CMC Regulatory Affairs — Insights and Career Advice from an Expert

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Chemistry, Manufacturing, and Controls (CMC) Regulatory Affairs (RA) plays a pivotal role in the development, licensure, manufacturing, and ongoing marketing of pharmaceutical products. In this role, CMC RA professionals help ensure that pharmaceutical products are consistently effective, safe and high quality for consumers. During an interview with Ashton Tweed, CMC RA career veteran Frederick A. "Simon" Golec, Jr., PhD, shares his insight on the most important CMC issues companies face today. He also offers some great advice for those considering a career in this area.

What is CMC Regulatory Affairs?

To conduct clinical investigations and market pharmaceutical products, Dr. Golec explains, pharmaceutical companies are legally required to obtain and maintain regulatory approvals. Regulatory Affairs is a discipline and strategic function within the overall organizational structure of a pharmaceutical company that directly interacts with government regulatory agencies concerning regulatory approvals. The Food and Drug Administration (FDA), European Medicines Agency (EMA), Japanese Pharmaceuticals and Medical Devices Agency (PMDA), for example, are government regulatory agencies typically involved in the approval process.

Chemistry, Manufacturing, and Controls (CMC) Regulatory Affairs (RA) is a specific area within RA that has the ultimate responsibility for providing CMC regulatory leadership and strategy required to achieve regulatory approvals. As a strategic function, CMC RA collaborates closely with multiple scientific, technical, quality, and commercial areas within a company or with external contract manufacturing organizations (CMOs). "To help companies effectively and efficiently achieve regulatory approvals," describes Dr. Golec, "CMC Regulatory Affairs provides knowledge, understanding, interpretation and utilization of regulatory guidances and regulations, as well as industry and government agency best practices and trends."

For example, CMC regulatory submissions may contain – but are not limited to – information associated with the Active Pharmaceutical Ingredient (API) and the finished dosage form, including:

- Names and locations of manufacturing and testing sites
- Characterization of the API and composition of the dosage form
- Raw materials used to manufacture the API and finished dosage form
- Description of the product and process development
- Description of the manufacturing processes
- Analytical methods and specifications used for testing and release of raw materials, in-process controls, container and closure systems, API and the dosage form
Release and stability testing data for both the API and the dosage form.

**What are the most significant CMC issues companies face and how can these be resolved?**

*New Molecular Entity Approval* – “For a New Molecular Entity (NME) regulatory approval,” says Dr. Golec, “managing all of the CMC Regulatory Affairs activities and requirements to achieve the preparation of a robust, regulatory submission is a very complicated process.” He points out that these activities occur within pharmaceutical and biotechnology companies – as well as externally with contract research organizations (CROs) – through numerous interactions with regulatory agencies during the entire process.

*Regulatory Documentation Changes through Product Approval* – In order to have a successful outcome (i.e., a product approval), an adaptive, regulatory strategy is required that continuously and prospectively details the progressive, regulatory requirements from the initial clinical trial, throughout the pre-registration, registration, post-approval, and life cycle management.

*Post Approval* – Even after marketing authorization approval, there are numerous CMC RA activities that are required to support CMC changes made to maintain the lifecycle of the approved pharmaceutical product. In addition, an efficient and effective change control process is essential to maintain product conformance and compliance.

“It’s very common for pharmaceutical companies to utilize CMC Regulatory Affairs consultants,” notes Dr. Golec. He points out that CMC RA consultants can “provide the knowledge, experience, guidance, and advice to help most effectively and efficiently achieve the highest probability of success in obtaining regulatory approval of a particular pharmaceutical product.”

**Who is CMC Regulatory Affairs a good career choice for, and how does one start a career in this area?**

“CMC Regulatory Affairs may be a good career choice for individuals working within the pharmaceutical industry or a closely related industry,” answers Dr. Golec, “who have a scientific or technical background, an analytical mind, problem-solving abilities, and strong negotiation and communication skills.” He also believes an understanding of the multidisciplinary complexity associated with the discovery, development, commercialization, and sustainability of a pharmaceutical product is essential.

CMC RA is a high value-added function within a company that is critical to successful development, registration, approval, and life cycle management of pharmaceutical products. Because of the importance of regulatory approvals for pharmaceutical products, Dr. Golec points out, individuals within CMC RA departments have high visibility at all levels of the organization and to the regulatory agencies with whom they interact. So they must also be comfortable and competent working in that type of environment.

“There’s no right or wrong way to start a career in CMC Regulatory Affairs,” Dr. Golec explains. Although the majority of people who start a career in CMC RA have worked in some capacity in the pharmaceutical industry, many of the personnel come from varied backgrounds, including working as biological or chemical scientists, engineers, lawyers, quality control and quality assurance staff, as well as in drug manufacturing and development positions.

In some cases, CMC RA staff members were influenced by individual leaders, Dr. Golec observes, or became interested in the variety and challenges of the work and opportunities provided within CMC RA. In other cases, people were more proactive – completing certification or degree programs in RA or quality assurance while employed within another area of the company to increase their chances for a move into an RA position.
Additionally, Dr. Golec encourages active membership in the following organizations as a way to network and learn more about a career in CMC RA:

- Drug Information Association (DIA)
- Parenteral Drug Association (PDA)
- American Association of Pharmaceutical Scientists (AAPS)
- Regulatory Affairs Professionals Society (RAPS)
- The Organisation for Professionals in Regulatory Affairs (TOPRA)

**How has CMC Regulatory Affairs changed, and what does the future look like?**

"The history of CMC Regulatory Affairs within the pharmaceutical industry is a story of continuous change," Dr. Golec observes. He believes collaboration – between industry and regulators, as well as global collaboration across regulatory agencies – is among the most positive trends.

In the United States in the late 1980s, for example, the FDA was involved in initiatives to rewrite the Investigational New Drug (IND) and the New Drug Application (NDA) regulations. "In fact, it was one of the earliest transparency initiatives requested by industry," Dr. Golec explains. At that time, however, the RA environment was very complicated because each country had its own unique requirements for conducting clinical trials, obtaining regulatory approval, and making post-approval changes to approved pharmaceutical products.

The first paradigm shift in the regulatory environment, Dr. Golec comments, was the collaborative initiatives – in the areas of quality, safety, efficacy, and multidisciplinary guidelines – commencing 20 years ago under the auspices of the International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use and still ongoing. This included joint participation from the regulatory agencies of the United States, the European Union, and Japan, along with these countries’ pharmaceutical industry trade organizations.

Yet, the ICH initiative may not have been possible without the establishment of the European Medicines Agency (EMA) in 1995. That, Dr. Golec explains, ultimately allowed for a product's regulatory approval in multiple European countries using a single dossier. Similar collaborative efforts have been ongoing among various regulatory agencies throughout the world, he adds, in the areas of information sharing on pharmaceutical products, inspections, and pharmacovigilance. In this way, regulatory agencies can better utilize their limited resources and collectively assure patient safety and product quality.

"Ongoing socio-economic and political changes will exert pressure on both industry and regulatory agencies to enhance collaboration in the continued development of regulatory requirements," says Dr. Golec. Advances in innovation, science, technology, regulatory sciences, and especially information technology and chemometrics, he concludes, will continue to be the drivers for enhancements in the future.

Ashton Tweed would like to thank Dr. Golec for this interview. If your company needs help in the area of CMC RA or from other members of the Ashton Tweed Life Sciences Executive Talent Bank, we can supply that assistance either on an interim or a permanent basis. Alternatively, we’d also like to hear from those who are CMC RA specialists looking for interim or permanent opportunities. In either case, please email or call us at 610-725-0290. Ashton Tweed is pleased to continue to present insightful articles of interest to the industry.

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Following a 33-year career in the pharmaceutical industry that included scientific and RA management and leadership positions, Dr. Golec founded CMCRegAff, LLC, in November 2010 to provide CMC RA consulting services to the biotech and pharma industry. Dr. Golec’s extensive understanding, knowledge, and experiences within the global pharmaceutical industry includes research, development, technology transfer, commercialization, as well as the registration, approval, life cycle management, and regulation of pharmaceutical products by global government agencies.

During his career, Dr. Golec authored or co-authored publications in organic chemistry and regulatory sciences, was an inventor or co-inventor on patents, was involved in gaining regulatory approvals for numerous marketed pharmaceutical products, and supported Pharmaceutical Research and Manufacturers of America (PhRMA) and International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use, and Product Quality Research Institute (PQRI) initiatives.