

# Regulatory Intelligence as a Business Partner

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Master's Candidate: Angela Yu

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*Disclaimer: The views and opinions expressed in this paper are those of the author and do not necessarily reflect the views or positions of any entities they represent.*

## **Introduction**

Regulatory Intelligence (RI) should be a valuable business partner at the highest corporate level and routinely included in all levels of Regulatory/Quality and Compliance position descriptions. A corporation's understanding of evolving rules, regulations, current compliance focus and other Food and Drug Administration (FDA) interests can contribute to an optimized time to market and efficient compliance. Furthermore, although RI shares a common goal of ensuring product safety through regulations and compliance, depending on the organization and several other factors, there are prominent variations in the scope and responsibility of a regulatory professional's job. With continuous scientific innovation and changing regulations and policies, RI enables industries to anticipate and better manage FDA requirements and trends as well as managing compliance more efficiently. This paper provides an overview of FDA's primary objectives, why senior RI should be represented at the table with top corporate management and examples of how the government and industry can fail to optimize opportunity.

## **Research Method and Rationale**

As part of the research for this paper, interviews were conducted with executive Regulatory professionals in the regulatory field.

A co-founder of the San Diego Regulatory Network (SDRAN, n.d.) was interviewed based on his strong interest in Regulatory education and RI. He started the conversation with a few anecdotes. He attended the original proposal meeting for regulatory certification at the Regulatory Affairs Professional Society (RAPS, n.d.), and reported that the goal was for the members to achieve a new certification. In 1992, this became known as the "Regulatory Affairs Certified (RAC)," with recertification in each three-year cycle ever since. This certification is a means to achieve and maintain, through renewal, a formal level of RI, but note that education on the topics in the field are highly diverse, especially when it comes to FDA trends. Upon

arriving in San Diego, he and a group of local Regulatory veterans realized that there was an educational deficit, especially since so much of the growing San Diego biotech community were start-ups and unable to afford the infrequent and expensive courses of the national society. So, they decided on a local educational organization and filed papers as a non-profit. This became what is known today as the San Diego Regulatory Affairs Network (SDRAN). The discussions in the formation of this group included consideration of a model for other communities with large biotech start-ups.

Beyond trade groups, another area of continuing education for RI includes topical publications. A recent one on diagnostics includes a chapter that can be summed up as “regulatory creativity”. Such creativity is the outcome of RI. With the permission of the referenced chapter’s author (Freiberg, 2020), here are some examples of the application of RI:

In two instances of innovation in the 510(k) realm, a regulatory professional proactively suggested to FDA that the submission be reviewed by an advisory panel. This is not typical for 510(k) products but provides the FDA review team “better grounds” to clear innovative applications. The two examples were a BTASTat<sup>®</sup> home use cancer test proposed as a 510(k) to monitor for cancer recurrence and the Boehringer-Mannheim (now Roche Diagnostics) Accu-chek<sup>®</sup> Voicemate prescription use only home point-of-care capillary blood glucose monitor for the blind. In each case, the company Regulatory head proactively suggested this new use of a 510(k) product be presented to an advisory panel. The proposals succeeded and the clearances went through expeditiously. So rather than following a formal guidance or regulation, these are instances of understanding FDA needs and applying innovative solutions, hence they clearly fall under the banner of RI.

Another area of innovation via RI is working with FDA in the evolutionary use of non-approved therapies outside formal clinical trials. FDA has at times been hesitant of this practice because of their desire for clearly controlled trials leading to submissions. Any use of

experimental products outside controlled trials potentially increases risk, could dilute data collection and could delay the application and review of new products. Examples follow.

The former head of Coulter Immunology Regulatory Affairs relayed an experience with what was then called a “compassionate” IND at the very beginning of the therapeutic monoclonal antibody industry. FDA was very hesitant to grant compassionate approval, but the request was granted and much learned. (At that time, the methodology to humanize an antibody was not known, but today many humanized antibody therapies are available). A few years after that was an experience with a compassionate IND for a cancer therapy. The AIDS lobby took on the Center for Biologics Evaluation and Research (CBER) with the help of many supporters to move the agency from strong resistance to “compassionate” INDs to the reluctant acceptance of “treatment” INDs. FDA eventually adapted; however, the resistance remains strong outside HIV/AIDS therapies and the current drive for “right to try” approaches while benefitting some patients may, in fact, delay formal data collection thereby delaying new and important therapies to larger populations.

Based on these feedback collected, involving RI with organizational leadership could help teams develop a clear strategy and cohesive execution plan to optimize continuous improvement and derive a timelier path for new opportunities from the beginning. The cross-functional education provided by the Johns Hopkins Regulatory Science Master’s program as well as local efforts like SDRAN and national efforts from the RAPS contribute significantly to regulatory professionals’ ability to participate and contribute. Training can help contributors at all levels understand the importance of the regulatory function as a whole outside of compartmentalized functions. Hopefully, in cases such as the “right-to-try” trend, the outcome will be the right balance between formal data collection and early safe and effective patient care.

### **Context of the literature in the field**

Outside the FDA purview are topics like patents and reimbursement/payment, RI needs to ensure these specialties are on the project plans in the correct time frames. An example of failure to do so was the patent dispute between Oncor and Vysis over a fluorescence in situ hybridization (FISH) genetics technology. The dispute was settled after three years with Vysis obtaining Oncor's FISH genetics program and Oncor agreeing to pay license fees (Business Journal, 1998). Typically, competitors will wait for product approval and income generation before filing a patent challenge; however, with cases like Oncor vs. Vysis, patent evaluations needed to be considered well prior to project approval.

On a similar note, on March 27, 2023, the Amgen patent for anti-PCSK9 antibody reached the US Supreme Court due to a dispute over the rights over the novel treatment for high cholesterol in people at risk of cardiovascular disease. Amgen claims their patent “includes not only a handful of specific antibodies, as defined by their amino-acid sequence, but also any other antibodies, regardless of their structure, that bind to the same region of the PCSK9 protein” (Nature, 2023). If the patent is revoked, it will keep the cost of the drug in check as multiple companies will be able to continue to produce and sell various versions of the drug. On the other hand, revoking the patent may discourage companies, like Amgen, from making similar investments in the future. When there is a failure to consider patents and reimbursement topics, product failure can occur. While the Regulatory team is not responsible for payment or patents, ensuring those activities are on considered in a timely fashion on project plans and budget is critical.

While these concerns may be outside the routine concern of a corporate management team, the RI effort should keep an eye on potential overlap that could affect the company and contribute such potential concerns to the conversation. As an industry issue, astute RI professional should also be raising such issues at trade group meetings for higher visibility.

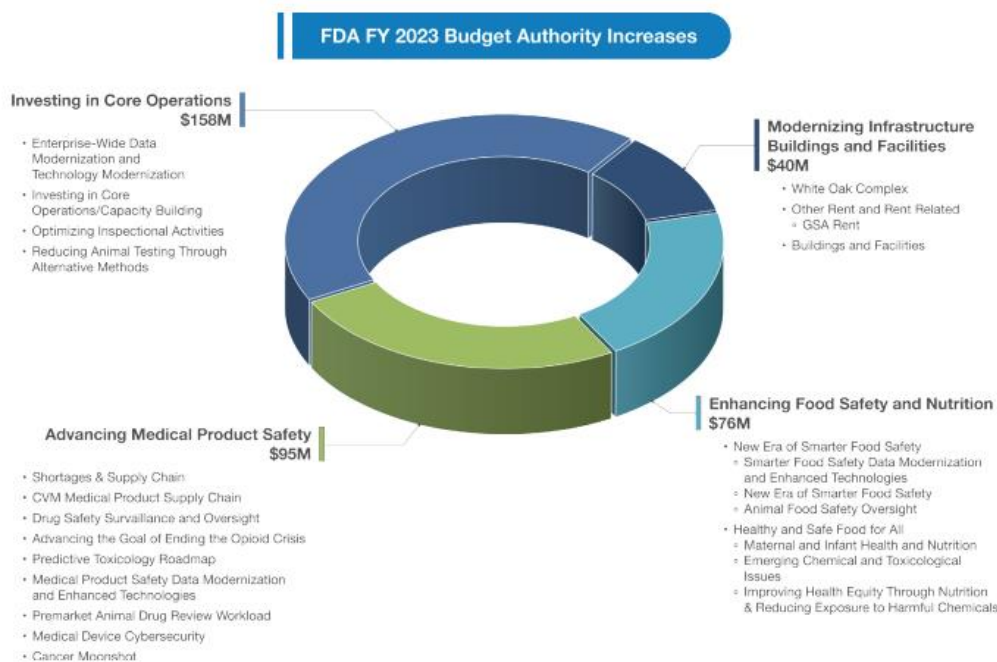
## **FDA's Primary Objectives**

The FDA recognizes their mission is to be “responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation. FDA is also responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health” (FDA, 2018a). RI is intended to address this conflict between “mission” and how FDA executes the mission to help accelerate safe and effective products to the market. Maintaining current knowledge of FDA’s thought-process, trends, recent decisions, and mission helps companies make efficient and well-informed business plans, budgets and related decisions.

## **Building Budget**

FDA’s responsibilities are ever expanding and more complex due to advances in food and medical product technology, new areas, such as tobacco, laboratory measurement ability to find ever lower amounts of contaminants, global supply chain complexity, and artificial intelligence, are directed by Congress. In 2022, the FDA announced it was requesting a total budget of \$8.4 billion as part of the President’s fiscal year (FY) 2023 budget (FDA, 2022a). The FY 2023 request, which covers the period from October 1, 2022, through September 30, 2023, covers initiatives which were previously requested in the FY 2022 budget request, as well as new efforts for high priority program areas such critical public health modernization, core food safety and medical product safety programs and other vital public health infrastructure, see figure below (FDA, 2023a).

**Figure 1. FDA 2023 Fiscal Year Budget Breakdown**



Part of the budget is geared towards “optimizing inspections and enhancing inspectional capacity” (FDA, 2022a). In the case of the infant formula, it is certain that FDA’s field operations will modify and redirect the inspection systems and resources for infant nutrition. This will enable safety problems to be detected earlier and better target interventions to prevent harm to consumers. RI also has the responsibility to respond more quickly and effectively to emerging safety problems, through better information, better coordination, and better communication.

**Patients and Consumers Accountability**

Over the past few years, amid the COVID-19 pandemic, several regulatory authorities have amended or updated their regulations with flexibility for accelerated pathways to approvals, such as the development of biologics and vaccines, ensuring the availability of the treatment or therapies for patients with COVID-19 worldwide. There have also been many guidelines around clinical trial conduct given the pandemic’s impact on the various aspects of such trial conduct, including trial participants, healthcare providers, and logistics. Patient groups



are also proactively engaging in the therapeutic area with disease experts and leading scientific researchers to create new models for medical progress (WSJ, 2023c). A key function of RI is keeping up to date on current trends and utilizing them for the benefit of the patients and company while identifying approaches - fast-track reviews/approvals, rolling submissions, Emergency Use Authorization - just to name a few, to expedite product availability. Relegating departmentally specific knowledge among the many FDA areas to individual departments or separating regulatory functions can often miss opportunities that the RI professional can provide to corporate management.

### **Artificial Intelligence as part of Regulatory Intelligence**

Artificial intelligence (AI) has the potential to transform every sector of business operations and the benefits of AI are apparent in the regulated healthcare industry, as seen from software as a medical device (SaMD) already approved by regulators. From the perspective of RI, adopting AI has the potential of time and cost savings for submission review, speeding up the process between sponsor and reviewer interaction. If the search of the data available is quick, reliable, objective, and valid, it could benefit all stakeholders. AI can be seen as another tool for RI. Here are a few thoughts on AI-driven RI questions for pre-submission processes:

- What is a typical sample size for a clinical trial for [X] product?
- What demographics are required for a clinical trial for [X] product?
- What complications have been reported for [X] product?
- Is [X] product currently marketed safe and effective?

In recent years, FDA has been advancing understanding and use of AI to support a diverse set of needs related to FDA-regulated products and leveraging knowledge management resources to improve regulatory review, and improve postmarket surveillance (FDA, 2022b). FDA hosts the Centers of Excellence in Regulatory Science and Innovation (CERSI) program to promote robust and innovative approaches to advance regulatory science and improve understanding of AI's potential and limitations. Through the CERSI program, FDA investigates the potential of AI

to improve the efficiency of reviewing regulatory submissions. For example, FDA applies natural language processing to regulatory submissions to classify its relative complexity (FDA, 2022b). The effectiveness of this will be dependent on how the questions are phrased, how the responses are interpreted, how the conclusions are validated and how regulators, manufacturers, and the public accept and adapt to this new technology.

## **Discussion**

As innovation occurs and regulations are revised or created, regulatory professionals must stay up to date and have the necessary skills and competencies to make meaningful management contributions to their organizations. Those who can successfully navigate this dynamic landscape remain in high demand. Although they share the common goal of ensuring optimal approval speed and product safety through RI and compliance, there are notable variations in the scope and responsibility of a regulatory professional's work, depending current role in the organization, on company size, product technology, portfolio, development timeline, and culture. In larger companies, RI may be part of a global policy function, whereas in small companies, RI may fall within the regulatory affairs department. RI is often conducted informally within a company and its value is not always recognized nor documented in sufficient numbers of position descriptions. A quick search on the internet reveals Senior RA position descriptions are highly variable, some requiring monitoring and disseminating RI (refer to [Appendix A](#)), while others do not (refer to [Appendix B](#)). Additionally, RI functions such as input of state affairs, federal affairs, Regulatory and Quality trends, assessing product related recalls across the world markets and regulators' guidance information needs to be incorporated to provide the intelligence as a missing parameter in common position descriptions for the benefit of the respective companies' executive teams. Additional consideration for the RI professional position descriptions may also include the following:

- Monitoring FDA-related issues:

- Does the internal audit program periodically consider FDA’s recall statistics and Warning letters to ensure hot topics in compliance, that is, FDA’s focus, is given special attention?
- Does the stability program adequately consider shipping conditions, especially in the growing prescription by mail programs?
- Does the sterility test program have adequate retest protocols and confirm “operator error” rather than just documenting “suspected operator error” and then not altering the retest process?
- Who is responsible for the Total Product Life Cycle Advisory Program (TAP)<sup>1</sup> and how is it represented within the organization?
- Is Marketing input documented from potential customers and not just from internal staff?
- What is the reimbursement plan?
- For clinical evaluations, are the differing needs of the Health Maintenance Organizations (HMOs) vs. the pay-for-service (PFS) providers addressed to prove their worth to those respective organization types?

Of course, to do so should not conflict with other functions like lobbying, legal, or clinical affairs, but still be at the table sharing information.

As part of the senior Regulatory Affairs role, RI responsibility considers all aspects of these FDA portfolio and potential impacts, benefits, opportunities, and risk on the business to advise senior management. If intelligence is cascaded throughout the organization, everyone is made aware of potential issues and can better plan for how they should be handled. More importantly, they know exactly what the rules are and often what regulatory reality is beyond the published rules. The efficiency of RI is increased if the organization is enlightened by the lessons learned from past experiences, whether they be successes or failures.

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<sup>1</sup> The TAP pilot program would allow manufacturers to get feedback from external stakeholders, such as physicians and insurers, on how to bring successful products to market (FDA, 2023b).

## **Conclusion**

RI is continuously evolving in terms of how it is conducted. There is no single source that provides collated information across markets; therefore, regulatory professionals are required to perform robust research for identifying appropriate sources to gather relevant regulatory information. Albert Einstein once said, “the true sign of intelligence is not knowledge but imagination.” Intelligence is not merely finding and storing the data, but thinking creatively on how to utilize the information. With the copious amount of data available, specialization to master the data can play an essential role in the profession. The hip surgeon may not replace knees and certainly the other specialties stick to their anatomy; however, in the corporate world, a generalist with broad background plays an important role in planning and strategy, hence, the need for RI to various degrees at every level of the Regulatory profession. Traditional Regulatory Affairs objectives at the entry levels may be to file submissions and/or conduct audits, but these are intermediary accomplishments. The more important objectives are to secure product approvals and conclude efficient inspections. As careers in the profession evolve, RI additionally requires the application of continuous education in the business environment contributing to corporate objectives and patient care.

Ongoing education, such as the JHU Master’s program, combined with mentoring, professional meeting attendance, trade group participation and Regulatory/Compliance department planning participation at the highest levels in companies should be conducted as business partners rather than just a submission or compliance service groups.

With their respective expertise and knowledge, Regulatory professionals play a pivotal role in the success of the business and must be an educator for cross-functional training. They must be generous with information, training and as an internal consultant. Technical skills, people skills and altruism are required for this role to be most effective. In summary, efficient RI is a key contributor to strategic planning and program execution achieving the overall goals of

Angela Yu

compliance, optimized approvals and making safe and effective products to benefit the company, shareholders, and patients across the globe.

## Appendix A

### Senior Director Regulatory Affairs

#### Primary Responsibilities:

- Provides strong regulatory and scientific leadership to the overall development team to ensure that the development plan provides for optimal scientific positioning and highest regulatory probability of success
- Interprets and applies regulations in the creation of timely and innovative regulatory strategies for US and international markets
- Represents the regulatory function on cross-functional development teams
- Plans, prepares, and reviews submissions to regulatory authorities including FDA, EMA and other global health authorities to support the conduct of clinical trials and approval of marketing applications (including but not limited to Investigational New Drug (IND), Clinical Trial Authorization (CTA), New Drug Application (NDA), and Marketing Authorization Application (MAA). Works with regulatory submissions coordinator to develop submission timelines and work with cross-functional teams to planned objectives
- Serves as the primary point of contact with Regulatory Authorities and develops strong working relationships with counterparts of FDA, EMA, and other regulatory authorities
- Interacts with regulatory agencies, coordinating the preparation and supporting documentation as well as leading meetings and other interactions; maintains correspondence and other records of interaction
- Manages all maintenance plans for regulatory investigative and marketing applications for assigned projects
- Acts as regulatory expert for diligence of external assets as part of business development activities
- Monitors, analyzes, and disseminates intelligence on regulatory matters that may affect ongoing development programs
- Provides regulatory guidance and/or training to external departments
- Prepares and revises internal procedures for continuous improvement
- Manages activities performed by regulatory

#### **Source**

<https://www.linkedin.com/jobs/view/3447541114>

Retrieved on 2023, Feb 27

## Appendix B



# Executive Director, Regulatory Affairs Strategy

### Your Contributions (include, But Are Not Limited To)

- Responsible for the regulatory leadership of one or more development projects, including responsibility for global regulatory strategy, IND/CTA preparation, maintenance and update activities, interaction with and preparation for key milestone meetings with regulatory agencies
- Develops integrated global regulatory strategies to ensure the earliest possible marketing approvals by FDA, HPB, European and other regulatory authorities
- For commercial products, provides regulatory guidance on all aspects of life-cycle management including strategic label development, safety label changes and regulatory management of the product
- Provides strategic guidance on global regulatory requirements to management and project teams
- Provides guidance to senior management and department VPs and directors within Research, Preclinical and Clinical Development areas on all regulatory issues for the strategic development, planning, compilation and submission of IND/CTAs and NDA/BLA/MAAs
- Provides strategic regulatory guidance for global product development, proposed claims, clinical endpoint selection and labeling
- Represents the company by leading interactions and negotiations with regulatory agencies during all stages of development, registration and commercialization
- Manages preparation of all regulatory submissions (IND/CTA/MAA/BLA/NDA)
- Reviews and approves non-clinical and clinical study reports and regulatory submissions
- Actively engages with stakeholder groups to help shape science based regulatory decision making
- Acts as strategic regulatory liaison with partner companies
- Leadership of a team of regulatory strategy professionals
- Selects, develops and evaluates personnel to ensure the efficient operation of the function
- Other duties as assigned

### Source

<https://www.linkedin.com/jobs/view/3482191316>

Retrieved on 2023, Feb 27

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