developed countries can help prioritize available limited resources for critical regulatory functions. DRA must collaborate with other law enforcement agencies in the country and take active role in the SEARN to derive maximum benefits from the network.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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