Universidade de Aveiro Secção Autónoma de Ciências da Saúde
2014

Liliana Marques Teixeira da Cruz

O PAPEL 'EMERGENTE' DO *MEDICAL SCIENCE LIAISON* NA INDÚSTRIA FARMACÊUTICA

THE 'EMERGING' ROLE OF MEDICAL SCIENCE LIAISON IN PHARMACEUTICAL INDUSTRY

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Relatório apresentado à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Medicina Farmacêutica, realizado sob a orientação científica do Doutor Luís Almeida, Professor Associado Convidado da Secção Autónoma de Ciências da Saúde da Universidade de Aveiro

On-the-job training report presented to the University of Aveiro to fulfill the requirements for the degree of Master in Pharmaceutical Medicine, conducted under the scientific guidance of Doctor Luís Almeida, Invited Associate Professor of the Autonomous Section of Health Science, University of Aveiro.

«*Let the future tell the truth, and evaluate each one according to its work and accomplishments. The present is theirs; the future, for which I have really worked, is mine*».
Nikola Tesla

O Júri

Presidente	Prof. Doutor Bruno Gago Professor Auxiliar da Universidade de Aveiro
Arguente	Prof. Doutor José Carlos Lopes Professor Auxiliar da Universidade de Aveiro
Orientador	Prof. Doutor José Luís de Almeida Professor Associado Convidado da Universidade de Aveiro

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Embora um relatório de estágio seja, pela sua finalidade académica, um trabalho individual, há contributos de natureza diversa que não podem e nem devem deixar de ser realçados. Por essa razão, desejo expressar os meus sinceros agradecimentos:

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Palavras-chave *Medical Science Liaison*, função, indústria farmacêutica, educação médica

Resumo O objectivo deste trabalho é a descrição de um *on-the-job training* como *Medical Scientific Liaison* numa Companhia biofarmacêutica multinacional, na área Cardiovascular (CV), e em apoio a uma marca líder de mercado em Portugal, com particular enfoque no desenvolvimento e implementação de programas de educação médica continuada e associada gestão de *Key Opinion Leaders* e *Opinion Leaders* regionais ou locais.

Keywords Medical Science Liaison, role, pharmaceutical industry, medical education.

Abstract The main goal of this report is to describe an on-the-job training as Medical Science Liaison in a multinational biopharmaceutical company, in Cardiovascular (CV) area, acting as support for a market-leading brand in Portugal, with particular focus on the development and implementation of continuing medical education programs and associated management of Key Opinion Leaders (KOLs) and regional Opinion Leaders (OPs).

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List of Abbreviations

CV	Cardiovascular
GPs	General Practitioners
HCP	Healthcare Professional
ISS	Investigator Sponsored Study
KOL	Key Opinion Leader
MAM	Medical Affairs Manager
MD	Medical Department
MP	Medical Plan
MSL	Medical Science Liaison
OP	Opinion Leader
P&T	Pharmacy and Therapeutics
SPC	Summary of Product Characteristics

1. Introduction

The present report describes my *on-the-job* training experience as a Medical Science Liaison at AstraZeneca and is submitted in partial fulfillment of the requirements for the Master's degree in Pharmaceutical Medicine. The internship was nine months long and started on 8th April, 2014.

Regarding structure and contents, the report is organized in six chapters:

The first chapter includes, apart from training objectives, a portrayal of AstraZeneca's structure, with a special focus on the Medical & Regulatory Affairs department.

Chapter two presents a brief description of new paradigms of organizational models in pharmaceutical industry, highlighting the most important changes occurred in the last few years and the impact of those across the most prominent world's markets.

Chapter three entails a description of Medical Affairs' activities in modern pharmaceutical companies and its approach on interfacing responsibilities and medical education.

Chapter four introduces the new emerging role of Medical Science Liaison, where its core responsibilities in science, communication, Key Opinion Leaders (KOLs) management, insights-driver and, more extensively, in medical education, underlining practice trends across pharmaceutical industry are presented.

The last chapters are reserved to detail the *on-the-job* training as Medical Science Liaison where, independently of other core activities related to the function, my role in managing of medical education projects are emphasized.

Additionally, in these final chapters, simultaneously as critical appraisal and conclusion, my expectations, achievements, major challenges and contributions during this experience as a trainee are also described.

2. New paradigms of pharmaceutical industry

There are different nature forces changing the way pharmaceutical industry will operate in the near future: pressure for lower cost medications, payer's mergers, healthcare reforms, uncertainty around delivering the promise of pipelines, extremely high costs associated to research and development, and regulatory demands are reshaping pharmaceutical industry's business model. In the United States of America and, similarly, in Europe, the increasing healthcare costs, the structural healthcare system reforms as well as heavier fiscal burdens are implying a thorough cost control by governmental authorities.[1]

These challenges have reinforced the need to demonstrate and communicate value beyond what was initially standard, based on the "orthodox" clinical development program and taking the classical "physicians stakeholders" into consideration only. Today, increasingly relevant players (e.g. payers, pharmacy & therapeutics (P&T) committee members) have an important decision role, and pharmaceutical companies have to be ready to communicate effectively with these stakeholders, using different and more sophisticated and complex evidence. [1] Also, as science evolves towards more specialized treatment options and personalized health care, new scientific concepts and technologies are at stake, and companies need to secure the right certified people and capabilities so that they can communicate product's value proposition. These changing forces have made clear to innovation-driven pharmaceutical companies the increasing relevance of the Medical Affairs teams and their evolving role.

Finally, as a result of regulatory demands for more transparency and higher public exposition of pharmaceutical industry, the way companies are engaging with Health Care Professionals (HCPs) and Public officials is being increasingly scrutinized, with physicians tending to refrain from being paid for participation as industry's speakers in sponsored events, fearing that it may affect their credibility and integrity, which underpins conflicts of interest matters and the need to properly address this as part of the daily business. [1] These regulatory pressures that ask for more transparency regarding access to patient data, and ethical interactions with HCPs and third parties, have also led pharmaceutical industry to create stricter compliance procedures, with a particular focus on Medical Affairs, due to its critical role in dissemination of data and external interfacing. [1]

3. Medical Affairs in modern pharmaceutical companies

In the recent past, the majority of strategic responsibilities resided on the commercial and marketing teams.[2] Over the last years, as a reaction to more restrictive regulatory demands and commitment to greater transparency, Medical Affairs emerged with a fully separated role from commercial departments, shifting their focus away from marketing support to KOLs interfacing and medical communication activities. Although marketing support traditionally represents a Medical Affair activity it is no longer considered its main focus, and much of the work is now included under KOL management, compliance activities and medical education. Progressively, Medical Affairs have taken a more strategic role within pharmaceutical companies, intervening not only in post-approval period, but in all drug lifecycle, including prelaunch phase, guarantying a stable and reliable foundation to its products commercialization. [3]

Currently, Medical Affairs include several medical activities, such as medical field teams (which include Medical Science Liaisons, who drive scientific exchange and deliver product information to medical community), post-launch clinical trials (including the planning and execution of phase IIIb/IV sponsored interventional and observational studies, investigator-initiated studies and pharmacoeconomic studies), medical information services, medical communications (including the support for peer-reviewed publications), medical education (including the identification of educational gaps about a disease, product or treatment, and implementation of external medical education programs according with the assessed needs, and the training of internal teams), medical strategic activities (including development of the medical plan for each product, collaborating cross-functionally with other departments to create a product life-cycle strategy). [1]

Examples of other Medical Affairs functions in a modern pharmaceutical company include: [3, 4]

- Ensure adherence to ethical standards, legal requirements and guidelines;
- Provide a medical perspective to product development;
- Provide medical insights to support marketed products commercial strategy throughout their life cycle;
- Management of KOLs and OPs;
- Response to HCPs medical queries regarding product safety or efficacy that is not addressed in a product's label;
- Support research initiatives outside labeled indications for marketed products;

- Work collaboratively and compliantly with different company departments (marketing, market access, regulatory affairs, training, legal) to ensure full medical support;
- Collect and report adverse events, and support to other pharmacovigilance activities;
- Promotional materials review and approval.

Medical Affairs may organize and structure themselves in different footprints. Many pharmaceutical companies choose to implement a centralized organization in which global teams implement and execute the strategies within global medical plans with a direct local market roll-out. In turn, other companies work with fully decentralized functions in which each country implement their own medical plans adapted to local market needs and characteristics. It is also possible to implement a hybrid structure and organization, with both centralized and decentralized characteristics, extracting each one's benefits. [5]

3.1. Industry and medical education

In post World War II period, in the 1950s and 1960s, there was an escalation of medical innovation and subsequent drug promotion on behalf of pharmaceutical industry. During these years, pharmaceutical companies developed broad intellectual and financial relationships with physicians, academic researchers and their institutions, relying on them to develop and maintain innovative research projects. In this partnership with physicians and academic researchers, pharmaceutical companies earned access to the forefront work being developed in the medical and biomedical research fields. Reciprocally, physicians and academic researchers gained access to fundamental research funds and sponsored medical education. The interactions between pharmaceutical companies, physicians, academic researchers, and their institutions developed mutual interests and shared needs. [6, 7]

Simultaneously, pharmaceutical industry realized the existence of a commercial opportunity in marketing its products to physicians. Companies felt that it was in their best interest to contribute to the spreading of new medical knowledge, while guaranteeing their visibility amongst HCPs. A partnership between medical community and pharmaceutical industry at physicians' medical education level emerged as a natural consequence of this interaction. Nevertheless, as industry sponsor for medical education grew, so did concerns about its commercial influence. Potentially seen as «incentives», these brought clear conflicts of interests. So, to protect patient's interests and to minimize pharmaceutical's commercial bias among medical community, strict regulatory

standards were progressively developed. Nowadays, sponsored medical education is highly regulated and follows high ethical standards to guaranty transparency and full separation between promotional and non-promotional contents. [6, 8]

Medical education can be defined as an activity « (...) *designed for, or performed by a physician for the purpose of acquiring, maintaining, or upgrading knowledge, skills, or attitudes to improve the quality of the healthcare that the physician dispenses to patients. (...) may be an individual or group action, based on a need or an interest, being a part of the learning process*». [9]

Medical education activities may take the form of a live presentation, internet-based presentation, videotape, teleconference, print medium, publications, Continuous Medical Education as scientific meetings (symposium, scientific updates, advisory boards, expert meetings, investigator meetings) or others, and may be certified by an accredited provider (academia, professional associations, medical education agencies).

These activities are strategically planned to support product and therapeutic area knowledge, and therefore establish the scientific basis for product differentiation. They also allow pharmaceutical companies:

- to build KOLs infrastructure (global, national, regional and local) through consulting, training and education;
- to publish and communicate key data and information;
- to present scientific and clinical information to target audience encouraging the improvement of patient outcomes;
- to use data, theory and experience to broaden the message and strengthen the product image.

Although Continuous Medical Education is crucial to enable healthcare providers to acquire new medical knowledge and skills after the completion of the academic training, in Portugal it has a voluntary character, unlike other European countries like France, Italy, and Germany where it is formally compulsory. [10, 11]

Despite the differences between Continuous Medical Education systems of European countries, healthcare authorities and medical associations are considered the main Continuous

Medical Education providers, leaving pharmaceutical industry sponsorships accounts for more than 50% of the programs.[11] In Portugal, Continuous Medical Education is largely driven by pharmaceutical industry. [12]

3.2. Ethics, compliance and regulatory standards

In the last years, incidents involving pharmaceutical industry and medical community highlighted the fragility of the prevailing regulatory framework, revealing obvious conflicts of interest in this interaction. These discussions brought to light public distrust regarding pharmaceutical industry and particularly its potential influence amongst physicians.

Ever since, pharmaceutical industry and governments made significant efforts to ensure compliant, ethical communication and transparent interactions with medical community.[13]

Concerning Medical Education, in Portugal, articles 150, 160 and 161 from Decree-Law nr. 176/2006 – *Estatuto do Medicamento* [14], article 19 from Decree-law nr. 330/90 – *Código da Publicidade* [15] and Deliberation nr. 044/CD/2208 [16,], establish the legal frame of the sponsorship of scientific and educational programs involving HCPs, having INFARMED as the regulatory authority. The deontological code from the local Pharmaceutical Association, APIFARMA - *Código Deontológico para as Práticas Promocionais da Indústria Farmacêutica e para as Interacções com os Profissionais de Saúde* in its articles 16 to 22 - supports in a more practical way the legal designations.[17]

Furthermore, each company has its own strict compliance guidelines, usually designated as conduct code, supported by different policies, guidance and standards, which are aligned with referent regulatory and legal requirements, ethical standards and company's values.

These documents have emerged to help industry to establish appropriate interaction with HCPs, and share a common perspective to protecting people's welfare and needs above commercial interests.

4. The role of Medical Science Liaison (MSL)

Most of major pharmaceutical companies have implemented field-based, customer facing medical support, composed by specialists with advanced training and degrees in life sciences that deliver a broad range of services to Opinion Leaders (OPs) and KOLs), clinical investigators and decision makers in healthcare institutions. As a consequence of their advanced academic training, and clinical and/or scientific background, field-based medical professionals are considered as more knowledgeable and verisimilar than sales representatives especially in what regards the exchange of scientific information. The role of field-based medical professionals has evolved over the years with the introduction of new and more complex products, and the increased sophistication of physicians' information requirements and education needs.[18]

These field-based specialists are commonly designed as Medical Science Liaisons. However each company structures the MSL role differently so there are several designations used for these positions: regional medical liaison, clinical advisor, scientific affairs liaison, scientific affairs manager, and regional medical associate, among others. [19, 20]

Regardless the designations of the MSL may be slightly different, the role definition shares common aspects:

The Medical Science Liaisons are «*specialists with advanced training and degrees in life sciences that are traditionally employed to educate healthcare professionals on a company's therapeutic capability in a given stage of a product's lifecycle*».[21]

«*Medical liaisons develop and enhance relationships with key opinion leaders within the health care community to contribute to improve outcomes for patients. Activities of medical liaisons include dissemination of medical information upon request, exploration of mutual clinical and scientific interests with health care providers, facilitation of professional education, and understanding the dynamics and unmet needs within therapeutic areas*».[22]

«*(…) field-based position whose main mission is to foster collaborative relationships with key opinion leaders (KOLs) and to facilitate the exchange of unbiased scientific information between the medical community and the company. (…) the major objective is to develop the professional relationships with the healthcare community, particularly KOLs, through peer to peer contact. (…) facilitate investigator-initiated clinical research proposals from approval until completion, presentation, and publication. (…) assist in the development, review, and follow-up of the clinical*

studies initiated within the relevant therapeutic area at the regional/local level. (…) lead regional/local clinical projects to ensure that all clinical trials are conducted in compliance with the International Conference of Harmonization Good Clinical Practice (ICH GCP) guidelines». [20]

While the common driver of the definition of MSL is KOLs management and scientific exchange, their scope of activities are varied, evolving and highly dependent on each company's perspective and strategy.[21]

4.1. Historical facts

Although considered as a new trend, first Medical Science Liaisons team was originally created in 1967 by Upjohn Company. It started with a small group of sales representatives with increased scientific background, and whose main objective was enhancing the company's image amongst researchers and KOLs, engaging them in peer-to-peer interactions, collecting insights on their needs and leveraging Upjohn products into research activities.[18]

Ever since, Medical Science Liaison role has been evolving in a way that current Medical Science Liaisons activities are impacting outcomes for patients in a widely scale. This is accomplished by dissemination of medical information, by searching mutual clinical and scientific interests with physicians, by encouraging medical education, and by apprehending the dynamics and unmet needs within therapeutic areas.[18, 23]

4.2. MSL function overview

Today, the MSL role comprises a wider scope of internal and external activities with different stakeholders. These activities are tailored according to companies' core business, pipeline, drug lifecycle phase, structure, organization, strategies and available resources.

Another relevant aspect of MSL role is related to geographical allocation of the teams, which may vary from small to large range geographies. The impact of large coverage territories implies high costs and time consuming travels. On the other hand, small regions coverage allows companies to optimize the MSL activities, both internally and externally.[24] Each company establishes its own criteria based on country specificities and KOLs' panel dimension.

The success of the MSL role depends upon its ability to accomplish the strategic objectives assigned on the medical plan while strictly adhering to all relevant compliance guidelines. As more

complex and demanding activities emerged, so did the necessity of an accurate MSL performance measurement able to evaluate competitive intelligence, insights and capable of demonstrating the real contributions of MSLs for company's internal value. [25]

Medical education, exploration of post-approval studies opportunities, KOL management and insight support to medical strategy, compose some of the different roles in which a MSL may be enrolled, and are described below.

4.2.1. Role in Medical Education

Medical education is considered a key activity of the MSL.[19] As they develop and enhance relationships with KOLs and other HCPs within medical community, MSLs promote scientific exchange, in-depth and cutting-edge information about products, presenting data in an objective, scientifically balanced, accurate and substantiated manner, ethical, truthful and free of promotional contents. Acting as KOLs' scientific partners, MSLs explore mutual clinical and scientific interests, identifying medical educational gaps and unmet needs, collecting these insights to build relevant and appropriate continuous medical education programs.[26] This interaction with HCPs promote advance in disease mechanisms and processes understanding and lastly, enhance patient access to optimal medical treatment and best use of it.

Interacting with the medical community in the context of medical education implies the following activities:

- Provide on-label information and deliver access to ongoing clinical trial information;[27]
- Respond to unsolicited requests for information about unapproved products or unapproved uses of approved products, which requires full transparency on the treatment's entire profile and a clear presentation of all risks and benefits, based on the latest status of medical and scientific research; [18]
- Implement appropriate continuous medical education activities by: targeting educational voids, identifying and engaging speakers, reviewing scientific data to prepare them; support several medical projects such as clinical trials, investigator-sponsored studies, non-interventional studies and scientific exchange meetings; provide recommendations for advisory board participants and present data. [21]

As result of their specialized role, KOLs state that MSLs are a very important resource for their practice, being able to discuss conceptually about overall disease state, efficacy issues and up to date research and science trends (Figure 1 – Importance of MSL Abilities and Attributes from KOLs' perspective). The results from a survey conducted to describe the MSL importance from a KOLs' perspective, show that the most valuable attributes of the MSL rely on their ability to act in an ethical manner, their awareness of specific therapeutic emergent products, their comprehensive knowledge about the disease state, their ability to address efficacy questions and to being up to date on current research trends. [21]

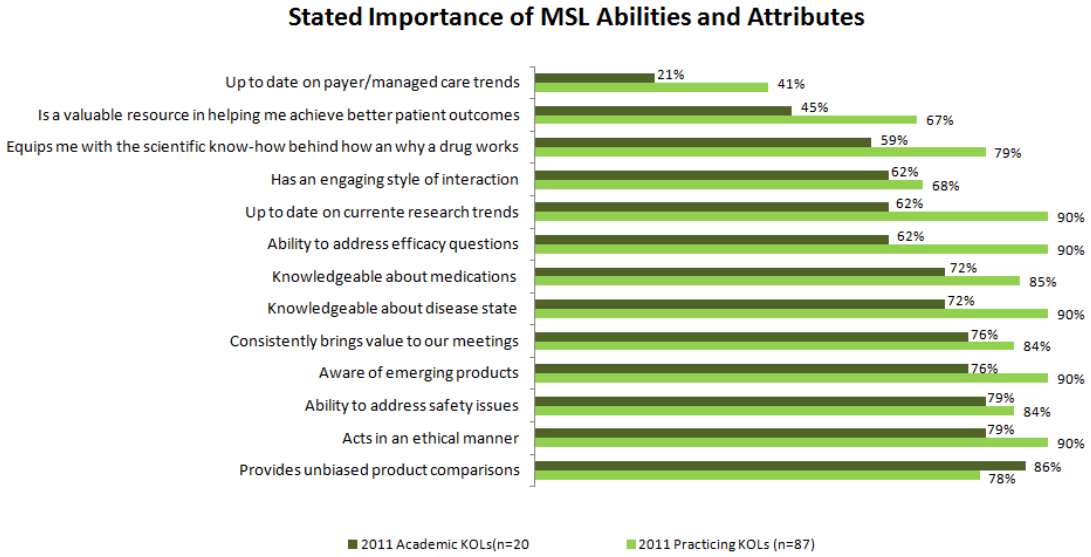

Figure 1 – Importance of MSL Abilities and Attributes from KOLs' perspective (adapted from Moss & Black, 2013)

The MSLs need to have a deep understanding of the KOLs circumstances, their challenges, needs and concerns. And it is based on this understanding that they can create value to KOLs practice, patients and institutions, being recognized as scientific drivers of valuable information that have significant impact on clinical practice and in patients lives. [21]

From companies' perspective, the interaction between MSLs, KOLs and other HCPs, in the context of medical education, brings important insights about medical community unmet needs and competitive intelligence that turns to be useful to better shape medical and brand plans, when integrated via Brand Teams or other cross-functional structure.

«*Currently, due to very restrictive policies governing the relationship between pharmaceutical industry and medical community, became mandatory the growth of medical affairs towards scientific excellence communication, guarantying high ethical standards between the parties.*

Among the many scientific tools that Medical Affairs make use of to sustain a highly ethical relationship with medical community, medical education projects are the "gold standard". Here the value of the MSL is unquestionable, being involved since early planning: giving very constructive scientific inputs - resulting from their expertise; streamlining with insights collected from KOLs tailoring the operationalization of projects, with respective micro-management of KOLs, as well as communicating scientific evidence contents back to physicians. We are living challenging times. And only companies with a well sustained Medical Affairs structure will survive to the scientific demands of medical community. Here, the MSL is certainly one of the values to success». Dr Rafael Fernandes, CV& Metabolic Medical Affairs Manager AstraZeneca

Bridging the gap of physicians' educational needs, the MSL reinforces the scientific bond between company and medical community and the shared purpose, which is putting patients on the center of everything they do.

4.2.2. Role in research

A potential expanding area for MSLs is clinical trials or research-related activities, which have been emerging as a focus for the future. These activities are intertwined with responsibilities in the support of investigator-initiated studies and company-sponsored trial. Furthermore, there are other types of studies supported by MSLs, which include health outcomes-related studies, health policy studies, and post-marketing studies. The role of MSLs within these activities goes from direct site management of studies supporting the start-up phases as well as recruitment, to problem-solving with clinical research organization (CRO), and also investigator meeting support (round table facilitation, data training presentations). [23]

Besides the support activities, the MSLs have also the responsibility of exploring new research needs for marketed products (phases IIIB and IV studies), which can include, in addition, the identification of potential investigators. In this context, MSLs assume the role of clinical catalysts.[25, 28]

Currently, the majority of MSLs are involved in clinical trials activities but only a small part of their daily work is related to these activities. This emergent involvement tends to grow as Medical Science Liaison support throughout all drug lifecycle continues to increase. [23]

4.2.3. Role in KOL management

The development and communication of breakthrough science and innovative compounds are core to the success of a innovation-driven company. To boost and optimize the strategic planning it is essential to build KOL and thought leader relationships.

KOLs and thought leaders are individuals who are considered references in research and in academic world, and are often seen as trendsetters and guides to their therapeutic areas by their peers.[19]

The engagement of these professionals starts, inevitably, with medical education. By delivering cutting-edge and valuable information, education and training, pharmaceutical companies grow as KOL's scientific partners. In turn, KOLs contribute with their insights to ensure that brand strategy maximizes the medical benefits for patients and physicians.

Moreover, engaging KOLs as speakers on behalf of the companies in medical education events has advantages not only to the companies in the dissemination of their information, but also to medical community, who gain access to unbiased, reliable, updated clinical and medical evidence.

The MSL embodies the formal contact between company and KOLs, and this contact is not only limited to scientific exchange but also to potential working collaborations with the company. This role is extended to many other physicians, with whom MSL interacts. And this particular aspect highlights the MSL role as an essential driver of medical education and a catalyst for product growth in the market.

The MSL may have a KOL proactive or reactive outreach strategy or approach. Interestingly, many companies have made a clear distinction between activities that can be considered proactive from the ones that are considered reactive, such as responding to unsolicited requests for information. While there is a consensus in separating these different concepts, the assumptions behind these two different approaches have a wide variation between companies.

Common to all visions is the fact that the MSL always acts in compliance with high ethical and deontological standards, and it is indispensable to avoid misunderstanding between the MSL role and the one of sales representatives.[19]

"Nowadays, MSLs are the human face of science for the pharmaceutical industry. They should be able to earn KOL's respect by managing human-to-human relationships with a scientific content on their speech. As such, MSLs are required to master skills in the areas of communication, science and human behavior in order to perform their job proficiently, thus giving a significant boost to their company's performance while bearing in mind that this business channel should maintain an arm's length distance from sales and marketing to prevent misperception between these different roles." Dr. Pedro Faber Branquinho, Senior MSL AstraZeneca

4.2.4. Role as internal thought leader

As stated before, Medical Affairs teams are assuming a more prominent role during early phases of drug development.[2] Within Medical Affair's teams, the MSLs provide important contributions across the product development spectrum; initially, prospecting and profiling KOLs and thought leaders for their companies, and exploring the therapeutic arena; subsequently, disseminating scientific data, facilitating clinical research and monitoring competitive landscape in their therapeutic specialty (Figure 2 – Contribution of MSLs across product lifecycle). [25]

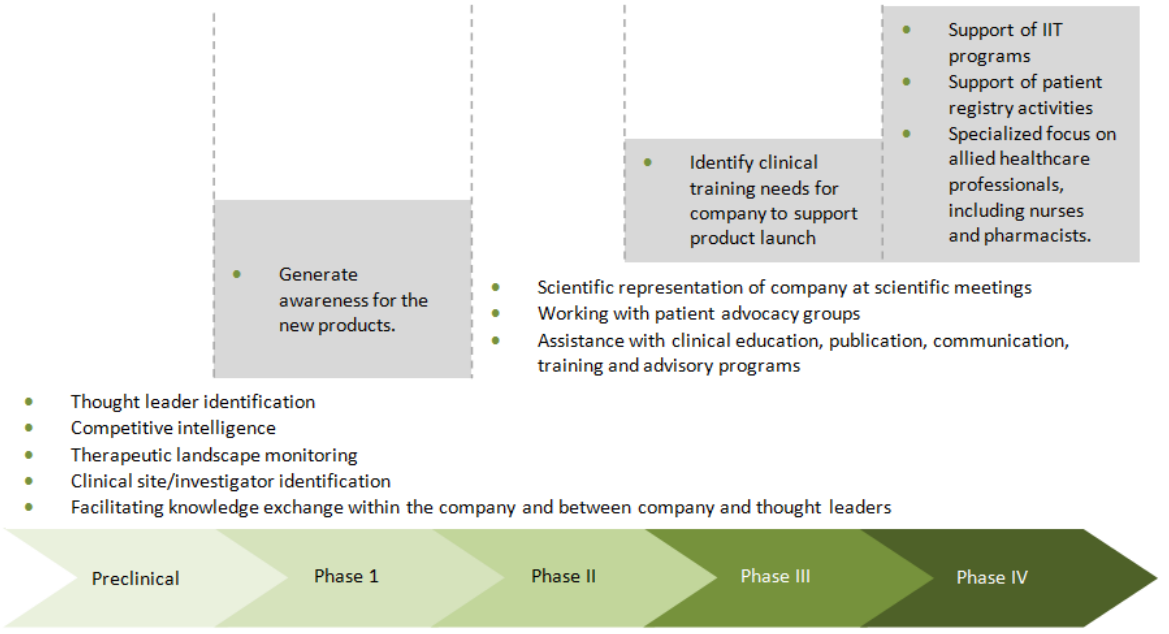

Figure 2 – Contribution of MSLs across product lifecycle (adapted from Chin, 2007).

The insights gathered by the MSLs in KOLs and thought leaders' interactions, along with their therapeutic expertise and competitive intelligence, enable companies to implement conscious and informed strategic decisions across multiple sectors, including R&D, Medical Affairs and Marketing. [25]

Furthermore, the MSLs have also the responsibility of identify internal training needs concerning product, disease and therapeutic area. As company's internal scientific and medical knowledge experts, the MSLs give their inputs to educational contents and provide specific training to sales force or other company's staff, as necessary. [25]

But the internal role of the MSL is not only limited to training and insight-driven performance. Many companies have implemented structured MSL mentoring programs in which a mentor (usually a senior MSL) is assigned to a *protégé* (new employee) with the purpose of introducing him/her to role expectations, providing a perspective of company's culture and values, facilitating team integration, and mentoring him/her towards the leadership mission. [26]

4.2.5. Compliance to high ethical standards

The pharmaceutical industry continues to undergo significant change with respect to how companies interact with medical community and HCPs. The increased pressures from regulatory authorities and demand for more transparency have made companies and physicians susceptible to investigation for fraud and misconduct.[29]

This new regulatory arena increased physicians' reluctance in collaborating with industry, fearing that it may jeopardize their credibility. It turns to be absolutely essential that pharmaceutical companies' approach to medical community has to be ethical, compliant and even stricter than the current regulatory dispositions and deontological guidances.

In Portugal, the MSL activities are regulated by Decree-Law nr. 176/2006 – *Estatuto do Medicamento*[14], Decree-law nr. 330/90 – *Código da Publicidade*[15], Deliberation nr. 044/CD/2208[16], with which Deontological Code from APIFARMA[17] is aligned. It is important to state that these regulations are not exclusive for Medical Affairs activities or MSL functions but represent promotional pharmaceutical activities as a whole, not making a clear differentiation between promotional or non-promotional activities, with the exception of Medical Information and Patient Safety activities which are clearly a legal requirement.

Therefore, companies opt to create their own interactions codes and ethical guides based on the interpretation of the regulatory standards and deontological codes. Moreover, it has been established that MSL interactions with KOLs must have a non-promotional nature and scientific exchange is required to be on-label, unless the physician has formally requested it otherwise.

The MSL should always comply with the established normatives, ensuring that its behavior adheres to the highest ethical standards, contributing to company's public recognition and reputation as trustful partner.

4.2.6. MSL performance metrics

Pharmaceutical companies are reformulating their hiring practices and organizational structure mostly due to regulatory compliance concerns. The focus shift from Sales and Marketing to Medical Affairs made companies face the challenge of developing and implementing metrics to assess MSL performance. However, measuring MSL activities is not an easy task due to the fact that relationship building, collaborative activities, value of ideas and insights are not quantifiable variables. [25] The current responsibilities and objectives of an MSL do not fit into the traditional field-based sales model.

«*I believe that we are still seeking for an ideal way to compare and evaluate the work of an MSL; and the current metrics, based on quantity of visits to a predefined KOLs panel do not reflect the richness of the work done, and do not show as well, by exclusion of qualitative metrics, the active involvement in the medical strategic product planning or the impact of the MSL role in generating and dissemination relevant scientific evidence*.» Dr Filipe Branco, Senior MSL AstraZeneca.

The MSLs consider frequency metrics as following a sales-centric approach and therefore unadjusted for compliance reasons, however qualitative metrics are perceived as insufficient from business executives' point of view. The fact is that quality matters for the purpose of appraisal of MSL performance. In contrast, quantitative metrics may be easily fudged and ultimately provide minimal insight into true performance. In an attempt to overcome metrics controversy, companies use a blend of qualitative and quantitative metrics to support and communicate MSLs value to corporate stakeholders.[25, 30]

Despite MSLs metrics include qualitative objectives there is a rising tendency to assess MSLs performance based on quantitative measurements, conferring the misperception that the nature of the MSL is analogous to the one of Sales Force Representative.

4.3. Practice trends across the pharmaceutical industry

Over the last years, the increasingly constraints of resources on healthcare systems and a product competitive landscape have pushed pharmaceutical companies towards a tangible demonstration of the medical and economic value of their products to medical community, institutions and society.[1]

In order to demonstrate value, Medical Affairs departments have availed themselves of field-based professionals with solid scientific backgrounds, MSLs, to collect insights from a broad range of medical influencers and decision-makers feeding back to companies' strategic plans, tailoring and continuously updating the definition of value. This movement allowed companies to better shape the communication of its products and also to create a stronger scientific bond with medical community.[1]

Although the function does not exist in every company or even country, in Europe there has been an increasing number of MSLs across industry. Up until 2010, multinational pharmaceutical companies have privileged the implementation of MSL teams on the USA market, with small expression in the European and Asian markets. Data from 2012 show that, globally, there were an exponential number of companies reporting the integration of MSL in their medical staff: 74% in Europe (compared to 64% from a study conducted in 2010) and 42% in Asia (21% in 2010).[5]

As the number of deployed MSLs tends to grow, so does their specialization. This trend towards specialization is more prominent in the USA market and thereby the MSL may assume different responsibilities:[30]

- Provide therapeutic area and/or health outcomes research support to Payer customers exclusively;
- Interact with external clinical investigators and potential investigators in the support of trials platforms, as Clinical Trials Liaison;
- Ensure broad coverage of HCPs below the KOL level targeting registered nurses, nurses practitioners and physicians assistants, as Clinical Education Liaison;
- Work in alignment with field sales, being responsible for supporting the brand while building relationships with thought leaders, as Thought Leader Liaison;

- Work in alignment with field sales, being responsible for developing speakers;

- Produce product training materials, disease-state materials and synopses from medical conferences, as Field-based Disease Education Resource Manager.

As MSL roles and responsibilities have evolved to fulfill a wider extent of demands, the profiles and educational backgrounds of MSLs are of critical relevance. In a survey applied to Medical Managers and Medical Directors conducted across the industry, when asked about the educational profile for MSLs, 66% referred that an advanced degree (MD or PhD) was essential to be integrated in theirs company's teams, 27% considered that an health-related undergraduate degree was sufficient, and 7% reported that non-health related undergraduate degree was the minimal requirement to accomplish MSL functions.[31]

Based on the historical evolution, the MSL role and responsibilities presumably will continue to develop, adapting to market demands, an increasingly more restrictive environment and a drift to specialty care focused business, as opposed to primary care business.

5. A journey into the pharmaceutical industry: my experience as MSL

5.1. AstraZeneca: host company profile

AstraZeneca is a multinational biopharmaceutical company, and one of only a handful to span the entire chain of a medicine from discovery, early and late-stage development to manufacturing, distribution, global commercialization of primary care and specialty care medicines, whose main focus areas include some of the most serious contemporary illnesses: Cardiovascular and Metabolic, Oncology, Respiratory, Inflammation and Autoimmunity, and also Infection, Neuroscience and Gastrointestinal diseases.

It employs over 50,000 people, in more than 100 countries, and its medicines are used by millions of patients worldwide.

Based in London, AstraZeneca was formed in 1999 when Astra AB of Sweden merged with Zeneca Group PLC of the UK. According to IMS[32], AstraZeneca is one of the top-five leading biopharmaceutical corporations in Portugal, ranking eighth in terms of sales worldwide. AstraZeneca Portugal is located in Queluz, in the outskirts of Lisbon, and employs 160 workers within several departments: Corporate Affairs and Market Access, Finance, Human Resources, Sales, Marketing, Medical and Regulatory Affairs.

The Medical and Regulatory Affairs Department integrates 21 professionals and it is structured according to specific functional units: regulatory affairs, medical information and patient safety, clinical research, quality assurance and five Medical Affairs therapeutic areas (respiratory, oncology, central nervous system, cardiovascular and metabolic).

Each company may structure its medical department differently, depending on the dimension and culture of the organization. The AstraZeneca Portuguese Medical and Regulatory Affairs Department (MD) is headed by a Medical Director, Dr Ana Rita Lima, who is supported by a multidisciplinary group of life-science and health-science background professionals and administrative staff (Appendix A – AstraZeneca's Medical and Regulatory Affairs Department Organogram). Within the Medical and Regulatory Affairs Department, these professionals take the roles of:

- Regulatory Affairs, Medical Information & Patient Safety Manager;
- Nominated Signatory;

- Patient Safety & Medical Information Specialist;
- Regulatory Affairs Manager;
- Regulatory Affairs Advisor;
- Clinical Research Manager;
- Quality Assurance Manager & Qualified Person;
- Quality Assurance Specialist;
- Medical Affairs Manager (MAM);
- Medical Science Liaison (MSL);
- Medical Assistant.

As Medical and Regulatory Affairs Department trainee, and specifically as an MSL, I was under the scientific guidance of the Medical Director, Dr Ana Rita Lima, and under supervision of the senior MSL Filipe Branco and the MAM Rafael Fernandes.

5.2. Internship

As an integrant part of the master degree in Pharmaceutical Medicine, the purpose of this internship was to blend real on-the-job experience with an extensive overview of the pharmaceutical industry environment and the competences gained during the curricular part of the master. This internship was held in the Medical and Regulatory Affairs Department of AstraZeneca Portugal, during the second year of the master's degree. It started on 8th of April 2014 and it is planned to last approximately nine months, until the 30th of November 2014.

5.2.1. Goals and description

The main goal of this internship was to develop key competences which will enable me to perform the role of a MSL in a multinational biopharmaceutical company, in Cardiovascular therapeutic area, acting as a medical customer-facing resource who supports a market-leading brand in Portugal; the focus of my role was particularly targeted to the development and implementation of Continuous Medical Education programs and associated management of KOLs and regional or OPs.

During the first weeks of the internship an induction program (Appendix B), common to all trainees and newly assigned employees, was rolled out. It comprised an introduction to AstraZeneca Portugal, held by representatives of different departments. Through this program it

was possible to get in touch with the company's structure, mission, culture and values. Afterwards, with a progressive grade of complexity, a handful of specific and comprehensive training (in-person programs, online training and self-study) required to the MSL performance and related therapeutic area of expertise were delivered.

AstraZeneca's knowledgeable mentors, senior MSL Filipe Branco and MAM Rafael Fernandes, have provided me with mentoring and on the job coaching while professional hands-on experience was being gained.

The internship was developed in the Cardiovascular area, in the dyslipidemia disease area, in support to rosuvastatin – a reference molecule commercialized by AstraZeneca as Crestor©, which although is seen as a mature end-of-lifecycle product, it represents 42.2% of the turnaround sales in Portugal. (Figure 3 - Rosuvastatin's lifecycle)

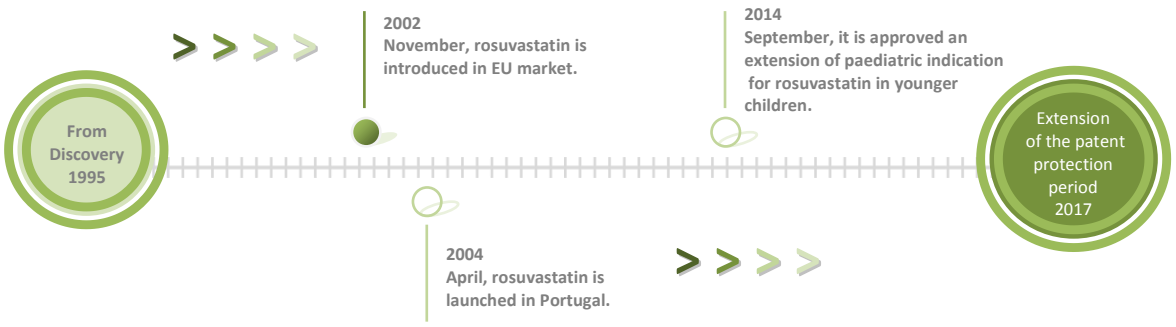

Figure 3 – Rosuvastatin's lifecycle

5.2.2. Core activities within Medical Plan

The management of a pharmaceutical product during its lifecycle requires an immense amount of operational planning and effective execution.

The strategic preparation of the market by Medical Affairs starts at least two years before a product's launch and continues throughout its lifecycle. From laying the groundwork of product understanding by the market, to prompting adjustments until patent expiry, Medical Affairs informs competitive product messaging, based on clear medical and scientific insight.

To facilitate planning, the Medical Affairs needs to be coordinated as a set of internal and external activities, defined by time frames and financial investment decisions, that are prioritized according to the product cycle phase and respective goals – the Medical Plan (MP).

The MP has a flexible and dynamic nature that is adapted to the characteristics of the product itself and its importance to the company portfolio and stakeholders. Although being a *die out* product, Crestor© is a blockbuster and it still represents a critical piece of AstraZeneca's business. In fact, it is still seen by the medical community as a standard treatment for hypercholesterolemia and the prevention of major primary cardiovascular events. The responsibility of having such a product implies that AstraZeneca continues to invest time and resources into it, especially in medical activities, in order to assure that patients who need continue to receive the best treatment available.

Each element of the Medical Affairs team is responsible and accountable for a different set of activities of the MP: Regulatory Affairs, Quality Assurance, Medical Information and Patient Safety specialists, Medical Managers and MSLs work to support the product medical activities and customers, serving the main purpose of educating internal and external stakeholders through the delivery of accurate, comprehensive and unbiased information on the product, while being compliant to the highest ethics standards and regulatory obligations.

The internal and external activities driven by the MSL in support to Crestor© MP are described below.

5.2.2.1. Internal

Crestor© internal medical activities were focused on developing sales force scientific capabilities, i.e. by training them on the medical unmet need, disease area, product and treatment algorithms and guidelines. Furthermore, as an MSL I had a clear role in providing medical and scientific expertise to support marketing activities (promotional material reviews, internal scientific updates, identification of potential speakers for promotional events), and also in response to medical information inquiries, as a scientific advisor of Medical Information.

My experience as MSL trainee allowed me to plan, prepare and deliver scientific training sessions to sales force and marketing representatives related to new clinical practice guidelines, the basis of anatomy, physiology and pathology, product characteristics, new indications and clinical studies updates. This was a dynamic process that allowed me to collaborate directly with

training department representatives, getting valuable feedback to my performance as a scientific trainer.

I was also involved in the support to marketing activities such as educational workshops involving healthcare professionals, and the review of marketing material, which provide me with a continuous interaction with the marketing department. The workshops has as a key target pharmacists, and had the main objective of raising awareness around cardiovascular risk and the importance of controlling major risk factors such as hyperlipidemia. My role in those workshops was to liaise with the speakers, usually Cardiologists, assuring an alignment of their communication and key messages.

Another activity that I had contacted with was the review of promotional materials. I was not able to do it autonomously but I could follow the process under the guidance of my mentors. This was is a very thorough process; all data were carefully scrutinized to guarantee that all information was on-label, scientifically accurate and balanced, according to all legal and regulatory requirements on promotional practices as well as company's policies and standards.

Occasionally, I was also requested to backing up medical information services with specific data required by HCPs. Most of these requests were related to new clinical studies or information about unapproved uses of rosuvastatin.

5.2.2.2. External

Crestor© external medical activities were focused on KOLs and OPs scientific exchange objectives (which included discussions about clinical practice guidelines, as well as potential new indications or areas of study whenever requested by HCPs), competitive intelligence (monitor literature and trial results, collect and report relevant insights gathered from KOLs about unmet needs, disease management, including treatment trends and competitors space) and medical education projects.

As MSL trainee, my activities were focused on the management of Continuous Medical Education projects, previously defined in the educational programs included in the MP, entailed to engage KOLs and OPs on scientific discussions around the unmet needs on CV risk management and dyslipidemia treatment, while building KOL advocacy, and to drive peer-to-peer communication and education, in a non-promotional context.

Strategically, and in line with the Marketing strategy and product positioning, the medical education programs were developed to reinforce Crestor's© positioning as a gold standard treatment in high cardiovascular risk patients, for patients who most benefit from it. This positioning was communicated to physicians of non-cardiovascular hospital specialties who frequently follow those patients but not seldom recognize that increased CV risk (e.g. Infectologists, Rheumatologists, Neurologists, Urologists and Gynecologists, Internists, as well as General Practitioners - GPs).

The management of Crestor's© medical education projects requires a strict coordination between several internal and external stakeholders where the MSL acts as the linking piece between all of them. On one hand, the MSL is responsible for engaging speakers – usually a regional or national OP –, aligning the scientific contents with the objective of the program, which has to follow the brand's strategy and positioning, and tailoring it to the audience needs and specificities; on the other hand, he/she coordinates the activity with the local First Line Manager and Sales Force teams making sure there is an adherence of the participants to the program; finally, an important planning activity seats with managing properly the third party or agency that is contracted to support the logistics and communication, which is particularly useful in bigger dimension meetings normally involving larger audiences outside of hospital setting (e.g. GPs regional meetings); collects insights and reports post-project feedback.

During my training, I had the chance to receive on the job coaching with the senior MSL Filipe Branco, by closely following the multidimensional management of these medical education projects. More recently I was given the opportunity to manage them autonomously.

The projects are described below.

Continuous Medical Education projects

«Porquê Arriscar?»

This was a Continuous Medical Education project whose main objective was to raise the awareness and educate GPs on cardiovascular risk assessment and management, delivered as smaller dimension local meetings. Key responsibilities of the MSL in this specific project included the engagement of regional or national KOLs, managing their contribution to the definition of the program agenda, and preparing them as speakers by means of a strong scientific briefing, as well

as aligning on a plan with the Sales Managers and Sales Force to mobilize resources and participants for the program.

«Pontes de Risco»

This project aimed at reaching out to physicians of hospital non-cardiovascular specialties (Infectious Diseases, Rheumatology) who manage patients with high cardiovascular risk. The management of this project involved the invitation of national KOLs and hospital physicians of non-cardiovascular specialty. After the invitation of the KOL, it was necessary to establish his/her contribution to define an agenda for the medical program, his/her preparation as a speaker, as well as the alignment with the Sales Managers and Sales Force team to mobilize resources and logistics to support the program participants.

«Sessões VIVA»

These sessions presented the results of an epidemiological population-based study conducted by the Portuguese Society of Cardiology to estimate the cardiovascular risk in the general Portuguese population. Along with the epidemiological data presentation and discussion, in each session there was an allocated time to raise awareness on cardiovascular risk which was done by discussing case-studies and training participants on cardiovascular risk calculation. The study investigators, representatives of the Portuguese Society of Cardiology, led these sessions. The «Sessões VIVA» where tailored and delivered to Internal Medicine physicians, and had an active involvement of the Heads of Department. The MSL role in this project included the invitation of the researchers who presented the study, the invitation and involvement of the Head of Department for the session, the discussion and establishment of the objectives for the session with both, as well as the alignment with the Sales Managers and Sales Force team for the mobilization of logistical resources and participants for the program.

«Sessões PGRx»

The sessions were led by a national KOL already pre-identified, and had the objective of training GPs in CV risk assessment and management, having as a basis and context the spreading of a recently published French real-world evidence (RWE) study in the statins area – the PGRx –, with discussion of real clinical cases. The MSL role was to brief the speaker on the session's objective and to liaise with the Sales Force assuring a good level of HCPs participation.

5.2.3. Other activities

During my internship I have experienced other enriching activities, although some not directly related to the MSL role, which must be mentioned due to the importance that they have had in my professional and personal development.

On a regular basis, AstraZeneca Portugal promotes internal scientific sessions open to all company's departments, integrated in a project named *Health Me*. These sessions take place during one week, several times a year, each of them focusing on a specific medical theme, introducing AstraZeneca's related portfolio and pipeline. All of these educational weeks involve the participation of KOLs or experts on a given field and Medical Affairs staff, who are also responsible for the planning and delivery of the events.

In this context, I had the opportunity to actively participate in the Respiratory Care sessions – "*Inspiration Week*" – where the basic disease concepts of Asthma and Chronic Obstructive Pulmonary Disease (COPD), national and worldwide epidemiological data, as well as the importance of screenings and healthy behaviors were presented. AstraZeneca's current and future pharmaceutical arming in these disease areas was also presented. Other highly interesting sessions were also delivered under the Oncology Care week – "*Courage Week*"; these sessions allowed employees from different departments to refresh and learn concepts about different types of cancer, the physiopathology underneath this disease, the numbers behind the facts, the screening and treatment options, AstraZeneca's R&D contribution through clinical studies for the evolution of cancer care, and AstraZeneca's portfolio and pipeline in this specific area. Until the end of the year, at least two more thematic weeks will be delivered – the "*Love Week*" and the "*Sweetness Week*" – covering Cardiovascular and Metabolic disease areas, respectively. I have already committed to actively contribute as a team member in the management of one of these thematic weeks.

As part of the launch of two new Diabetes products, a one-day training, led by a senior MSL – Ana Penha – and an Endocrinologist – Dr Laura Guerra –, was delivered. This training covered the diabetes basic mechanisms, epidemiology, treatment options, new drug's mechanism of action, and differentiation versus insulin treatment. This training was directed to all internal stakeholders involved in the Metabolic area and, despite being allocated to other therapeutic area, I also had the opportunity to attend this training session. This allowed me to get a deeper knowledge about this fascinating disease, which it-self contributes significantly to the high CV risk of many of our

patients, and to have a glimpse on the best therapeutic options available to manage this multidimensional disease.

Another project in which I was personally involved came out unexpectedly and it was concerned to Safety, Health and Environment. Being my-self an HCP with many years of clinical practice in the public sector, my ultimate goal is to contribute meaningfully for people's wellbeing and health improvement. For that reason I gladly accepted the invitation to collaborate in the production of an ergonomic guide to AstraZeneca's employees, giving my insights and contributing with my technical expertise.

Over this period I was also given the opportunity to receive training in the hospital setting l and have had contact, as an observer, with cardiac catheterisms – a minimal invasive surgical procedure with both diagnosis and intervention purposes at the coronary arteries level, in Hospital de Santa Cruz, under the guidance of Dr Manuel Almeida, Cardiology KOL. Behind the obvious contributions to deepen my knowledge in the CV area, this experience allowed me to interact directly with many other Cardiologists, collecting insights about their clinical practice, its limitations and unmet needs.

To complement my internship, I have also done side-by-side coaching with Sales Representatives and senior MSLs. The coaching with sales representatives was very valuable. It allowed me to experience their field interactions with physicians, the objections that are raised during the visit, learn how to effectively use triggers to get the message across, and collecting insights related to the medical needs of those physicians. The visits also allowed me to introduce myself and thus have my first contact with some KOLs and OPs. To sum up, this experience has allowed me to have a better understanding, from a purely commercial perspective, of the dynamic between AstraZeneca's Sales Force representatives and the medical community at the hospital level.

Another activity in which I was enrolled in, and that was not initially included in the induction plan, was the MSL certification process. This process was implemented globally across AstraZeneca as a way of standardizing MSL capability building and development across markets, and represented a valuable way to validate key competences and skills of the MSL, which are essential to his/her performance. Globally, my communication skills and my ability to present scientific contents to medical audiences were evaluated. My performance was rigorously scrutinized by the Cardiovascular & Metabolic MAM, Rafael Fernandes, the MSL mentor, Filipe

Branco, and the Training Department Coordinator, Paula Serralha, who kindly reported back the results in a very positive and constructive way. This was a very important milestone in my professional development, since I have obtained rich and valuable inputs in what regards the planning, preparation and presentation of scientific sessions, which really had an impact in my daily work.

Finally, the engagement in one-to-one training sessions with top KOLs was another important part of my experience as trainee. These sessions were directly related to the cardiovascular area of expertise and have contributed significantly to increase my scientific and medical knowledge, and grow the enthusiasm for being part of AstraZeneca.

Results and Critical Appraisal

Being responsible for rosuvastatin's (brand name Crestor©) medical scientific liaison plan allowed me to develop the following activities:

- I have written and updated eight training documents/manuals specifically designed for supporting the scientific preparation of different internal stakeholders, such as Sales Representatives and other staff from marketing and sales departments, concerning the following topics:

    ∴ Rosuvastatin clinical studies – Galaxy

    ∴ Cardiovascular Anatomy, Physiology and Pathology

    ∴ Cardiovascular risk in elderly people

    ∴ Cardiovascular risk in autoimmune diseases – Lupus, Rheumatoid Arthritis, Psoriasis

    ∴ Update on 2013 American Guidelines on Blood Cholesterol

    ∴ Update on 2012 European Guidelines on Dyslipidemia Management

    ∴ Rosuvastatin Summary of Product Characteristics (SPC)

    ∴ Update on rosuvastatin clinical studies – new indication

- I have conducted scientific training sessions directed to Sales Representatives and other staff from Marketing and Sales Departments related to the themes I had previously prepared (mentioned above).

- I have been involved in marketing material reviewing, specifically in the review of an interactive detailing (iD) for Sales Force use, concerning Acute Coronary Syndromes.

- I have been present in several AstraZeneca's external Marketing and Medical events:

    ∴ Pharmacies workshops

    ∴ Heart Beat interactive platform events

∴ «Porquê Arriscar? »

∴ «Sessões VIVA»

∴ Hospital clinical sessions

- I have liaised with KOLs and OPs in the context of marketing activities and medical activities (medical educational projects), setting the scientific agendas, discussing meeting objectives, and aligning on key messages:

  ∴ Pharmacies workshops

  ∴ «Porquê Arriscar?»

  ∴ «Sessões VIVA»

- I have also cooperated with AstraZeneca's Medical Information and Patient Safety services in specific unsolicited medical requests related to rosuvastatin, namely off-label uses and clinical studies requests.

Regarding the internship limitations, it was not always clear how much support or how much autonomy I should have had. Sometimes it was difficult to understand the expectations and where to start for some of the medical activities I had to assure as a trainee. To overcome this difficulty, I have begun to define very clearly the requirements and deadlines for all medical projects under my responsibility, and developed structured spreadsheets with action points and status for the activities planned. This was a great way to define timelines and plans of actions, but also to keep projects information organized and updated.

These activities, which were delivered in close cooperation with internal and external stakeholders, have given me the chance to sharpen my communication and presentation skills, to raise my self-confidence when interacting with KOLs and OPs, to acquire a comprehensive knowledge on dyslipidemia and CV risk management, as well as on CV therapeutic area as a whole, strengthening my scientific preparedness in a disease area that is close to my heart. Moreover, the experience of working in an inter-departmental cross-functional environment was really challenging and, simultaneously, rewarding, having allowed me to develop my ability to define priorities and to build on my natural strengths – collaborative, problem-solving focused, team player, customer oriented, results driven, and strong communication skills.

6. Closing remarks

Clearly, due to increasing regulatory pressures, healthcare systems restructuring, more transparency in all pharma companies activities directly related to patient data and HCPs engagement, as well as socio-economical changes observed both in Europe and North America, we are observing a strategic shift in pharmaceutical industry, where the focus is no longer directed to commercial teams only, but it is progressively being allocated to Medical Affairs teams.

Medical Affairs teams have become a privileged source, and actually a privileged channel, of interaction with medical community. The MSLs are considered to be the propellers of these collaborative relationships and scientific knowledge exchange, acting as reliable and trusted partners of KOLs, collecting and reporting their insights back to pharmaceutical companies, which ultimately are translated into more tailored strategic plans. Thinking of the value they deliver to the medical community, the MSLs help physicians to stay up to date, by delivering higher quality, relevant and balanced medical information, as well as cutting-edge science to address unmet clinical needs and provide better patient care.

The presence of MSLs in companies' Medical Affairs teams has been continually increasing over the last years, however it cannot be truly considered a new emerging role, since it does exist since the late 60's. But, now more than ever, with the featured role of Medical Affairs, MSLs are becoming an unquestionable essential resource. And it is interesting to note that there is also an increasing trend towards MSLs specialization, mostly related to clinical trials support, education resource management objectives, and health outcomes research needs, especially since we are seeing the increasing need to communication value to new customers, as is the case of payers. Despite core MSLs functions resemble between companies, there are aspects that differ concerning metrics and management responsibilities, and each company shapes the function according to its Global strategic vision, lifecycle phase of its portfolio and pipeline, and local market specificities. Unfortunately, in Portugal there is no benchmarking data on MSL groups across pharmaceutical industry. Therefore, it was not possible to analyze the past or current state of the function, nor the inherent particularities of this role in Portuguese market.

Regarding physicians' Continuous Medical Education, pharmaceutical industry plays an important role, and more so in Portugal. The value of this core pillar of the Medical Affairs activity is not only due to the scientifically solid nature of the physician-MSL interaction, but also due to

the investment of time and resources behind the implementation of relevant Continuous Medical Education programs, with HCPs consensually recognizing the benefits of such programs to their continuous training and development, with an impact on patient care management. Although outside of the scope of this report, it is worth mentioning that there is a lot more to explore concerning Continuous Medical Education, especially because of the marked contrast between countries' accreditation systems, professional impositions and the challenging role of pharmaceutical industry in those contexts, not to mention the different funding systems in different countries.

As a result of a deeper involvement in all drug lifecycle, with more cross-functional responsibilities and an intensive KOL interfacing, the MSL is gradually assuming a critical role in pharma companies business success, not only in pre-launch and launch phases, but also in managing the life cycle of more mature brands when these are still relevant to the business as is the case of Crestor®. The MSL is therefore an internal thought leader, clinical catalyst and external voice, and these different roles' relative weight is more or less prominent depending on the lifecycle of a given product.

However, some challenges still remain, and this was also observed during my trainee experience. The demarcation of MSL role from a sales representative role, which can work against cross-functionality and create silos, the demonstration of the real MSL value to companies' business leaders, the development of appropriate metrics that really reflects the nature of the role, and finally the need of an appealing career development path.

During my almost nine-month long experience as Medical Scientific Liaison trainee, I had the chance to progressively undertake more responsibilities, initially developing my scientific knowledge and building on my educational and professional background, and subsequently preparing and delivering scientific training and managing medical education projects more autonomously.

During this transition time, I took a wide variety of tasks that covered almost all of the activities performed by an MSL. Although the emphasis of this internship has pivoted around the role of the MSL in Medical Education projects, it was possible for me to experience other related activities, namely internal ones. Within the MSL role, I would have valued to have had more contact with clinical research activities, but this was understandably not possible due to the end-of-cycle stage of Crestor®.

At AstraZeneca the MSL time allocation takes into account the customer facing nature of the role and therefore 70-80% of the time is spent in interaction with physicians. During the internship period my interactions with KOLs and OPs were all related to projects' management. Peer-to-peer scientific discussions require a high level of expertise that is only achieved with intensive training and years of practice. As someone said to me: «*Every expert was once a beginner. You are just getting started*». Nevertheless, I had the chance to accompany a senior MSL in the field, to better understand the dynamic and the primness of these scientific interactions.

This internship was an excellent way of putting in practice and developing in a real-life setting concepts acquired during the master, and a chance to contribute with my knowledge, background experience, resilience and dedication to AstraZeneca's values and purposes. In every task I was assigned to, aiming at small or great achievements, I have always strived to reach excellence. It was also a great opportunity to develop a personal and professional networking and to collaborate with a fantastic team of very talented people.

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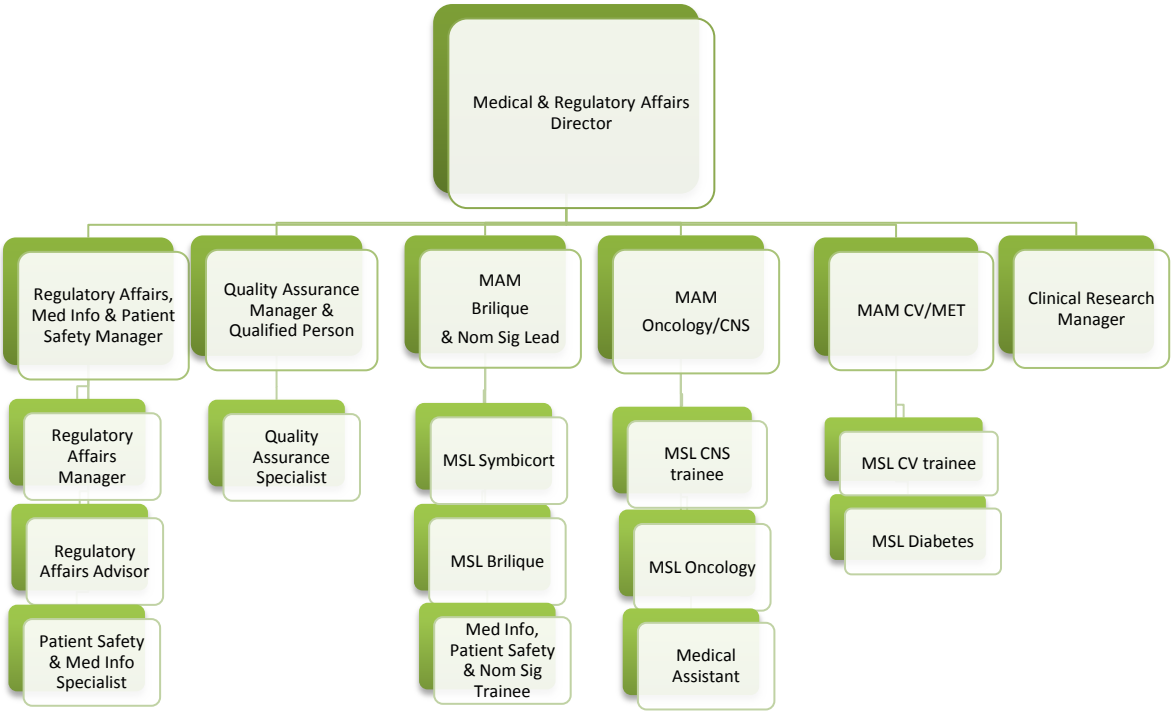
Appendix A – AstraZeneca's Medical Department Organogram



Appendix B - AstraZeneca's Induction Programme

Induction Plan Liliana Cruz
Inicio - 08 Abril 2014

Activity	Objectives	Delivery Method	Documents / Links	Timing / Date Meeting Room	Self Check & Comments / Notes
IS / IT Material & Tools	IT Tools Acesso Remoto Wireless - opções disponíveis Acessos às Drives Public, Departments, etc IS / IT code of conduct	Meeting with Miguel Rodrigues	Politica Safeguarding Company Assets & Resources	1st week	Sessão não realizada
			Computer_usage_policy__PT	1st week	Sessão não realizada
Processo de Admissão	Contrato de Estágio	Meeting with João Dias		2nd Week	Sessão Realizada
AZengage - Ferramenta de RH	Validação de Dados pessoais e preenchimento dos restantes		Página AZengage		Sessão Realizada
Telemóvel Procedimentos	Realizar procedimentos relativos ao Telemóvel	Meeting with Raquel Sousa		2nd week	Sessão Realizada
Missão e Visão	Conhecer a Missão e a Visão da AZ Posicionamento Cientifico	Consulta de informação	Mission & Vision		
		Consulta de informação	Our science		
AZ Institutional Comunicação Interna	Obter uma Visão Global sobre a AZ Portugal Iniciativas Internas	Meeting with Célia Machado			Sessão Realizada
Overview da AZ - Global e Local	AZ performance - Objectivos e Prioridades Estratégicas	Documentos para consultar	Portugal Scorecard 2014	Semana 21 Abril Filipe Branco	
		Meeting - Orientador do Estágio	Your:AZ_Global Scorecard 2014	Semana 21 Abril Filipe Branco	
Overview do Departamento	Departamento - Objectivos e Prioridades Estratégicas Contextualização do Estágio	Meeting Orientador do Estágio Diretor do Departamento		Semana 21 de Abril	
Politica SHE	Apresentação da Politica SHE e SHE Committee local	Consulta da documentação e Meeting Area SHE	Politica SHE		Sessão Realizada
	Actuação em situações de emergência		Politica Edifício Sem Fumo		Sessão Realizada
	Primeiros socorros		Safety		Sessão Realizada
			Localização e responsáveis pelas caixas de 1º socorros		Sessão Realizada
			Equipa de Apoio Médico		Sessão Realizada
	Registo de Acidentes e Incidentes		Form. de registo acidentes		Sessão Realizada
	Recolha selectiva de resíduos		Folheto		Sessão Realizada
			Regras separação		Sessão Realizada
Business Continuity Plan	Risk Management Business Continuity Plan	Meeting with Alexandra Nunes	IRM / BCP Local page		Sessão Realizada
Politicas AZ	Conhecer as Politicas Globais e Locais	AZ Global Intranet	Global Policies		Documentação - Leitura realizada
		AZ Local Intranet	Corporante Governance		Documentação - Leitura realizada
Politicas AZ	Realizar formação em Data Privacy	E-Learning - Data Privacy	Data Privacy - Protecting Personal Information	incluido no treino de MSL	E-learnings - Concluído
Código de Conduta Procedimento sobre report de Incidentes	Conhecer a Politica: Código de Conduta	E-Learning - Código de Conduta	E-learning - AZ Code of Conduct		E-learnings - Concluído
Compliance Formação em CDTI	Overview área de Compliance na AZ Conhecer a politica de Interacções externas e seu impacto	Meeting with Paula Serralha	CDTI Intranet page	11-Abr-14	Sessão Realizada
Continuous Assurance	Conhecer processo de Continuous Assurance Compreender o papel de colaborador AZ	AZ Local Intranet Meeting with Cláudia Sousa	Continuous assurance Intranet page		Sessão Realizada
Quality Assurance Product Security	Qualidade dos produtos Procedimento de gestão de queixas				Sessão Realizada
Nominated Signatory overview	Nominated Signatory - Papel, responsabilidades e desafios	AZ Local Intranet Meeting with Inês N Guedes	Nominated Signatory Page Intranet local		Sessão não realizada
Contratos na AZ	Processo de Contratos na AZ	Meeting with Sara Macedo	Intranet_Contratos		Sessão Realizada
Formação de procedimentos na Área Financeira	Submissão de Despesas Mensais	Meeting with Susana Santos (on the job)	T&E Intranet	2nd week	
	Conhecer o processo do Doa´s (Delegation of authorities)	Leitura da informação e documentação	DoA_Intranet		
Farmacovigilância Info Med	Procedimentos	Meeting with Isabel Cruz / Ana Paula Rita		confirmar quais os treinos on line que deve fazer	Sessão Realizada
Formação Patologia e Produto	Formação em Crestor	Meeting Treino - Lourenço Pereira MSL - Filipe Branco			Sessão Realizada
Overview Área de Vendas	Estrutura de Vendas Primary Care e Objectivos 2014	Meeting Anibal Carvalho			Sessão não realizada
Overview Marketing	Estrutura Marketing e Objectivos 2014 Objectivos Crestor	Meeting Sofia Correia Igor Costa			Sessão não realizada
Clinical Trials	Desenvolvimento Clinico do Medicamento	Meeting Sandra Barbosa			Sessão Realizada
Formação em Atlas	Submissão de projectos Consulta de material disponível da AZ Global	E - Learning e Treino presencial - Line Manager	LM solicita ao Global Commercial Services: GlobalCommercialServices@astrazeneca.com - a criação do utilizador, enviando o PRID e Endereço de Email.	Esta formação não será realizada numa 1ª fase. Avaliar posteriormente se justifica o terino	Sessão não realizada
Formação em Veeva	Ferramenta para a actividade dos MSL´s	Presencial		11 Abril, 8 de Maio e mais uma data	Sessão Realizada
Formação em Condução Defensiva		Classroom and Driving training		A considerar se utilização de carro AZ	Sessão não realizada

Sessão realizada

Sessão não -realizada