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The Drug Regulatory Affairs Professional (With an insight into the Albanian context)

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Abstract

The Drug Regulatory Affairs profession was born as a need of governments to ensure public health, to enable the drugs that reach patients to be safe, of good quality and efficient. With a history starting at the second half of the past century, it can be considered a relatively new profession. However, due to developments in the manufacture of drugs, the rising number of pharmaceutical companies and their global reach, the increased potential of the sector to bring income, the enforcement of multiplied, complex, regulatory norms, this profession has developed rapidly, occupying a prominent place, not infrequently even a key one, in various professional teams. To better understand this professional, its educational background, core competencies as well as role and responsibilities are thoroughly analyzed. The development and the importance it has reached up to now in our country is also a point discussed.

In a globalized world, where there is a high public concern for safe and effective medicines, regulatory compliance is increasingly becoming a trend of the future. Due to the primary mission of drug regulatory affairs professionals to safeguard public health, it is in the general interest that every stakeholder involved supports the empowerment of this profession.

Keywords: drug regulatory affairs, professional

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"To work without rules is the most tedious and difficult job in this world."

Alessandro Manzoni

INTRODUCTION

The Drug Regulatory Affairs (DRA) profession did obviously not exist in the world before drugs were regulated. In the USA, being referred to as the "gold standard" of drug quality, federal regulation of drugs began in 1848 with the entry into force of a law that regulated only imported products. Some of the first main revolutionary milestones of USA drug regulation, were:

- the signing by president Theodore Roosevelt of the Food and Drugs Act on 30 June 1906; the law prohibited interstate commerce of misbranded and adulterated foods, drinks and drugs, however, there were no requirements to submit information to the authorities before marketing;
- the passing by the Congress of the law of 25 June 1938 after the dramatic event of 1937, the death of 107 people, most of them children, from the sulfanilamide elixir, law that required manufacturers to file an application with the FDA showing the safety of the drug they claimed to market;
- its amendments of October 1962, after the tragedy of thalidomide in western Europe, through which before marketing the drug, companies no longer had to demonstrate only drug's safety, but also real evidence of its efficacy in the proposed indication; this evidence would consist of appropriate and well-controlled studies;
- making the package insert leaflet mandatory in 1970 for the first time, and so on (1).

A similar pathway was followed in Europe after the tragedy of thalidomide in the early 1960s, regulating the procedures and obligations of pharmaceutical companies before placing any medicinal product on the market.

This was the beginning of a new era, where drugs, in order to be marketed, had first to be registered by a state authority, a practice that still continues today.

The DRA profession was born hence as a need of governments to ensure public health, to enable the drugs that reach patients to be safe, of good quality and efficient. With a history of drug registration starting at the second half of the past century, it can be considered a relatively new profession. However, due to developments in the manufacture of medicinal products, the rising number of pharmaceutical companies and their global reach, the increased potential of the sector to bring income, the enforcement of multiplied, complex, regulatory norms, this profession has developed rapidly, occupying a prominent place, not infrequently even a key one, in various professional teams.

We find DRAs in the pharmaceutical industry, consultant companies, pharmaceutical distributors, affiliate offices, regulatory authorities, but also in the academic world. Based

on the importance it holds in the pharmaceutical sector, the number of employed professionals and the complexity of the tasks, the DRA professional in the pharmaceutical industry is mainly of reference in this paper.

Through the presentation of the DRA professional, the aim of this publication is to give a comprehensive overview of its key role throughout the drug lifecycle, to influence the perception of the pharma and academic community about this role and its multifactorial implications, and to provide the foundation for subsequent publications pertaining to regulatory science in the national scientific bulletins as it already happens in international journals.

METHODS

To better understand this professional, the extensive own experience of the author in the field has been the base for a clear description and thorough analyze of the DRA educational background, core competencies, role and responsibilities. Furthermore, a worldwide literature research has been conducted, critically selected and finally reviewed. In Europe, the available professional literature for DRAs is not extended. In Albania, publications on the topic are almost totally lacking, therefore the development and the importance that this profession has reached up to now in our country is also a point discussed.

RESULTS

Professional background

Professional background worldwide

Worldwide, DRAs come from different professional backgrounds. The majority have advanced degrees, mostly in a scientific field. Additionally, they commonly have experience in other careers before moving into Regulatory Affairs (2). In USA, Europe, India etc. there are several university degrees or certificate programs in Regulatory Affairs and related disciplines.

In Europe, four universities, those of Copenhagen, Basel, Hertfordshire and King's College, London have initiated a cooperation project to start a common European Master Program in Drug Regulatory affairs. A common program and syllabus will be implemented with contribution from representatives of universities, pharmaceutical companies, professional associations and different regulatory authorities in Europe (3).

There are three major international professional organizations, with membership opportunities, for DRA professionals:

- Drug Information Association, DIA, http://www.diahome.org
- The Regulatory Affairs Professionals Society, RAPS, http://www.raps.org
- The Organization for Professionals in Regulatory Affairs, TOPRA, http://www.topra.org

offering education and training, professional development and certification (2, 7, 8).

History and professional background in Albania

In Albania, the change of the political and economic system in the early 1990s brought significant developments in pharmaceutics. Until then, the drugs circulating in Albania were controlled, but not registered. The evaluation of drugs that would circulate in the country was done by a committee made up of doctors and pharmacists based on theoretical criteria and the experience of doctors (4). Even in the first years of democracy, there was a lack of an authentic pharmaceutical legislation. The regulation of pharmaceutical activity was done through the decisions of the Council of Ministers, orders and rules issued by the Ministry of Health (4).

In cooperation with international organizations such as the World Health Organization and the World Bank, the Ministry of Health drafted a modern pharmaceutical legislation, sanctioning the registration of drugs among other pharmaceutical activities. The registration of drugs became regulated therefore through the Law no. 7815 / 1994 "On Drugs". In the same year was established the Registration Sector at the National Drug Control Center (NDCC) (4,5).

Although the pre-market requirement for pharmaceutical companies to submit the registration dossiers to the NDCC was stated in the Order of the Minister of Health no.121, of 5.6.1995, outlining in a sense the beginning of the DRA profession in Albania, it was only the later Regulation "On the Registration of Medicinal products in the Republic of Albania" (hereinafter "Regulation"), that made it official specifying that the company applying for a Marketing Authorization had to authorize a person to submit the documentation to the NDCC.

Starting from 1994, the Law for Medicines in Albania has been approved every 10 years:

- Law no. 7815 / 1994 "On Drugs"
- Law no. 9323 / 2004 "On Drugs and Pharmaceutical Service"
- Law no. 105 / 2014 "On Drugs and Pharmaceutical Service"

with amendments between them, continuously expanding the object, field of activity and concepts, as well as detailing the requirements. Despite law improvement, in recent years, guidelines and other documents have been approved, such as: guideline for clinical trials, guideline for obtaining Marketing Authorization of homeopathic medicines, the list of OTC medicines, etc., making it more and more necessary not only the presence of regulatory professionals, but also the expansion of their technical-professional knowledge and the competences they cover.

The current Regulation, dated 8.4.2015, determines that the responsible person authorized by the company for the official communication with the National Agency of Drugs and Medical Devices, must have a university degree in

medicine, pharmacy, dentistry (6). The majority of pharmaceutical affiliate offices and pharmaceutical distributors have only one person employed for regulatory affairs, but there are also those structures with more extensive activity, such as the pharmaceutical industry, which have real regulatory sectors with several employees. These professionals are not subject to the obligation of the above point of the Regulation and their educational background remains at the choice of the employer. Typically, in all these years, this position has been held by newly graduates and preferentially pharmacists, who have had the trend of constancy in continuing this career, thus forming some of the first consolidated DRAs in Albania.

In our country, despite a scientific degree, master's type postgraduate qualifications or dedicated, professional courses and seminars on the topic are completely absent. Basic training is usually offered by mother companies, nevertheless, experience remains a key asset for all these professionals.

The competencies, responsibilities and role of the regulatory professional

These three components can be analyzed in the following contexts:

- competencies on a domain-based perspective;
- internal and external responsibilities;
- role during the lifespan of the drug.

Competencies on a domain-based perspective

The graphic below is an illustration of the seven knowledge domains in which a regulatory professional pursues professional competency and of their relationship. Leadership and Ethics are the foundational domains, providing the underpinning for professional success. The cross-functional domains, Business Acumen and Scientific and Health Concepts represent knowledge content that is broadly relevant to those employed as regulatory affairs professionals.

The technical domains, Product Development and Registration, Regulatory Framework and Strategy and Post approval/Post market, specify the competency needs that reflect the specialized responsibilities of regulatory affairs work (7).

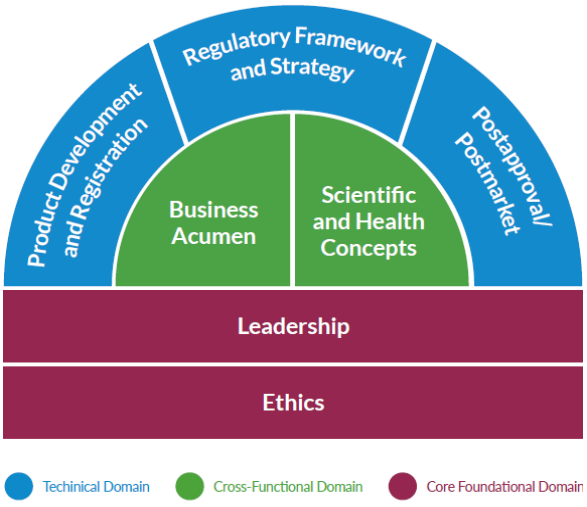

Figure 1. Regulatory competency framework (Source: https://www.raps.org)

Internal and external responsibilities

Internal responsibilities

Strategically, the main responsibility in this regard is finding the best way for the drugs of the company to reach the market safely and in the shortest possible time, while technically collecting information and data from other departments, necessary for the compilation of documentation as well as archiving of registration dossiers and keeping them in an updated status, archiving Marketing Authorizations and approved variations.

The regulatory affairs professional interprets legislative norms and guidelines, predicts their effects on day-to-day individual and group work, as well as proposes reasonable strategies to enable business success.

External responsibilities

The DRA officers are the interface between the pharmaceutical company and the regulatory authorities, those who take care that the documentation that accompanies the drug in all stages from development to post-marketing is according to well-defined rules, in order to achieve their registration and marketing, a function that ensures in parallel the company's regulatory compliance and safeguarding the health of patients.

They are constantly updated with new regulations, either local, international, or of specific company's export countries. These regulations are numerous, detailed, complex, in different languages, differing from each other and requesting challenging deadlines for implementation.

Role during the lifespan of the drug

In the context of the lifespan of the drug, the role of the DRA can be assessed at the pre-registration and post-registration stages (figure 2).

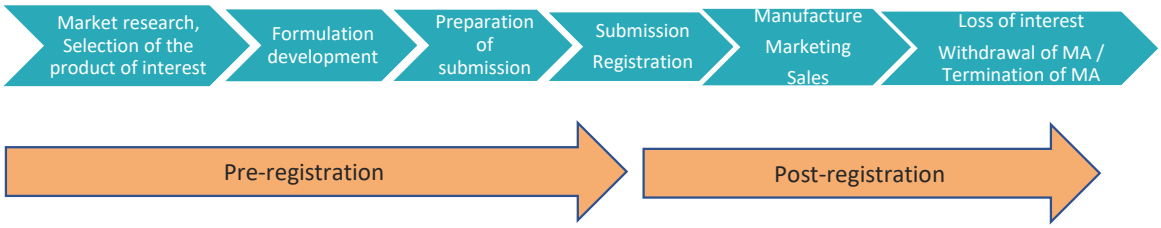

Figure 2. Lifespan of the generic drug

The responsibilities of the DRA professional at each stage are summarized in the table below (table 1) (9 – 13):

Table 1. Main responsibilities of DRA professional during the lifespan of the generic drug

Main DRA responsibilities prior to drug registration	**Main DRA responsibilities after drug registration**
• Identifies, based on current recommendations of authorities or professional literature, if there are problems with the expected use of the drug. • Identifies if there are problems for market access. • Proposes the regulatory strategy. • Advises cross-functional project teams, orienting them towards regulatory compliance. • Drafts, reviews and approves the core prescribing information. • Collects and collates information and data from other departments. • Prepares the submission for registration. • Submits the application and follows-up. • Compiles and writes reports for the authorities.	• Defines the regulatory strategy in case of changes to the information stated in the registration file. • Provides regulatory input and support during audits and inspections. • Approves information in promotional materials. • Cooperates with the pharmacovigilance department for post-market surveillance. • Submits request for withdrawal of the MA at the regulatory authority when there is such a decision. • Keeps up to date the regulatory database.
• Establishes and maintains a Good Regulatory Practice inside the company.	

Career pathway in Drug Regulatory Affairs

As in every other job, in DRA there are different work experience levels. Each of them comprises different regulatory competencies as presented in the tables below (table 2, 3).

Table 2. Work experience levels in drug regulatory affairs

Level	Job title	Work experience (years)
Entry (1)	Drug Regulatory Affairs Associate / Specialist	First 2
Intermediate (2)	Drug Regulatory Affairs Senior Associate / Specialist	2 - 4
Mid – level (2)	Drug Regulatory Affairs Manager	4 +
Advanced (3)	Drug Regulatory Affairs Director	10 - 15
Executive / Expert (4)	Vice president / Executive Director	Minimum 15

Table 3. Overview of the Regulatory Competency Framework for each level (Source: https: //www.raps.org)

	Level			
	1	2	3	4
Description	Professionals at this level acquire knowledge related to the regulation of healthcare products, including regulatory frameworks, requirements, legislation and processes. Key Skills: Basic project management, communications, interpersonal skills and the ability to understand scientific and health concepts.	Professionals at this level have a strong foundation in the regulatory profession, including scientific, legal, policy and regulatory process management. Key Skills: Well-developed regulatory technical knowledge and skills. Regulatory Affairs Certification (RAC) is targeted to professionals at this level.	Professionals at this level understand and translate regulatory, scientific, operational and business knowledge into effective implementation plans and strategy. Key Skills: Integrates technical knowledge with management and strategy. Models desirable competencies to colleagues.	Professionals at this level take on the role of the strategic regulatory lead while developing new approaches for achieving or defining business objectives. Strategic planning and working with other teams throughout the product lifecycle—both within and outside the individual's organization—are among the most important responsibilities. Key Skills: Navigates ambiguity and demonstrates agility and other executive characteristics. Possesses and communicates strong understanding of the requirements, opportunities, risks and alternatives for developing and maintaining products. Sets the tone for ethical standards of behavior.
Proficiency	Foundational/ Operational/ Novice	Intermediate	Advanced	Expert
Learning Objective(s)	Acquire knowledge	Comprehend and apply knowledge	Analyze and synthesize knowledge	Evaluate knowledge
Private Sector	• Coordinator • Specialist • Associate	• Senior Specialist • Supervisor • Junior Manager • Manager	• Senior Manager • Director (private sector) • Senior Director • Asst. VP • "Head of" Roles	• Senior Director • Vice President • Executive Director • CRO (private sector) • Head or Chief of Regulatory • Global Vice President • Corporate Officer

Skills required for the DRA position

Not everyone can excel in DRA. The types of tasks that are required, as a consequence of the competencies, are very wide (figure 3). The position needs the acumen to understand and interpret laws and regulations, negotiation skills to achieve goals in the shortest possible time, ability to work with exceptional volume under pressure of strict deadlines, ability to lead and motivate others, confidence to report truthfully to upper management, intrinsic desire to continuously learn and contribute, accuracy, attention to detail, and strong written and spoken communication. The mastery of several influent foreign languages is an added value for these professionals (14).

A DRA professional who correctly understands this role and takes upon oneself full responsibility of fulfilling it, is also the person who maintains the delicate balance between loyalty to the company and commitment to the success of its business on the one hand and the principles of professional ethics on the other. Accomplishing something like this is not easy. It requires good knowledge of the issues it covers, critical thinking, sound judgement, clear communication, determination, courage and honesty, traits that build a balanced personality.

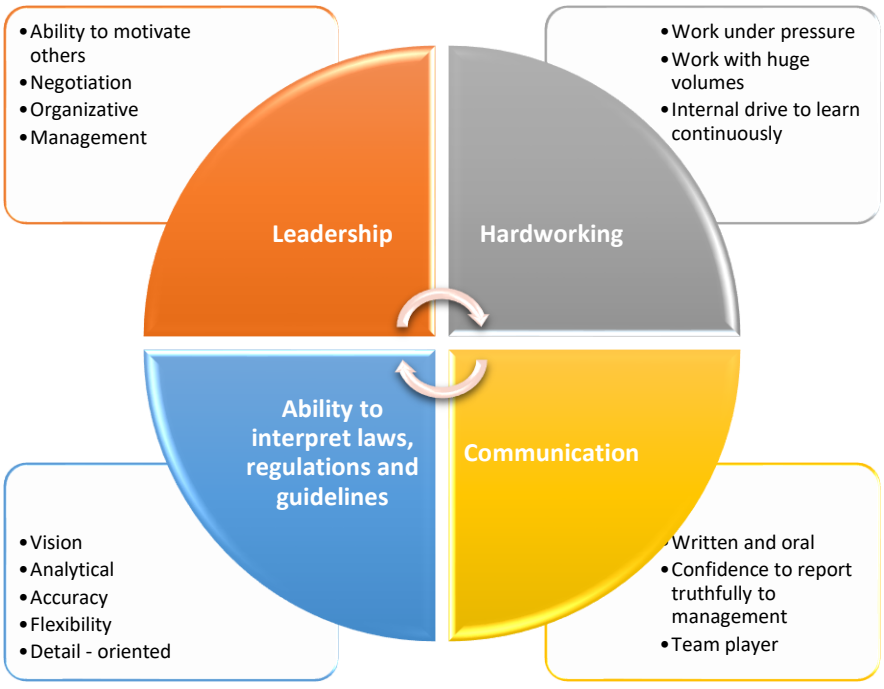

Figure 3. Skills required for the DRA position

Importance

The pharmaceutical industry operates in an increasingly complex regulatory landscape, and regulatory professionals are its vanguard. New scientific developments and technological advancements lead to further changes and these professionals are of great help for the industry to ensure its adaptation with the new situation. Without these valuable assets, improving, life-prolonging, life-promoting drugs would not make their way to market safely and in compliance with standards.

Ensuring that the company has in place qualified regulatory affairs personnel guarantees that its products are not subject to sanctions by the authorities, e.g. market recall, which would damage the company in several ways:

- the economic damage of the market recall and eventual free replacement of the product to the subjects where it was sold (distributor, pharmacy, hospital);
- the economic damage of not selling the recalled product;
- damage to the image of the company and its credibility with the authorities, associates and patients, the recovery of which would be difficult and prolonged in time.

The presence of such a department is a strong reference point for other departments, relieving them of the burden of maintaining regulatory compliance independently.

They help the company avoid problems such as inappropriate thinking, badly kept records or poor presentation of data (15).

Moreover, regulatory affairs officers contribute to the development of regulatory standards and tools.

DISCUSSION

Despite this importance, regulatory professionals are often silent heroes and their value is recognized only when problems arise, e.g. when the medicinal product fails to succeed in registration, a scenario that would cost a lot of money to the company. In a globalized world, where there is a high public concern for safe and effective medicines, regulatory compliance is increasingly becoming a trend of the future, as an essential tool for economic survival, especially of small or medium-sized companies.

Nevertheless, the DRA professional is not on the same scale everywhere. The position, role and competencies are directly related to several factors:

- the number and complexity of regulations in the country operating,
- their degree of execution,
- the professional expertise level of different stakeholders,
- general standards of that country, especially the economic status,
- as well as the size and experience of the hiring company.

In the Albanian context, due to the factors listed above which currently pose serious limitations, the role of the DRA professional has not yet reached the prestige it enjoys in other countries. It is often seen as a secondary role, the performance of which can be realized by other persons who do not have the relevant qualification or experience. Institutional support from the Authorities is compulsory to raise the awareness of the actors of the sector for solidifying this role.

Limitations

This article lacks a detailed information on the total number of DRA professionals in Albania and the specific number of pharmacists, doctors or dentists that currently cover this role. Such information was not made available from the competent Authority seeing it as a statistics for which they don't have specialized structures. This information gap constitutes the main limitation of this article.

CONCLUSIONS

Regulatory professionals are becoming increasingly important, exceptionally those individuals highly talented and skilled. Due to their primary mission to safeguard public health, it is therefore in the general interest that every stakeholder involved supports the empowerment of this profession.

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All claims expressed in this article are solely those of the author and do not necessarily represent those of her affiliated organization..

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