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GLOBAL REGULATORY SOLUTIONS & SERVICES
AN ISO 9001 & 27001 COMPANY

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# CONNECT

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## Regulatory Centralization: The Game Changer for Life Sciences Companies

**REGULATORY:** INTELLIGENCE | AFFAIRS | LABELING | ARTWORK | SUBMISSIONS | COMPLIANCE AND AUDIT | MEDICAL WRITING | SOFTWARE | CONSULTING

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# What's Inside?



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# FOREWORD

**Dear Patrons,**

Greetings, and thank you for your continuous support.

We hope that you and all your loved ones are happy and healthy!

We are in the most crucial time of the year. Perhaps, it is the time is to build strategies, define market entry pathways, set targets, etc. At this juncture, being at the forefront of all things Regulatory is the need of the hour for any life sciences or medtech organization. Enabling you to put the best foot forward with end-to-end insights on global compliance best practices, we are pleased to bring to you the latest Issue of Freyr CONNECT, Volume 10.

With this Issue, we showcase all the Regulatory aspects of Life Sciences, from strategy to submissions to lifecycle maintenance. Starting with a specialized focus on the need for Regulatory centralization, this edition takes you through a thought leadership article on the EQUATOR Network. It highlights key perspectives on preparing Clinical Evaluation Reports and paperless Regulatory submissions in China, followed by eCTD 4.0 objectives.

In addition, we are happy to bring to you Freyr's increased hiring plans when the world is facing the challenge of job-market uncertainty. The plan clearly states how Freyr is aligned with customers' growing needs and employee well-being. It also highlights how Freyr has become a proven Regulatory partner, with its exclusive case studies and creative presentations of various global Regulatory aspects of Pharmaceuticals, Medical Devices, Cosmetics, and Food and Dietary Supplements.

To add it all up, we hope this Issue will give you a better scope to re-evaluate your Regulatory strategy and compliance best practices.

**Happy reading!**

Best Regards,

**Suren Dheenadayalan**

CEO

Center of Excellence
**Global Pharmaceutical Regulatory Services**

# REGULATORY CENTRALIZATION:

## The Game Changer for Life Sciences Companies

A streamlined business model leads to defined workflows and processes, thus enhancing productivity on any given day. Various factors, such as location, product(s), size, budget, global market share, etc., help businesses choose the best operating model to meet their predefined goals. For life sciences and pharmaceutical organizations, compliance with the competent Heath Authority (HA) regulations is a major influence on choosing the ideal business model. .

Companies involved in developing and marketing medicinal products need a foolproof Regulatory strategy. Over the years, such organizations have implemented Regulatory centralization in their functions to emerge successful. A lot depends on the efficient centralization of Regulatory departments, which in turn translates to best results in terms of cost, time-to-market, global market access, etc. In this context, let us understand Regulatory centralization and why it is the most-preferred operating model in the present times.

## What is Regulatory Centralization?

As mentioned earlier, pharmaceutical and life sciences companies must adhere to HA regulations and requirements. In such a scenario, harmonized processes gain prominence. Conformity with the prevailing mandates is possible only when processes and workflows are standardized, and everyone follows them in their day-to-day activities. Thus, a controlled approach is the key tenet of Regulatory centralization.

## Benefits of Regulatory Centralization

When everyone in the organization follows different procedures at each predefined stage, chances of missteps or errors increase at every phase, leading to delayed approvals or even rejection of applications.





With Regulatory centralization, the key functions are consistent at all times. Here are a few advantages of Regulatory centralization:

- **Harmonization** in processes and workflows.
- **Transparency in information-sharing,** which in turn leads to an **effective information management** system.
- An **enhanced operational model**.
- **Cost reductions** with **outsourced functions**.
- **Optimal use of Regulatory software and tools.**
- **Compliance best practices**.
- **Faster implementation of decisions**.

The below table explains the benefits in detail:

## The Advantages of Regulatory Centralization

| ADVANTAGES | DESCRIPTION |
|---|---|
| **Harmonization** | When all the processes are harmonized, everyone in a specific team adopts a common workflow, as the role of each employee is defined. As a result, companies can achieve maximum employee productivity. |
| **Effective Information Management** | Information management is a major factor that ensures the implementation of standardized processes across the organization. A capable and transparent communication channel is the ideal scenario. |
| **Enhanced Operational Model** | When there is harmonization in processes and information-sharing, each centralized procedure is predefined, which gives rise to an ideal business model. |
| **Cost Reductions** | It becomes easier to identify specific processes that can be outsourced, thus leading to reduced costs of the overall operational model. |
| **Optimal Use of Regulatory Software and Tools** | Most companies use digitized tools to ease out workflow, and these can be used optimally in a model that is based on Regulatory centralization. Automated workflows result in error-free and seamless processes. |
| **Compliance** | The ultimate goal of any life sciences company is compliance with the prevalent HA regulations. A centralized Regulatory system ensures the same and results in faster product approvals. |
| **Faster Implementation of Decisions** | Decision-making is more effective as there is an open communication channel throughout. This, in turn, makes the implementation process faster, which is ideal in the ever-evolving life sciences Regulatory field. |

Several Regulatory functions can be centralized for better results. These include Dossier Preparation, Publishing and Submissions, Lifecycle Management (LCM) of Medicinal Products, Regulatory Information Management, Chemistry, Manufacturing, and Controls (CMC), and Labeling and Artwork.

- **Dossier Preparation:** Whether it is an Investigational New Drug Application (INDA), a New Drug Application (NDA), an Abbreviated New Drug Application (ANDA), a Biological License Application (BLA), or a Marketing Authorization Application (MAA), every submission made to the HA is required to follow the International Council for Harmonization (ICH) Common Technical Document (CTD) format. A centralized Regulatory system ensures that there are customized CTD dossier templates for each type of drug and submission. This saves time and decreases any chances of errors.

- **Publishing and Submissions:** In continuation with the above point, customized CTD dossier templates, based on the application type, can help in managing submissions effectively. When it comes to metadata (the drug description that includes dosage form, strength, etc.), customized templates for respective HAs can help meet the specific requirements and prevent any delays. Regulatory experts can comprehend the prevalent regulations and guidelines in the metadata and follow the best practices for faster product registrations.

- **LCM of Medicinal Products:** Once a product is approved, the manufacturer/marketer needs to ensure effective LCM. This is accomplished through a series of Regulatory submissions like the Adverse Drug Event (ADE), change in formulation, change in suppliers, contact detail changes, etc. These submissions are best managed with the help of a centralized Regulatory system that has a standardized process in place. From planning the publishing to tracking the submission dates, no deadlines are missed, and this leads to seamless LCM activities.

- **CMC:** The content in the medicinal product dossiers/applications is changed whenever the manufacturers feel the need to reduce their operational costs. These post-approval CMC changes must receive prior approval from the competent HA. The company's post-approval Regulatory Affairs team creates and files the relevant submissions. Under the circumstances, the ideal Regulatory strategy is to have a centralized repository of various submission formats. This would save both time and effort.

- **Labeling and Artwork:** Most drug manufacturing companies rely on labeling tools to effectively communicate safety and efficacy information to the HA initially (during the development and clinical trial phases), and then, subsequently to the end users. A centralized labeling tool that is transparent and allows manufacturers to make real-time changes makes labeling activities much easier and Regulatory-compliant.

  Artwork is yet another function that can benefit much from a centralized Regulatory system. Compliant artwork that is content-driven and based on digital tools is the need of the hour! Automated artwork tools can help create and manage artwork activities well. Such tools also enable collaboration between teams and contributors, thus making artwork management seamless.

**Conclusion**

A decentralized business model creates confusion at each employee level in a life sciences company. Following the mandatory Regulatory norms becomes quite challenging in an uncontrolled business environment.

Small, mid-sized, and large life sciences companies must gear up (if they haven't already) and implement the centralization of all their Regulatory functions for enhanced efficiency. How can you accomplish the same? Get in touch with a proven partner like Freyr, who can help design the ideal centralization program and offer end-to-end support with your Regulatory activities.






# FINDING THE NEEDLE:

## The Challenges and Solutions of Effective Regulatory Intelligence (RI) in Pharma

If only Regulatory Intelligence (RI) was about the proverbial "Finding a needle in a haystack." A decent metal detector – or specialist database and search engine – and ping, ping, you have your updated guidelines on achieving Market Authorizations (MAs) for pediatric drugs in Brazil.

The challenge for Regulatory Affairs professionals is not finding needles but finding the right needle. Now that almost every article, white paper, guideline, and Royal Decree (seriously) is digitized and online, a combination of the right tools and strategies is needed to navigate a very complex and ever-changing Regulatory landscape. This article looks at these complexities, shares some of the challenges and questions Freyr consultants face, and offers some approaches you can take.

Try this! Search for 'Regulations' on PubMed, fda.gov, and ema.europa.eu. For the European Medicines Agency (EMA), you get 10,077 results relating to 'humans,' or 20,113, if you include literature sources. The United States (US) Food and Drug Administration (FDA) produces 20,098 entries, and PubMed is far more complex, with 3,201,321 results going back to 1,802 and including a vast array of publications, trials, and legislations, to name three (03) of the many sub-categories.

This leaves us with the central challenge of RI data being vast, diverse, time-critical, and complex.

## Humans and Machines

At Freyr, RI is the backbone of nearly everything we do, from publishing and submissions work to labeling and Periodic Safety Update Report (PSUR) support services. To achieve 100% compliance and zero recalls, it is necessary to know exactly what local Health Authorities (HAs) are looking for and what they have updated and released recently. The materials and sources must be found, read through, and considered in detail.

A quarterly review won't do. Auditors will not care if your PSUR was missing key data just because your RI sources were not updated when you compiled the report. Thus, one of the first criteria Regulatory professionals need to consider is just how "live" and "up-to-date" their data needs to be and how current their sources are.

Freyr is increasingly using AI "bots" and web crawler technology to provide near-real-time refreshing of its data sources. The same technologies can also scan, extract, and collate all the oncology-related updates in Southeast Asia to compile them into a report for a particular customer.

We have learned over a decade that the right tools, platforms, and sources are only half of the solution; human expertise and experience – Subject Matter Experts (SMEs) – are also vital. To achieve the result, SMEs ideally need to

be local, and Freyr works hard to establish either hubs or local representation. Where we cannot have our people, we set up strategic partnerships with in-country experts. We have branded this affiliate network, calling it FreyrX. Recent projects involving FreyrX include PSUR support, monthly scientific literature searching, Marketing Authorization (MA) and Marketing Authorization Holder (MAH) support, and MAH transfers in three (03) countries in the Far East.

At Freyr, we let humans and machines do what each does best. Machines are best at repetitive, scalable tasks, whereas humans can be prone to boredom and making errors. We use AI and bots for data collection from websites as well as for data monitoring; and humans – Regulatory professionals and SMEs - for decision-making and complex tasks such as data curation, interpretation, and deciding what to include and omit from a report.

## One Size Does Not Fit All

Different organizations have different needs. Therefore, for customers looking for purely RI services, we offer the following three (03) delivery models:

- **Infrastructure as Service Model** is typically best for larger organizations looking to cut back on their digital footprint and too many siloed software tools. Here we deploy Freyr IMPACT, tailored as per customer needs, including workflows, data sources, and reporting.

- **Managed Services Model** is a fully outsourced service where the customer stipulates when there is a need for reports or insights, whether or not it is a one-off project or a regular one – daily, monthly, quarterly, etc. – Freyr provides only data in this model.

- **Custom Solution** will typically be a combination of the above two. Often, Freyr takes on ad-hoc projects with urgent delivery timelines or special requirements, such as product launches in an entirely new market.

Whichever model suits you best, your in-house Regulatory team needs to find the right partner - one that has operational flexibility and can work the way they work. Many a times, we found that stakeholders of a new RI platform either only reluctantly use it or revert to web searches and spreadsheets if they feel that their needs haven't been met. This means that the partner must really understand their workflows and processes and be willing and able to configure – at the very least – their platform to accommodate these business needs.

A recent Freyr IMPACT implementation for a global pharma group with multiple stakeholders required a partnership development of a policy module with built-in workflows and reporting functions. Benchmarking and highlighting RI findings against their internal policies and SOPs were vital to the company. The good news for other customers is that new and innovative functionality developed for a particular configuration or customization effort invariably finds its way into a general release update.

## Don't Forget the Data!

RI pulls in data and insights from many sources. It is then processed, analyzed, and finally pushed out into a multitude of formats for consumption by different stakeholders. This could be the senior management looking for new markets to launch an existing drug or a safety team that needs to include every Rheumatology scientific paper and citation for inclusion in a PSUR report to ensure compliance in an upcoming audit.

Freyr understands that data has multiple dimensions, which we cover and curate based on client needs. The data can include geography, Regulatory functions, product types, and diverse HA sources, and then, the reporting can vary in terms of granularity level.

The business requirements are also complex. Effective dashboards are useful for users who need a clear overview of what is happening in their world. Then the functionality needs to offer the ability to almost endlessly sort, filter, and drill down to the individual paper, HA update, or data set that they need. Cross-reference can be done, based on the results, with their internal data.

At Freyr, we are wary of single tools claiming to provide a one-stop-shop type solution for RI. Think of the sources as well as the main free industry sites from the FDA, EMA, MHRA, and all the HA sites of individual countries. There is a myriad subscription sources from providers offering collections HA publications, white papers, citations, patent data, and more - Cortellis, Citeline, and Tarius, to name a few. Finally, companies have their own internal datasets, policies, local and regional market intelligence, TA data, and competitive commercial insights.

It means Regulatory teams need to be asking themselves two (02) fundamental data-related questions. First, what sources do they need in terms of geography, therapy area, and detail of coverage? Second, how granular and specific do they need their RI search results to be?

To meet these needs, we developed Freyr IMPACT, an open cloud-based architecture that provides secure access



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with easy-to-import capabilities. Therefore, searching records from free-to-source sites such as the EMA are as straightforward as pulling data from subscription services and other platforms. Our wide and growing library of industry Active Pharmaceutical Ingredients (APIs) enables this capability. Freyr not only believes that this platform approach is the right one, but also understands that we are part of a wider ecosystem that must be interoperated with alongside.

## Measuring Success

Whether you are looking for an entirely new platform, or you feel like outsourcing and paying for RI data that better suits your needs, or you want a mix of these two, the overall solution should deliver real and measurable benefits.

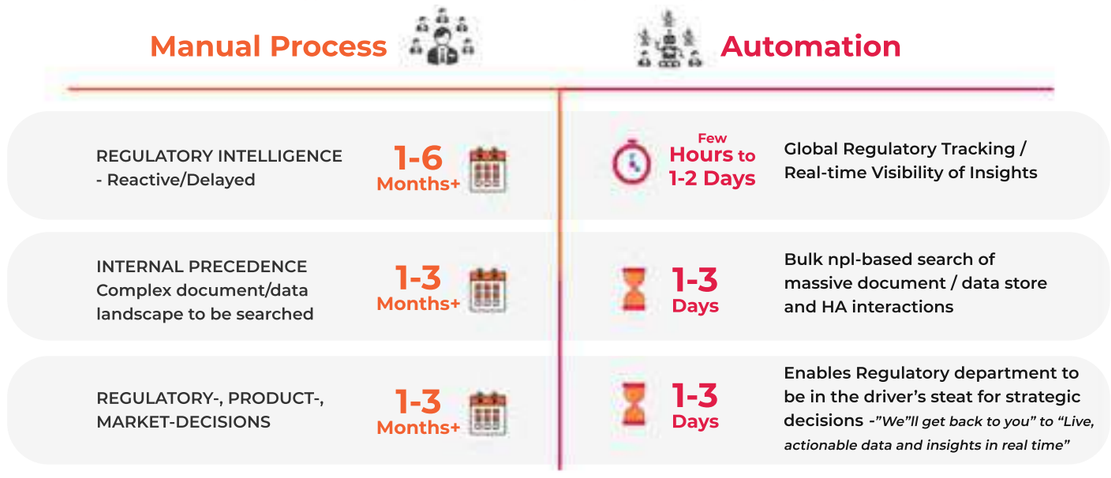
RI is by its nature, like other domains of Life Sciences, made up of disparate silos of data and processes. External databases output Computer System Validation (CSV) files, which in turn are filtered and sorted, invariably manually, and then reimported into other systems, and so on. In a recent Freyr IMPACT implementation, we replaced a complex end-of-life RI ecosystem made up of SharePoint applications as well as tools, including Excel, Word, and PowerPoint templates – over fifteen (15) separate tools, in all. Thus, our motive is not to add complexity but look to simplify, streamline, and speed up.

Your measurement and success criteria could be as simple as "We want to replace all our applications and data sources with one platform." We recommend you focus on the following success criteria while choosing the RI platform:

- Time efficiency
- Cost efficiency
- Better decision-making and collaboration through data centralization and shareability
- Workload reduction
- User experience

## The Results

We are going to end with a simple graphical showcase based on a real customer implementation and the value or savings that can be made. More importantly, the graph illustrates the possibility of achieving near-real-time global Regulatory compliance.




We have similar showcase examples in other service areas, including scientific literature review and labeling, with time and cost savings of up to 60%.

Our RI platform – Freyr IMPACT – reimagines and applies a smarter use of visualization, dashboards, analytics, and reporting. The most important aspect is partnering with our clients to understand their processes, business needs, and the data they want to access inside and outside the business, and finally, delivering a faster, more cost-effective solution.

For more information on technological solutions for Regulatory aspects, consult Freyr Digital.


# ENHANCING THE QUALITY AND TRANSPARENCY OF HEALTH RESEARCH (EQUATOR) NETWORK

The UK-based EQUATOR network that started in 2008 is a global initiative aiming at improving the trustworthiness and value of published health research by fostering transparent, accurate, and comprehensive reporting for reproducibility and applicability. It is an "umbrella" organization that brings together researchers, medical journal editors, peer reviewers, developers of reporting guidelines, research-funding bodies, and other collaborators who want to improve research publication quality.

## Advantages

- The EQUATOR enhances "the applicability of existing scientific evidence."
- This approach has enabled groups like the Cochrane Collaboration and the National Institute for Health and Clinical Excellence (NICE) to undertake systematic reviews and clinical guidelines.
- EQUATOR also helps research funders get the most out of the new data from the research they fund.

EQUATOR is a "long-term program of research support and enhancement" rather than a project with a predetermined duration. Ongoing EQUATOR initiatives are anticipated to boost the applicability and value of published findings in both clinical practice and research, in turn maximizing the Return On Investment (ROI) in health research.



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## EQUATOR Network Library

EQUATOR Network Library is a comprehensive, searchable database of health reporting guidelines being published since 1996. The library also has other resources and web links related to research reporting.

Complete, accurate, and transparent reporting is "integral to responsible research." Reporting guidelines are essential strategies for obtaining high standards in reporting health studies. Researchers/authors, editors, and peer reviewers must frequently and extensively apply reporting rules to reach their full potential. Research funders and Regulatory organizations must provide robust support to this endeavor.

## EQUATOR Toolkits

The EQUATOR network also offers practical help and resources to support:

- Writing an excellent research paper using reporting guidelines
- Selecting the appropriate reporting guideline for an article
- Deciding whether a research manuscript contains enough detail for its quality to be judged
- Developing a reporting guideline
- Supporting the journal in publishing transparent, usable research papers

The EQUATOR Network is currently working on methodological guidance for developers of reporting guidelines, examining barriers and facilitators to applying reporting guidelines inside journals, and establishing a tool for the critical appraisal of available reporting guidelines. The EQUATOR network of the Consolidated Standards of Reporting Trials (CONSORT) group enhances reporting. EQUATOR pertains mostly to reporting rather than design and quality evaluation; the positive implications of a better study design are likely provided in the table below:

### EQUATOR Reporting Guidelines for Major Study Types

| Name of the Guideline | Applicable to | Type(s) of Study design | Applicable Sections of the Manuscript |
|---|---|---|---|
| PRISMA | Systematic Reviews and Meta-analyses | Systematic Reviews/ Meta-analyses/ Reviews/HTA/Overviews | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results<br>• Discussion<br>• Other Information |
| CONSORT | The Parallel Group Randomized Controlled Trials | Clinical Trials, Experimental Studies | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results<br>• Discussion<br>• Other Information |
| STROBE | Observational Studies in Epidemiology | Observational Studies | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results<br>• Discussion<br>• Other Information |

| Name of the Guideline | Applicable to | Type(s) of Study design | Applicable Sections of the Manuscript |
|---|---|---|---|
| MOOSE | Meta-analysis of Observational Studies in Epidemiology | Systematic reviews/ Meta-analysis/ Reviews/HTA/Overviews | • Background<br>• Search strategy<br>• Methods<br>• Results<br>• Discussion<br>• Conclusion |
| STARD | Standards for the Reporting of Diagnostic Accuracy | Clinical Trials, Diagnostic and Prognostic Studies, Experimental Studies, Observational Studies | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results<br>• Discussion<br>• Other Information |
| TRIPOD | Reporting of Studies Developing, Validating, or Updating a Prediction Model, whether for Diagnostic or Prognostic purposes | Diagnostic and Prognostic Studies, Observational Studies | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results<br>• Discussion<br>• Other Information |
| SPIRIT | Defining Standard Protocol Items for Clinical Trials | Clinical Trials, Experimental Studies, Study Protocols | • Administrative Information<br>• Introduction<br>• Methods<br>• Ethics and Dissemination<br>• Appendices |
| CARE | For Completeness, Transparency, and Data Analysis in Case Reports and Data from the Point of Care | Observational Studies | • Title and Abstract<br>• Introduction<br>• Patient Information<br>• Clinical Findings<br>• Timeline<br>• Diagnostic Assessment<br>• Therapeutic Intervention<br>• Follow-up and Outcomes<br>• Discussion<br>• Patient Perspective<br>• Informed Consent |
| AGREE | Reporting of Clinical Practice Guidelines | Clinical Practice Guidelines | • Scope and Purpose<br>• Stakeholder Involvement<br>• Rigour of Development<br>• Clarity of Presentation<br>• Applicability<br>• Editorial Independence |



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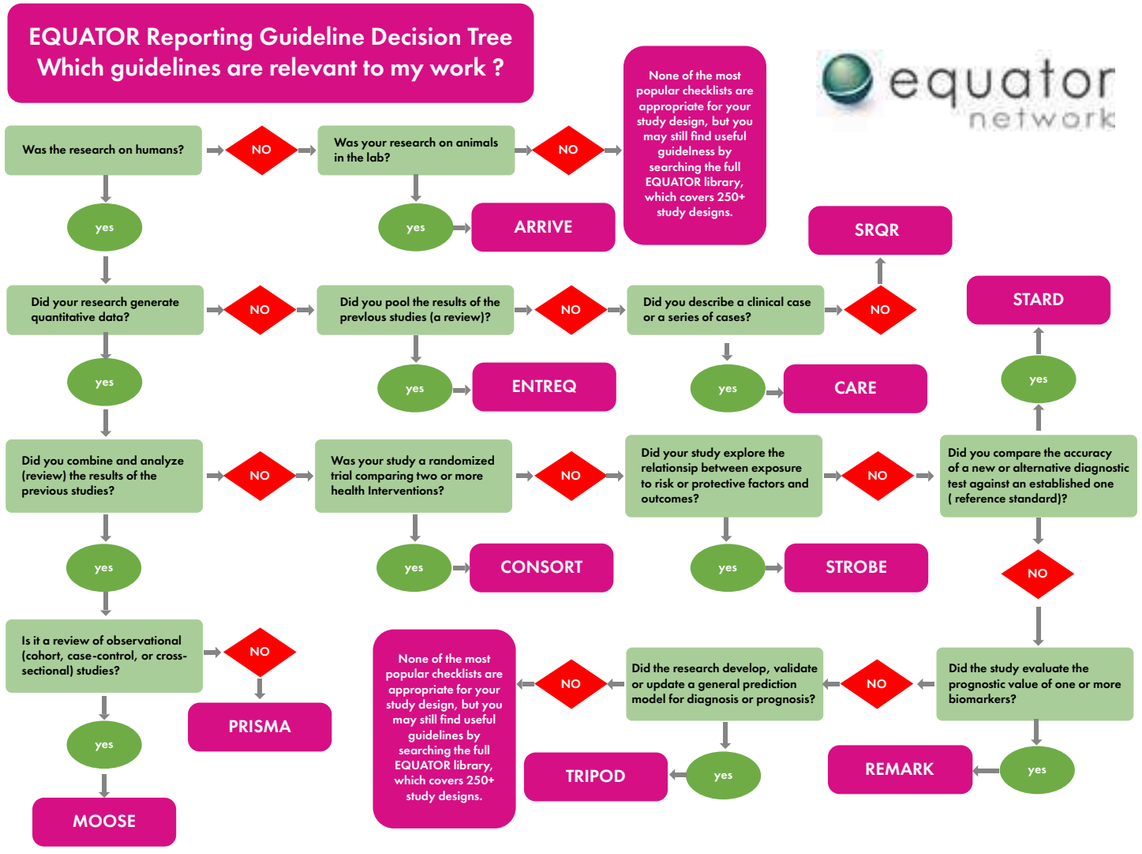
| Name of the Guideline | Applicable to | Type(s) of Study design | Applicable Sections of the Manuscript |
|---|---|---|---|
| SRQR | Reporting of Qualitative Research Studies | Qualitative Research | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results/Findings<br>• Discussion<br>• Other Information |
| ARRIVE | Reporting Any Area of Bioscience Research using Laboratory Animals | Animal Pre-clinical Research | • Title and Abstract<br>• Background<br>• Objectives<br>• Ethical Statement<br>• Housing and Hhusbandry<br>• Animal Care and Monitoring<br>• Interpretation/Scientific limplications<br>• Generalizability/ Translation<br>• Protocol Registration<br>• Data access<br>• Declaration of Interests |
| SQUIRE | Quality Improvement in Healthcare | Quality Improvement Studies | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results<br>• Discussion<br>• Other Information |
| REMARK | Tumour Marker Prognostic Studies | Diagnostic and Prognostic Studies, Observational Studies | • Title and Abstract<br>• Introduction<br>• Materials and Mmethods<br>• Results<br>• Discussion |
| CHEERS | Economic Evaluations of Health Interventions | Economic Evaluations | • Title and Abstract<br>• Introduction<br>• Methods<br>• Results<br>• Discussion<br>• Other Information |

## Decision Tree




*Source: equator-network.org*

The decision tree has significantly impacted the reporting quality of numerous forms of medical research. Specifically, it has been underlined that modifications must be made to implement the guidelines. There are obstacles to effectively expressing the benefits and drawbacks of compliance with rules. Authors are responsible for ensuring that the proper guidelines are followed when reporting research results.

Another result of reporting guidelines is the exclusion of research reports. Presently, some research does not get published because the rules make it abundantly evident when a study has flaws or does not reach the desired conclusion. In this instance, reporting requirements prevent inferior research from being published in high-impact publications and then cited (high-impact journal articles primarily cite articles from the same or other high-impact journals).

### Conclusion

Establishing reporting guidelines in medical research is aimed at providing authors with a roadmap to follow, one that facilitates transparency, uniformity in reporting, and a more objective evaluation of the trustworthiness of the results. Even if this goal has been accomplished in part, it is critical to maintain a healthy dose of skepticism whenever evaluating any scientific study. The editors, authors, and reviewers may need to meet to figure out how to use the various reporting requirements and provide recommendations.

For compliance best practices, reach out to Freyr.



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# REGULATORY AFFAIRS STAFF AUGMENTATION: EXTERNAL EXPERTISE FOR YOUR INTERNAL SUCCESS

Regulatory Affairs Staff Augmentation is a trusted and proven staffing model that infuses the right talent at the right place at the right time into the life science organization's flexible workforce plan.

It is intended to provisionally enhance the internal team with expert resources cost-effectively and flexibly to meet the specific Regulatory Affairs staffing needs and solve the complex issues around urgent project deadlines and critical skillset shortages.

In this era of unprecedented market uncertainty, where we are witnessing hiring freezes and corporate layoffs, life sciences organizations need to be more flexible and agile than ever to adapt to the changing market dynamics and resource needs.

To this end, the evaluation of "flexible staffing models for talent management," as the range of staff composition varies according to specific needs, becomes necessary. It must meet both long-term and short-term staffing needs and provide a strategic framework for adding and removing staff in an efficient, timely, and cost-effective manner.

Staff Augmentation has established its importance over the years, and there are numerous ways and benefits to achieve this.

## Benefits of Regulatory Affairs Staffing Outsourcing


## RA Staffing Models for Life Sciences

**Functional Service Provider (FSP) Model**

In this type of staffing model, pharmaceutical companies are flexible in choosing the staff as per their requirements. If the company wants full-time staff for a project, it can choose to contract out staff on a full-time basis till the work is done. However, if the company wants partial staff for a specific task, it can choose to contract partially. This model gives the organization flexibility to pick and choose which services to outsource to which FSP partner based on its expertise. Hence, companies can either outsource the staff for all RA-related tasks, such as submissions, drug safety, management, and HA monitoring, or a few tasks, such as validation and SOP writing.

**Types of FSP models:**

- Full-Time Equivalent (FTE) Staffing Model: This is a comprehensive analytical staffing strategy that allows pharmaceutical companies to have highly skilled staff with Regulatory expertise. In this model, the number of working hours required to complete a project is considered rather than the number of working staff. Through this model, experts can provide their expertise across the globe as well as across different time zones. This approach towards staffing is beneficial when there is a short, or mid-term need for staff due to time-bound projects.

- Fixed Price (FP) Model: In this model of staffing, the budget of the contract is agreed upon in advance, regardless of the time and expense. The organization knows the total cost for finishing all the assigned tasks to the employees. This model also allows organizations to control costs and risks. Hence, the vendor is obliged to complete the contract.



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| Pros | Cons |
|---|---|
| A single contract can support many projects for the company. | Staff management burden on the organization as the expansion of the team requires oversight and management. |
| Improves administrative transparency and reduces associated costs. | There is a chance of process handoff issues if the various FSPs are involved in multiple RA requirements. |

**Full-Service Outsourcing (FSO) model:** In this type of staffing model, pharmaceutical organizations usually outsource either majority of the research-oriented tasks or the whole research work to RA experts. Contracts are more unit-based rather than FTE-based in the FSO. In this model, organizations outsource full responsibility to the staffing partners within the scope of the preferred relationships with the vendor. Hence, organizations outsource the entire drug development process to a full-service provider.

**Type of FSO Model:** Unit-Based Staffing Model: In this model, the organizations pay for the units of work which are delivered by the staff. The model is used where the volume of work or tasks flexes up and down for a specific period. The hours per unit and volume of work are predictable, well-established, and understood. Resources are carefully measured and utilized in this model.

| Pros | Cons |
|---|---|
| Reduces management burden on the organization as the whole work is outsourced at once. | Contracts per project may reduce efficiency, as the staff is sometimes not ready for add-ons. |
| The workforce requires constant change, and the organization is flexible in bringing additional staff to address the business needs. | No control of the organization over staff, as the staff is outsourced, and the internal manager might not be aware of employees' specialties. |

Having a Staff Augmentation Model in place facilitates flexibility, control, and cost-effectiveness in the system. Whether you are looking for Regulatory experts to help in your business or want to scale up the expertise of your existing RA team, we have global reach and Regulatory expertise to meet your demands to eliminate skill gaps and reinforce your projects. Contact Freyr.

# IN A WORLD OF UNCERTAINTY, BE CERTAIN OF YOUR CAREER WITH FREYR – *WE ARE HIRING*

In today's challenging and uncertain times, many organizations are laying off their employees through company-wide restructuring plans. With companies announcing that they would be letting go ~**20%** of their workforce by June 2023, speculations on job security have reached an all-time high.

On the other hand – contrary to all the market trends – Freyr, one of the largest, global, Regulatory-focused solutions and services companies, announced that it is increasing its hiring plans because of the need it sees from its customers and its plans to invest in emerging technologies.

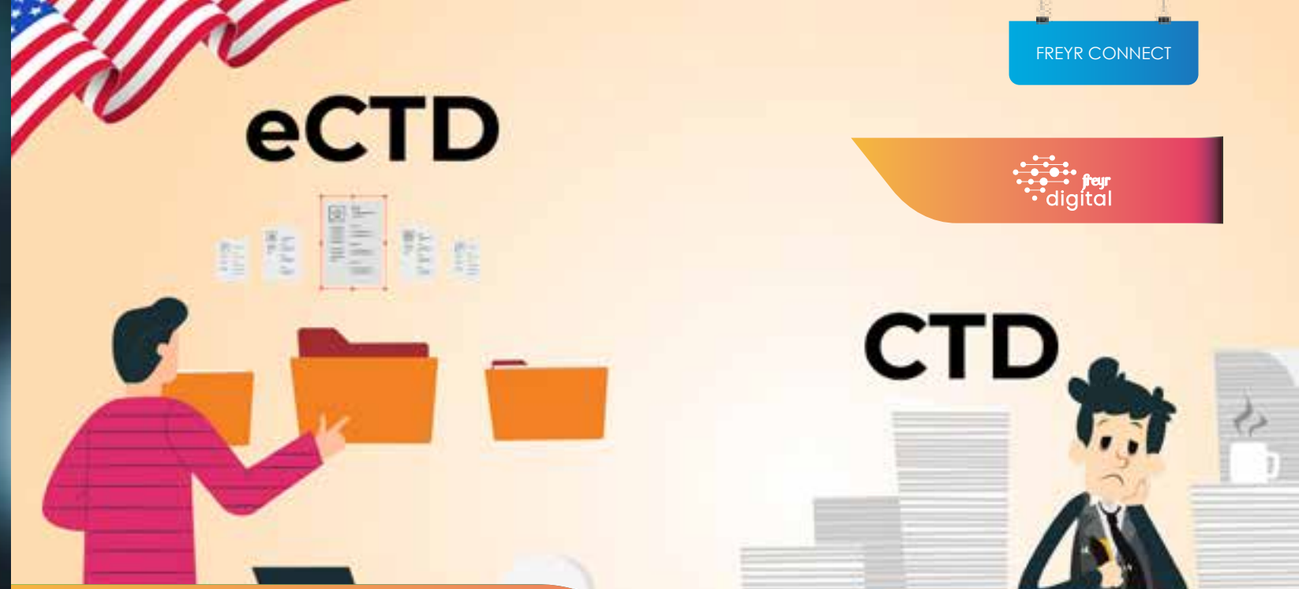
Here is a quick snapshot of the hiring trends at Freyr:

- In the past six (06) months, there has been a 32% increase in Freyr's workforce.
- Freyr is aiming for a 100% growth in employee count in the upcoming year.
- By 2030, Freyr is aiming at becoming a Regulatory powerhouse with 15k+ professionals.

"Freyr is reimagining Regulatory services. "And there's never been a better time than now to hire," says Suren Dheenadayalan, the Chief Executive Officer (CEO) of Freyr. "Freyr is looking for individuals who are dedicated, talented, and passionate about their work. We encourage interested candidates to visit our website to learn more about the available opportunities," he added.

To know more about current opportunities, visit - https://www.freyrsolutions.com/careers/current-positions






# eCTD AND CTD FILING PROCEDURES FOR THE US AND CANADA: CHALLENGES AND HOW TO AVOID THEM

A multitude of challenges are faced by Regulatory departments since the move from paper-based to eCTD submissions happened, and that continues around the world. Most of the life science companies are struggling hard to keep up with the USFDA standard for using the eCTD format and meet the specified deadlines. The compulsion of the eCTD format in the US and Canada has enhanced the submission procedure and made it easier by bridging the gap between time and the market, which in turn is helping to minimize expenses on electronic submissions to the pharmaceutical industries. Though the benefits offered in this kind of submission are many, it is still quite challenging for the life science companies. Some of the setbacks that are faced in the USFDA eCTD submission publishing are discussed below:

- **Annual Reports**: The eCTD doesn't easily allow the annual report to be authored as one document for this approach, which lead to validation errors and issues and can set the application up for a rejection.
- **Clinical Study Reports (CSRs)**: The preparation of a CSR allows the reviewers to easily navigate and track so that even if the section is updated the report need not be replaced.
- **Hyperlinking**: One of the most common issues that publishers face due to typographical errors during document authoring is the attempt to hyperlink a section which might not exist at all.
- **Report Numbering** : When a study data scan takes place across multiple reports, it is important to insert a unique study ID to ensure that if there are any cross-references in the summary sections referring to the content, they are clearly set and easily identified.

## Challenges Involved in eCTD Submission Management

Pharmaceutical companies are under immense pressure, dealing with the logistical challenges of managing (IT) applications and systems to submit error-free documents within stringent timelines. This becomes an even bigger challenge when the costs increase or cause delays to the approval, and at worst result in the receipt of a Refusal to File (RTF). Even though the publishers might be highly experienced, Regulatory publishing teams typically encounter the following problems:

- **Conflicting Information for Publishers:** Depending upon the experience of the Regulatory team, critical information required in the publishing process is necessary to showcase to the publishers but might also be ambiguous, even though it is included in the content of the submission. For example, eCTD submissions rely heavily on the use of metadata, which are included in critical capacities such as folder paths in the final eCTD, which provides additional information about the elements. An easy way to prevent potential rework is by using well-designed procedures and forms, by providing this information to the publishers at the same time as the source files.
- **Inappropriate Granularity:** An eCTD publishing document, produced using a quality template with the appropriate level of granularity, has a huge effect on publishing. On planning to submit a section as multiple leaves, they should be supplied as the corresponding number of source documents rather than being complied into a single file to be segregated at the time of publishing. Every source document that must be sent back for reformatting is just another small opportunity for the project to be delayed.
- **Inappropriate Submission Validation Process:** An inappropriate validation may arise if there are any system or publisher errors while downloading the files. The main benefit of the eCTD is the ability to check its technical conformity upon submission by the applicant or the agency.
- **Incorrect Document Versions:** To complete publishing a submission with the right document or the document version with more intensive QC reviews is the goal. Stringent procedures are required for the groups that use file shares for publishing repositories. Publishing teams that use a closed Document Management System (DMS) in their publishing workflows generally avoid this issue as only those versions marked as 'approved' can be published.
- **Nonlinear Delays:** Not only are delays sometimes inevitable, but they can also result in adverse effects on submission timelines. Given a situation, the slot for publishing the project cannot be moved back by even a day or two due to delay of other projects, then it is bound to extend the delay even further.
- **Short Publishing Timelines:** Due to an exceedingly long submission process, time lost in the previous stages is often expected to be recovered during publishing. One of the most time-saving techniques of leveraging the risk in the submission process is by independently publishing the modules or sections of the submission.
- **Source Document Incompatibility:** During the process of scanning source documents to automatically extract information differing from Word/PDF file types and tools from different vendors, source files are scanned and elements such as internal document links, existing bookmarks, and heading/outline styles are processed and collected into the software's database to create bookmarks and hyperlinks in the published output. If source files are not set up as per the publishing software expectancy, this process might take extra time, and post-publishing, manually adding navigational elements may be required.
- **Technical Problems with Legacy Files:** Although in the most critical times legacy files may have been printed without any issue in the past, electronic publishing is extremely efficient in highlighting technical issues. The issues are generally not difficult to solve but are time-consuming and cause a delay knowing the fact that the most important tool in the publisher's toolbox is time. Such a situation can be addressed well beforehand if publishing submissions teams use incremental builds to catch up on time that are causing issues in the process.
- **Quality Control:** By the time publishing begins at the right time, the source file content should be final and approved, as changing a document during the publishing process can extend the project timeline even further. A few of the quality control points that needs to be set clear throughout the project to ensure that they are appropriate to the task to make an eCTD submission are:
  - Mandatorily quality check all source documents before they enter the publishing workflow.
  - Independently review the submission structure (the assembly/outline) within the publishing software prior to any publishing.
  - Review all published PDF files on the screen.
  - Check bookmarks and links in published PDF files.
  - Always validate the eCTD submissions prior to any submission.



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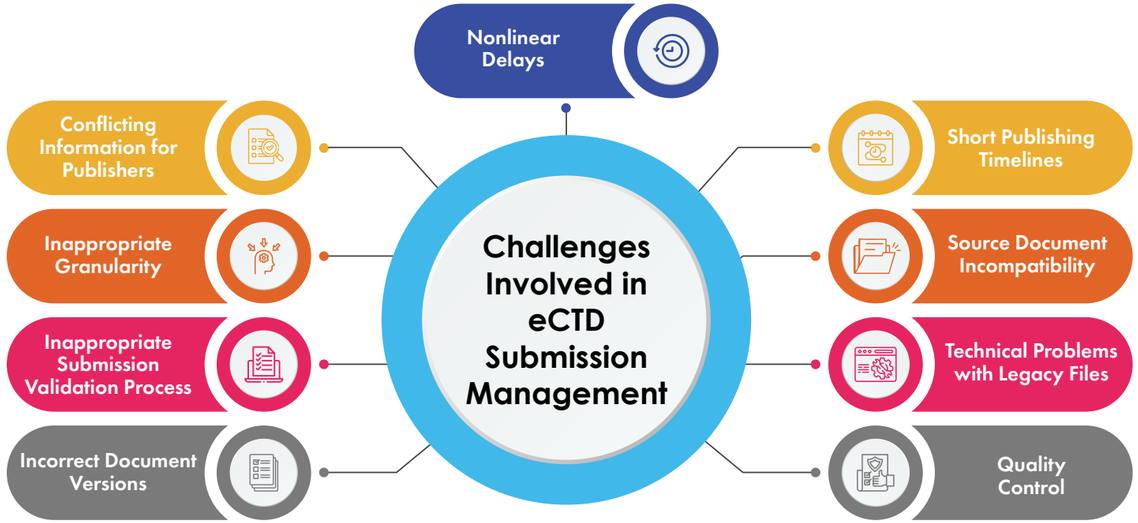
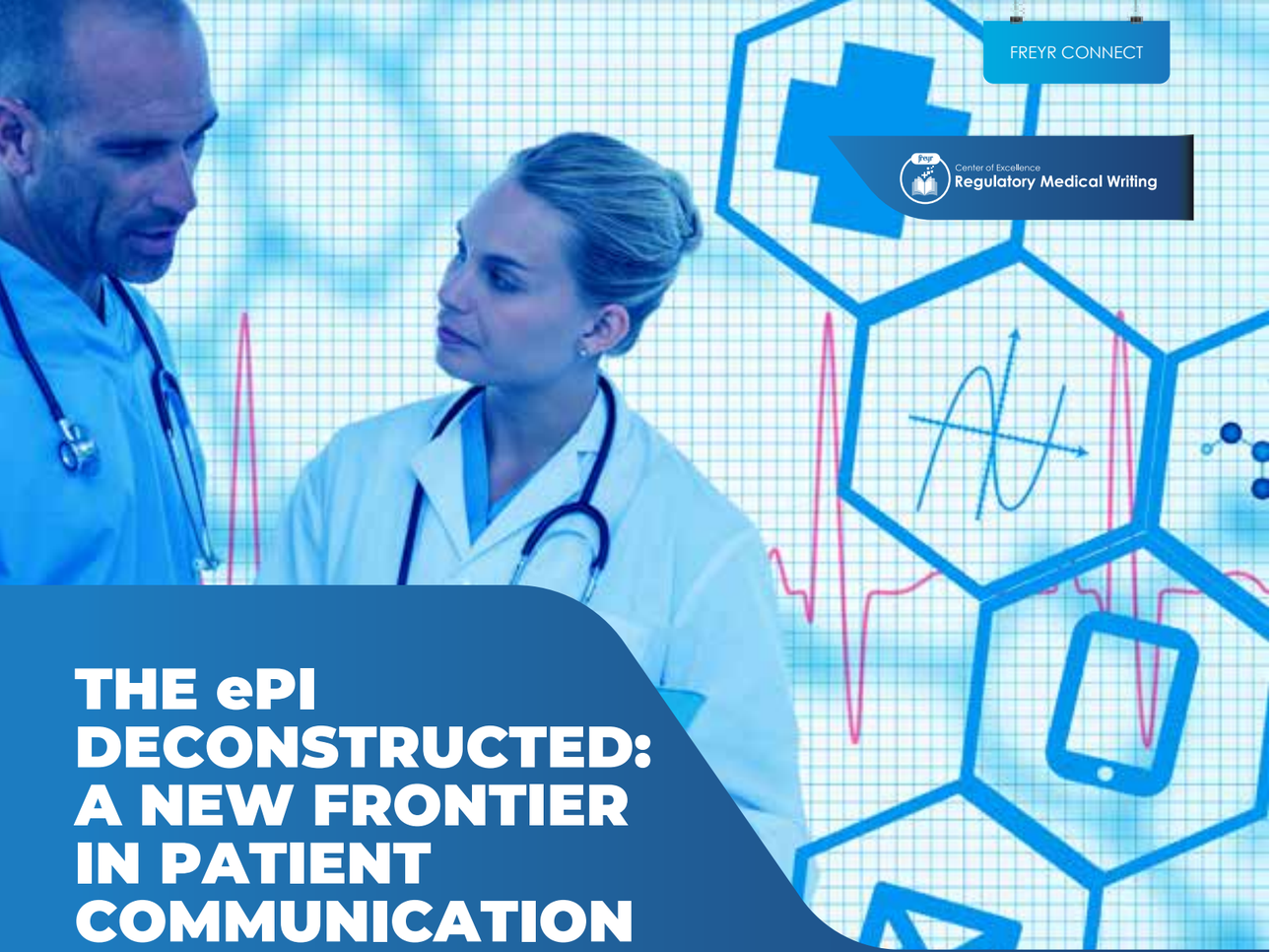



Freyr Digital has a solution to all the challenges listed above for your organization's publishing and submission-level activities. Freyr SUBMIT PRO, a cloud-hosted eCTD software, makes it easy for our Regulatory operations team and eCTD publishing specialists to provide additional support when you need it the most. Freyr ensures efficient, timely submissions through our eCTD software supported by an in-built eCTD viewer and validator.

Would you like to learn more? Request a demo.




# THE ePI DECONSTRUCTED: A NEW FRONTIER IN PATIENT COMMUNICATION

Pharma manufacturers face several challenges when it comes to labeling, both in terms of design and production. As the label size tends to increase every year, adding clarity, consistency, and appeal is becoming increasingly difficult. Pharmaceutical manufacturers also face new legislative and Regulatory requirements, on top of the existing challenges. The information that patients need, thus, can sometimes get lost because there is simply no space on the label. This is where electronic Product Information (ePI) comes in. It is essentially a digital version of the Product Information (PI).

The ePI opens new doors to include extremely creative story telling on a pharmaceutical pill or capsule while meeting all the Regulatory requirements. It is a significant step in moving the pharmaceutical industry away from pages of printed text on the back of prescriptions and Patient Information Leaflets (PILs) towards highly engaging, interactive digital communication, potentially replacing entire leaflets.

## The Global Scenario

In Belgium and Luxembourg, the ePIL pilot is now a collaborative effort between both the pharma industry and government bodies. The European Commission (EC) supports and encourages it. During the proposed two (02)-year-long pilot, the print leaflets of a variety of prescription drugs confined to inpatient use and commercialized in Belgium and Luxembourg are not included in hard copies but can be checked online via reputable websites.

In Japan, to formally adopt eLabeling, the Pharmaceuticals and Medical Devices Act was amended. Paper labeling was replaced, and a necessary framework was added to provideaccess to the most recent and up-to-date labeling information to all Healthcare Professionals (HCPs).

European regulators have established high-level, key principles that will direct future work in establishing common electronic standards, processes, governance, etc., which will in turn profit patient safety. The principles were developed in collaboration with other key stakeholders.

On August 19, 2019, the Health Sciences Authority (HSA) in Singapore published the electronic labeling guidance. In the guidance, eLabeling refers to Product Information (PI), including Package Insert (PI) and Patient Information Leaflet (PIL); it is made available electronically via a barcode or web address on the packaging, which ties to a safe web system disclosing the product data in a digital format.

The Taiwan Food and Drug Administration (TFDA) publishes labeling information on its website. In 2016, the TFDA released an app that allows users to contact medication manufacturers using a mobile device.

Furthermore, trade organizations in certain Asian nations, including Malaysia and Thailand, have begun to form eLabeling collaborations and want to further explore eLabeling ideas with their respective Health Authorities (HAs).

The United States Food and Drug Administration (USFDA) has shown a keen interest in using digital platforms for prescription drug labeling meant for doctors and pharmacists for a long time, and we may see electronic PIs being adopted soon.

## Moonshots for ePI in Pharma Companies

- To enhance content reuse, govern the way reused information is updated, and provide a deep degree of transparency, and automated output without any post-translation formatting or Direct-to-Patient (DTP). Pharmaceutical firms can employ content management systems to create, manage, translate, and publish PIs. This might ultimately lower cycle times by 30-40% and translation expenses by 30%.
- The translation and submission of PIs have traditionally been handled via Word and PDF formats, but ePI would be shared and updated in an XML format. Modern Computer-Assisted Translation (CAT) tools are already well-suited to handle this file type, and thus, translation agencies should not have much difficulty handling the texts in the new format. The same holds good with all developments relating to product information.
- Improving compliance with dosage regimen via interactive (Digital Therapeutics) DTx solutions plugged into the ePI.
- With the ePI, pharma companies can create a dynamic and interactive PIL that engagingly delivers important PI and advice. The ePI also allows product managers to provide innovative solutions with added value, with the inclusion of video, games, 3D visuals, animation, online tests, questionnaires, animated graphic sequences, interactive tools, and more. The possibilities are endless, and pharmaceutical companies can tailor the contents to align with the product, diagnosis, or situation.

For companies with extensive product lines, the ePI might just be the key to reducing product complexity and using pharma salesforce resources more efficiently.

## For HCPs

- Use cases include instant access to detailed pharmaceutical administration instructions, focused ePI searches for specific medical illnesses and treatments, and notifications for revisions to safety information.
- By using ePI, medication information is presented to health professionals clearly and concisely so that they can efficiently educate, prescribe, and administer medication.

## For Regulators

- ePI will improve the efficiency with which the PI is managed throughout Regulatory procedures. The ePI might remove several manually performed processes and inconsistencies, which are possible causes of mistakes, by allowing PI updates to be made throughout all applicable PI annexes and products.

## For Patients

- With the ePI, there are important opportunities at play, such as cross-border prescription, making medicines easily shareable between member-states, which was of particular importance during the pandemic. Products could be shipped from Country A to Country B, and a patient would have access to the PI in their language. Translations can appear “automatic,” providing the right information to people traveling or emigrating , thus removing the need to have multi-language packages for countries like Belgium, which in turn leads to PILs that are hardly readable.

- In a world becoming increasingly digitized, the ePI could also be used alongside other strategies such as e-prescriptions and smartphone applications. For example, a barcode on the side of a carton or packet could make the most up-to-date ePI available immediately on any smartphone, in any language.

## Challenges

Multiple questions need to be answered to ensure that the system is brought to a place where the ePI becomes a success, and then, gradually, a norm. A few of them are as follows:

- What risks do we face while running two (02) parallel systems globally – one of the ePI and one of the traditional paper package leaflets/SPC – that will have to be simultaneously maintained, at least in the short term? How long will the transition period be?
- If it is considered local integration for eg., how long will it take to harmonize the various national efforts to produce an EU-wide ePI and portal?
- Is there a risk of leaving behind patients who are not technologically savvy on out-of-date product information?

## On the Future of Electronic Information

Digital imaging enables pharmaceutical manufacturers to present a whole array of additional, often interactive, information directly on the pill or capsule label. The pill or capsule itself could be equipped with digital imaging technology, for example, by attaching a tiny camera to the it. The patient would then take a photo of the pill or capsule, which is captured on a low-cost HD or OLED digital display. This creates an interactive experience by linking the patient to the PI. The interactive screen could be arranged anywhere on the label and could be designed to fulfill all Regulatory requirements.

Learn more about ePI and compliance best practices. Get in touch with Freyr.



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# TOP 10 FAQs ON THE Q-SUBMISSION PROGRAM

## 1. What is the FDA Q-submission Program?

Q-submission FDA program refers to the system that tracks the collection of interactions with the FDA. It helps manufacturers of Medical Devices and in vitro diagnostics (IVDs) to obtain feedback from the FDA on the Regulatory processes and requirements for the product during its development.

## 2. What is the Difference between a Pre-submission and a Q-submission?

Pre-submissions or Pre-subs form a subset of Q- subs. They are only interchangeable when referring to Pre-subs. Other types of Q-subs, as per the updated final guidance released in 2019, are:

- Submission Issue Requests (SIRs)
- Study Risk Determination
- Informational Meetings

Other Q-sub types are technically submitted under the Q-sub process but have their guidance documents -PMA Day 100 Conference, Agreement and Decision under the United States Food and Drug Administration Modernization Act (FDAMA) Meetings, breakthrough device program submissions, Safer Technologies Progam (SteP) and accessory classification requests.

## 3. Is it Mandatory to have a Pre-sub Meeting with the FDA before a Pre-Market Notification?

The program is **completely voluntary** on the part of the submitter. However, early interaction with the FDA on device design, technology characteristics, predicate device, and its substantial equivalence for careful consideration of the FDA's feedback may improve the quality of subsequent submissions, transparency, shorten total review times, and facilitate the development process for your device.

## 4. What is the FDA Q-submission Fee?

The FDA **does not** charge any fee for Q-submission meetings.

## 5. What are the Contents of a Q-sub Application for Requesting a Meeting?

First and foremost, all the Q-sub documents must be in the English language. The content for Q-submissions as per the Q-submission guidance, includes:

- Cover letter
  - Contact information
  - Q-sub type (only one Q-sub type to be included in each submission)
  - A draft agenda proposing topics to be presented and the estimated time for each agenda item
  - Meeting format (in-person or teleconference)
  - Three or more dates or times when you're available to meet
  - Planned attendees, including their position, title, or affiliation
- Purpose
- Product description
- Proposed indications for use
- Regulatory history

## 6. How Many Pre-subs Can I Submit for a Single Submission?

There is no limitation on the number of pre-submissions for a single device submission. However, you cannot do more than one pre-submission at the same time. You need to wait for the FDA's feedback on the previous pre-submission before doing the next pre-submission

## 7. What is the Next Step if the FDA Rejects My Pre-submission Request?

If the acceptance review by the FDA determines that the request does not qualify as a Pre-submission, the submitter will receive a notification of this decision along with the reasons for refusal.

The submitter may respond to a Refuse to Accept (RTA) notification by submitting **additional information** to the Document Control Centre (DCC), which will be logged in as an **amendment to the Q-Sub.** Within fifteen (15) days of receiving the newly submitted information, the FDA staff will **conduct the acceptance review again.** The subsequent acceptance review will assess whether the new information makes the submission complete, according to the Acceptance Checklist.

## 8. Does Pre-sub Guarantee Approval or Clearance of Submissions?

Review of information in a Pre-Sub **does not guarantee** approval or clearance of future submissions. Additional questions may be raised during the review of a future submission when all information is considered as a whole, or if new information has become available since the Pre-sub.

## 9. Does the FDA Modify its Feedback on Pre-sub under any Circumstances?

Modifications to the FDA's feedback will be limited to situations in which the FDA concludes that the feedback given previously is not addressing important new issues that have emerged since the time of the FDA Pre-submission, and that is materially relevant to the determination of a reasonable assurance of safety and/or effectiveness, substantial equivalence, or other relevant Regulatory decisions.



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## 10. Is the submission of Meeting request for a Pre-sub Same for Single Entity Devices and Combination Products?

Requests for meetings regarding a combination product should be submitted to the lead center for the product, following that center's corresponding processes. Accordingly, Q-submissions should only be submitted for device-led combination products assigned to the Center for Drug Evaluation and Research (CDRH) or to the Center for Biologics Evaluation and Research (CBER). If the classification or center assignment for a medical product is unclear, the submitter should submit an RFD or Pre-RFD to the Office of Combination Product (OCP), and then submit their meeting request to the center determined to be the lead center.

In case of any more queries and assistance for Q-submissions or device registration in the US, you can reach out to a Regulatory expert like Freyr.

Stay informed, stay compliant!


# THE SIGNIFICANCE OF THE DRUGS AND MAGIC REMEDIES (OBJECTIONABLE ADVERTISEMENTS) ACT, 1954.

India is a diverse country with a rich heritage and stories of miraculous healing of life-threatening diseases with magical powders, talismans, magical shields, etc.

Taking advantage of these belief systems, in recent years, a shift in marketing strategies by industries has been observed. There is a rise in toxic and misleading advertisements, which are flooded in every kind of media, suggesting miraculous healing of diseases and toxifying the minds of people and their emotions.

To protect the interests of innocent people from being exploited, an Act was imposed by the Indian government on drug advertisements to prohibit the use of "magical" terms for matters connected therewith. In India, this is done through the Drugs and Magic Remedies (Objectionable Advertisements) Act, 1954. The objective of the Act is to prevent self-medication and the practice of self-treatment by the general public and to restrain such advertisements, which have caused unfortunate incidents.

## The Act is divided into 16 Sections:

- Sections 1 and 2 describe general information such as the title or definition used in the Act for the so-called "magic remedy".
- Sections 3 to 6 describe the prohibitions under this Act.
- Section 7 briefs about penalty.
- Section 8 briefs about provisions for powers of entry or search and seize by state government authorities.
- Section 9 covers the offenses by companies.
- Section 10 details punishable jurisdiction for offenses.
- Section 11 is aimed at deemed officers.
- Section 15 focuses on powers to exempt from the application of this Act.
- Section 16 has provisions to make rules under the Act.

Sections 3 to 6 are of the prohibitions under this Act, which clearly state the kind of advertisements that are prohibited:

1. Miscarriage/prevention of conception in women.
2. Enhancement of sexual improvement and pleasure.
3. Correction of menstrual disorder in women.
4. The diagnosis, treatment, remedy, or prevention of any disease/condition/disorder specified under the schedule or the rules of the Act.

According to Section 4 in the Drug and Magic Remedies Act, no person shall take part in the publication of an advertisement that contains any false claim related to the original drug. A total of fifty-four (54) diseases/disorders are listed under Section 4(d), which are of serious nature, and prohibit advertisement, suggesting the use of the drug to cure, diagnose, treat, mitigate, or prevent any disease, disorder, or condition.

As per Section 7, if any person acts against the Act, they will be subjected to a penalty. In the first case, it can be only six (06) months or more of imprisonment, or can be a fine, or both. During the conviction, it may result in one (01) year of imprisonment, a fine, or both.

## Amendment to the 1954 Act for Advertisement

Mainly, this Act was challenged in the Supreme Court, and the Court struck down a part of Clause(d) of Section 3 and the whole of Section 8 as invalid. This Act was therefore amended to eliminate the defects pointed out by the Supreme Court in the case, Hamdard Dawakhana vs Union of India. An Amendment to this Act was presented by the Union Health Ministry on February 03, 2020. From then on, the Act has been called "The Drugs and Magic Remedies (Objectionable Advertisements) (Amendment) Act, 2020".

In Section 2, the definition of "Advertisement" has been amended.

Section 3 was amended to get guidance experts with proper tests and validation for Ayurvedic, Siddha, and Unani drugs from the Technical Advisory Board constituted under Section 33C of the Drugs and Cosmetics Act, 1940. And the true character was to be reflected by the object of its promotion.

The penalty in Section 7 was amended. In the case of a first offense, the penalty is up to two (02) years of imprisonment and a fine of up to 10 lakh rupees. In subsequent offenses, it is imprisonment of up to five (05) years and a fine of up to 50 lakhs.

In Section 8 of the proposed bill, "Code of Criminal Procedure, 1858 (5 of 1898) has been substituted by 'the" Code of Criminal Procedure, 1973(2 of 1974)."

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The number of diseases and health conditions mentioned in the schedule of the Act has also increased.

Reinforcement of the amended law is in process. One needs to have laws to strictly monitor any false claims and to protect people from becoming prey to these claims. After seeing such advertisements, people will be more aware of such quacks and stop practising self-medication. There are many things that can be done as remedial procedures to prohibit drug and magic remedies misleading advertisements if we seriously ensure that the existing laws are enacted.

For reviewing and creating advertising and promotional material, get in touch with Freyr now!

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Regulatory Medical Writing

# INVESTIGATOR'S BROCHURE (IB) AND CHALLENGES FOR MEDICAL WRITERS

A comprehensive compilation of clinical and non-clinical data on the investigational product (drug, supplement, device, or any other product) provides a brief description of the drug substance and the formulation, including the structural formula (if known). An Investigator's Brochure (IB) is an essential document maintained by a drug developer or investigator throughout the drug development process, and it contains the body of information acquired before and throughout a drug trial. The IB is updated whenever new information about an investigational product becomes available.

## Purpose of the IB

The IB's goal is to combine pre-clinical and clinical data to furnish the investigator with the background information required to manage study conduct and study subjects during a clinical trial. It ensures that the investigator and other staff involved in the trial process understand the rationale behind the study and work in accordance with the study protocol. It provides clinicians or potential investigators with information, which is concise, basic, objective, balanced, and non-promotional, and this is required for the proper conduct of the study, such as dosages, dosing frequency, administration techniques, etc. It also supports the clinical management of study participants during the trial, such as safety monitoring measures. The IB helps the investigator to evaluate the appropriateness of a trial in an unbiased and independent manner so that the investigator can make a neutral risk-benefit assessment.

## General Information that an IB should Include

The IB must include the following for each investigational medicinal product:



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- Information about the sponsor's name and the product's identification (research number, Generic and trade names)
- A confidentiality statement instructing the investigator's team, review boards, and ethical committees to consider the document confidential
- A collection of results from non-clinical and clinical investigations on the investigational medicinal product
- Background information on the investigational medicinal product's properties and history

## Contents of the IB

Section 7 of ICH E6 gives information on what should be included in a table of content that is almost always used in its entirety. The highest-level sections are as follows:

- Table of contents
- Summary
- Introduction
- Physical, chemical, and pharmaceutical properties, and formulation
- Non-clinical studies
- Effects on humans
- Summary of data and guidance for the investigators

## Updating the IB

The editing of the IB should be overseen by a medically certified practitioner. An IB should be evaluated once a year and amended as needed, in accordance with the written requirements of the sponsor. If new material is significant enough, it must be communicated to the investigators and the Human Research Ethics Committee (HREC) before it is included in the updated IB. The sponsor guarantees that the investigators have access to an up-to-date IB, while the investigators are responsible for presenting an updated copy of the IB to the necessary Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs).

An IB update is never "simply" an IB update. Depending on the circumstances, you may be obligated to provide a detailed overview of the IB changes. This detailed overview is known as a "summary of change document," or simply an SOC, and it uses strikethrough and bold font to illustrate the changes done. A thorough SOC should not be mistaken for the summary of changes that is frequently seen at the beginning of an IB and provides a high-level overview of the changes made. The method of developing a thorough SOC varies for each firm.

## Challenges for Medical Writers

When preparing an IB, the overarching issue is to produce a clear and focused presenting style while striking an acceptable balance between completeness and readability. Of course, the IB should be both comprehensive and readable, to this end, but this takes time and effort. As a result, given the limited time, an IB may grow bloated with information in order to appear thorough, but the result is frequently unreadable. To ensure conciseness, the contents of the entire IB should be evaluated at each update; not just in terms of what should be included, but also in terms of how much of the present information can be reduced or eliminated. Logically, the initial edition will focus on non-clinical material with no clinical information. Simultaneously, when more clinical information becomes available, the quantity of detail for non-clinical information may be reduced as the clinical performance of the investigational product will be better known. So, preparing a quality IB that balances the necessary non-clinical and clinical information, which facilitates the proper conduct of the trial, is challenging.

The IB is a live document that must be updated on a regular basis, providing writers with an exciting opportunity to connect with a broad team drawn from a variety of tasks contributing to the development of the investigational product. This variety can exacerbate the logistical issues associated with getting the materials required to prepare the IB. Depending on the IB preparation process, the writer may be involved in coordinating and modifying text contributions received from other team members or may be expected to create some or all of the IB content based on reports and other material received as source information. Regardless of the process, the main challenge and responsibility for preparing an IB are to confirm that the information captured in the IB is as concise, complete, readable, and focused as possible, and is correctly structured to efficiently communicate what an investigator needs to know for the proper conduct of the study and for assessing the benefits and risks of using the investigational product. Hence, a partnership with a Regulatory service provider with an efficient pool of medical writers who have a thorough understanding of the clinical development process compliant with ICH guidelines and who can timely deliver a high-quality submission-ready, right-first-time IB with a satisfactory response from the client is important. Consult Freyr for compliance best practices.


# DEEP DIVING INTO PERIODIC SAFETY UPDATE REPORTS (PSUR) OF EU MDR AND EU IVDR

The establishment of the European Union Medical Devices Regulations (EU MDR) 2017/745 and In Vitro Diagnostic Devices Regulations (EU IVDR) 2017/746 posed additional requirements. The significant aspect highlighted was implementing the Post-Market Surveillance (PMS) system. Enabling PMS will ensure the devices's safety even after being launched in the market.

PMS is a continuous process that includes deducing the plan to implement and maintain the system. The Periodic Safety Update Report (PSUR) is an essential tool in the process. It is a document that summarises the results and conclusions of the data gathered during the PMS and details any preventive and corrective actions, if taken. This document will be maintained for each device or each category/group of devices (wherever applicable).

PSUR is applicable to both medical devices and IVDs, but it is generally maintained only by the manufacturers of Class IIa, IIb, and III under EU MDR and Class C and D under EU IVDR. Article 86 in EU MDR and Article 81 in EU IVDR outline the requirements for PSUR. The overall goal of PSUR is to demonstrate the data that manufacturers have deduced and implemented in their surveillance system, ensuring the safety and efficacy of the devices placed on the market.

Let us look into the details that should be incorporated into the PSUR. Also, note that the amount of data incorporated may vary, but the skeleton of the report should always contain the following components:

- The findings deduced from the Post-Market Clinical Follow-up (PMCF) {Post-Market Performance Follow-up (PMPF) in case of IVDs}
- Conclusions that are drawn from the benefit-risk analysis
- Descriptions of the preventive and corrective actions taken (if any), and justifying the same
- The volume of the sales of the device
- Evaluation of the users (size, characteristics, usage frequency, etc.)
- Executive summary – the gist of the overall analysis

These documents must be updated frequently under the obligations mentioned in the regulations. As per EU MDR, Class IIb and III devices must update these reports on a yearly basis, while Class IIa devices should be updated at least every two (02) years. Similarly, under EU IVDR, Class C & D devices must be updated annually.

Further, according to Annex II and III, these reports are considered to be part of the technical documentation (except for custom-made devices). Class III devices/implantable devices and Class D IVDs are required to submit PSUR via EUDAMED (electronic system) to the notified bodies involved in the conformity assessment. Notified bodies will review these reports and provide their assessment and the actions taken (if any). These reports and assessments by notified bodies are available to the competent authorities via EUDAMED.

In the case of other remaining devices (Class IIa, IIb, and C), the reports shall be produced to the notified bodies involved in the conformity assessment and to the competent authorities upon request.

The importance of PSUR must come into the limelight, as even though it is a single document, the placeholder of it in the PMS system is quite essential. Failure to write PSUR effectively may further raise potential queries and concerns from the notified bodies or competent authorities.

Having a systematic approach to designing the reports is always beneficial! Freyr, with over ten (10)+ years of experience, has streamlined these processes, enabling quality and success for the manufacturers!

Partner with Freyr today to conquer the post-market surveillance hurdles!

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Global Food and Food Supplements Regulatory Services

# NON-CARBONATED WATER-BASED BEVERAGES (NON-ALCOHOLIC) AND STANDARDS UNDER THE FSSR 2011

As per the regulation on Non-carbonated Water-based Beverages (Non-Alcoholic) released by the FSSAI on July 26, 2021, all Food Business Operators (FBOs) were required to comply with the amended provisions by February 01, 2022. According to the amendment, "non-carbonated water-based beverages" (non-alcoholic) refer to drinks made with water, which meet the requirements for packaged drinking water or mineral water but without the addition of carbon dioxide. These must also contain a certain ingredients, either solely or in combination.

On January 12, 2023, an official notification was released, directing all regional directors to carefully review all the licenses issued for the category of "Non-Carbonated Water Based Beverage," with non-compliant cases to be reported to the FSSAI HQs by January 31, 2023. All non-compliant FBOs will receive notices directing them to either make the necessary changes to the product to bring it into compliance or stop manufacturing any unsatisfactory products after taking the necessary actions.

The licenses will be scrutinized to verify if non-carbonated water-based beverages are produced using water that complies with packaged drinking water standards or mineral water as a base and if they are required to contain the ingredients listed in the regulation, either individually or in combination. Additionally, non-carbonated water-based beverages will be closely examined to ensure that they do not use the word "water" in any way, including on their product names, labels, advertisements, or any other forms of representation. They must adhere to the vitamin and mineral limits specified in the standards for packaged drinking water or mineral water.

Stay updated with the recent updates on the regulation for Food and Food Supplements. To know more, contact Regulatory experts at Freyr.



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# HOW TO PREPARE CLINICAL EVALUATION REPORT (CER) UNDER EU MDR 2017/745

The clinical evaluation is a procedure for demonstrating the safety and efficacy of the medical device. The documentation of the clinical evaluation process is called a Clinical Evaluation Report (CER). CER holds a significant position when placing or distributing medical devices in the European Union (EU). The report aims at establishing the device's intended benefits for users when weighed against the associated risks.

The CER is submitted as a part of the CE technical file to the Notified Body (NB) during the conformity assessment. Under EU Medical Devices Regulations (MDR) 2017/745, Article 61 and Annex XIV detail the requirements for the clinical evaluation process.
Transitioning from MDD or MED DEV 2.7/1 REV 4 to MDR is complicated. One may question the similarity between the MED DEV 2.7/1 REV 4 and the MDR. The requirements seem to be quite identical from a bird's eye view. However, the microscopic view shows a different scenario, and the requirements vary excessively.

Given the importance of drawing out an effective CER while placing the devices in the EU market, some of the key pointers that one should focus on are the following:

## 1. Deduce and draw a plan

A Clinical Evaluation Plan (CEP) is vital to the CER. The CEP defines the scope, methodology, and approach for the clinical evaluation process, which will then be documented in the CER. The CEP includes details about the device(s), specifications on the intended use of the device, indications, contraindications, intended users, clinical benefits, and clinical outcome parameters. This CEP document can further guide the clinical evaluation in carrying out stepwise activities.

## 2. Identify clinical data

Most of the time, the misconception can build over the fact that themore data is included in the CER, the more effective

the report will be. There is no limit to the data that can be incorporated into the CER. However, including accurate data is always beneficial. For this, a thorough literature search is required via a robust database. Other than that, support from additional clinical data such as clinical experience, clinical trials, as well as internal data (meeting excerpts, ongoing clinical studies, etc.) can also supplement the report.

## 3. Creating a checklist

Understanding the gaps between the requirements and the data collected is quite crucial. Creating a checklist that suits the requirements is always advisable. One of the ways would be to first create a template in accordance with Article 61. It helps in assessing the potential missing areas in the reports.

## 4. Legibility of the Report

Writing a CER is not easy and requires quite a bit of expertise in the field. Report writing can vary, depending on several factors, such as the device, its classification, etc. However, the skeleton of the report should include the following elements:

- Device information which includes device type, manufacturer name, device designs, and other relevant data
- A technical description like intended use, user population, classification, therapeutic indication, etc.
- Identified clinically equivalent devices and justification on the same
- Methods used for clinical evaluation
- Analysis and conclusions that are drawn, based on the data collected, demonstrating the safety and efficacy of the device

## 5. Updation of CER

CER must be updated continuously even after the device is placed on the market. The report goes as a Post-Market Clinical Follow-up (PMCF), a part of the post-market surveillance system. Potential changes to any new clinical data or evidence, including hazards, benefits, claims, etc., that might have a relevant impact on the clinical evaluation process, must be documented.

Drawing up and maintaining a compliant CER can be a cumbersome process. An ineffectual report can heavily impact the conformity assessment procedure, leading to failure in placing the device on the market. Being a partner to Freyr can ensure that all your needs are supplemented correctly and create a high-quality document.

Consult Freyr for any further queries on medical writing.




# ICH'S eCTD 4.0 OBJECTIVES AND VENDOR CONSIDERATIONS

Electronic Common Technical Document (eCTD), a standardized submissions format, was established based on the Regulatory Product Submissions (RPS) standard (HL7 standard) with advice from the ICH. The current eCTD version 3.2.2 will soon be replaced by version 4.0. With various modifications designed to simplify the process for sponsors and Regulatory authorities, eCTD V4.0 has officially been issued. The primary goal is to implement changes that speed up the Regulatory submissions process, enhance communication between agencies and sponsors, and improve global harmonization of the format. Therefore, it becomes crucial for the sponsors to keep up with the release of stepwise ICH updates.

Timelines for mandatory implementation of eCTD V4.0 are not yet specified for several nations such as the United States (US), Canada, Japan, Switzerland, Brazil, and Australia, as well as for non-centrally approved products in the European Union (EU), which further hinders prospective planning. In certain cases, nations like Thailand, South Africa, and the region of the Gulf Cooperation Council (GCC) have not offered any plan for their V4.0 adoption. In conclusion, it appears like the eCTD V4.0 deployment will be a drawn-out process that will continue to change well into the 2030s.

## Why is eCTD V4.0 Efficient?

- **Enhances communication between agencies and sponsors:** The upcoming eCTD version 4.0 enables two-way communication between sponsors and agencies, and vice versa, which facilitates a comprehensive picture of the application's complete lifecycle, including all inquiries and information requests, in one place.
- **Harmonized information source:** A single, standardized XML backbone will be used to transmit all data and metadata of messages. It will facilitate information reuse for regulated industries and more effective information exchange or evaluations for national Regulatory authorities.
- **Communication management:** In eCTD V4.0, the lists of valid submission metadata (controlled vocabularies) are preserved in separate files, and the submission metadata from the XML backbone files are separated. This implies that updates or changes to the lists will not impact the backbone file. As a result, national authorities and providers of eCTD tools benefit from simplified maintenance. It will also make updating less expensive.

- **Repurposing of the content using UUID:** Each document will receive a Universal Unique Identifier (UUID) under eCTD V4.0. Future sequences can reuse the document with this identifier rather than having to submit the content repeatedly.

## Need help? Get help!

Advances in the eCTD submissions can make the sponsors feel apprehensive. However, any Regulatory change should be viewed positively. This helps the sponsor evaluate their efficiency and adds sophistication to the submission plan.

Pharmaceutical manufacturers must understand that the transition from eCTD V3.2.2 to V4.0 can be a tedious affair, and hence, they must collaborate with competent vendors in simplifying and streamlining Regulatory publication operations at each level of the process while adopting eCTD V4.0. Organizations can replace primitive human operations with automation, enhancing data quality, and accelerating the publication of regulations to launch products faster.

Collaboration with an entrusted vendor ensures:

- New assembly templates to support the new V4.0 structure and update the Document Type Definition (DTD).
- Updation of validation tools to ensure that all criteria, including the rules relating to the association of controlled vocabularies and sender-defined keywords, are included.
- Provision to focus on viewing tools, ensuring the capabilities to review both the content and the structure of the eCTD V4.0 format.

The necessity to link to multiple controlled values as well as the utilization of the same list of values for both IDMP and published by organizations with integrated registrations and publishing - as well as any future initiatives requiring those same values - will be extremely helpful.

## What Next?

The industry will start to gain from some much-needed reforms to the Regulatory submissions procedure as eCTD V4.0 becomes a reality. This will result in streamlined approval processes and quicker patient access to new products. A seasoned Regulatory partner can help facilitate the compilation of information needed to ensure compliance throughout the lifecycle of the products being marketed. Contact us to delve into the specifics of eCTD V4.0.


# HOW TO CHOOSE THE RIGHT eCTD SUBMISSIONS VENDOR: A COMPREHENSIVE GUIDE

The process of submitting Regulatory documentation to Health Authorities (HAs) can be complex and time-consuming. Many organizations partner with a vendor that offers a submission tool to ease this process. With so many options in the market, it can be difficult to know who the right strategic partner is for your submission requirements.

This blog will discuss what you should consider when selecting an appropriate electronic submission service vendor. By considering the following factors, you can ensure that you find a vendor who can provide the right support, best procedures, and efficient tools for successful submission.

## Company Presence

***First, does the company have a strong presence in the submissions and publishing space?***

A well-established company with a track record of success stories is the foremost attention-seeking factor any organization would intend to look at because it holds not only market leadership, but also broad expertise in the Regulatory operations and submissions space.



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## Comprehensive Contract

***Is the contractual agreement vendor friendly?***

A clear agreement between the organization and the submissions vendor helps to ensure that both parties have understood the scope of the project. The contract should be clear and elaborate on roles, responsibilities, and timelines.

## Credentials

***How essential is it to have strong credentials?***

The major assets that can help to derive the selection of a vendor are case studies, success stories, testimonials, and clients. One can contact references to verify their quality of work. Thus, reliable credentials help decide on a vendor for the process of submissions.

## eCTD Jurisdictions

***Are all the templates available to support various eCTD jurisdictions?***

It is a huge plus when the submission vendor has multiple templates to choose from! Such templates can be re-used to reduce the challenges faced in the submission components when a submission must be filed each time.

## Integrated Services

***Will one vendor be able to offer all the support services?***

A team full of submission experts who can guide throughout the submission process and can support publishing activities through technical expertise is all an organization needs. If vital factors like teamwork, financial outlook, and partnering have been taken care of by using just one vendor, what more can an organization ask for?

## Onboarding Process

***How speedy is the onboarding process?***

When it's time to begin the process, selecting a vendor who can ramp up the onboarding activities smoothly could make a big difference between the missing and the meeting of a Regulatory submission deadline.

## Publishing Support

***How flexible and scalable is the publishing support going to be?***

Round-the-clock publishing support is every organization's need to meet submission deadlines. An efficient vendor can help to seamlessly move the project forward. Look for vendors who can handle several submission challenges with flexible software and sound support services. The vendor should be able to scale up and down as per the need of the organization to meet the most challenging deadlines.

## Regulatory Experts

***Are they specialized Regulatory and consulting experts?***

Look for vendors that help strategize and advise on the submission type. The Regulatory operations team must have thorough expertise in the submission publishing process and should know how to utilize technology to assist it.

## Security and User Authentication

***How advanced is the security, and how strong is the user authentication?***

Security is the priority, and demonstrating that the software applications undergone the certification process is of utmost importance. Secure software is to be designed to secure the entire project data, including Advanced Encryption Standard (AES-256) encryption for data at rest and transfer.

## User Interface

***Does the platform have an easy-to-use interface and innovative technology?***

Faster and efficient utilization of technology to gain a quality output is the ultimate focus of any organization from their submission's vendor. While employing a simple user interface, key aspects that any life science organization considers looking at include whether it would save time or improve accuracy and quality. The vendor should be able to provide the Regulatory operations team with an efficient Regulatory submissions software.

| Vendor Expertise | Submissions Management Suite |
|---|---|
| Company Presence | ✓ |
| Comprehensive Contract | ✓ |
| Credentials | ✓ |
| eCTD Jurisdictions | ✓ |
| Integrated Services | ✓ |
| Onboarding Process | ✓ |
| Publishing Support | ✓ |
| Regulatory Experts | ✓ |
| Security and User Authentication | ✓ |
| User Interface | ✓ |

In conclusion, when selecting an eCTD submissions vendor, it is important to consider factors such as efficiency, cost-effectiveness, and the ability to meet Regulatory submission deadlines. Freyr Digital meets all requirements and acts as a strategic partner in your Regulatory submissions journey. With an integrated product suite, including Freyr SUBMIT PRO, Freyr SUBMIT Track, and Freyr rDMS, you can efficiently handle all aspects of Regulatory data and document management. Book a demo with our in-house specialist to experience Freyr Digital's benefits.



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# SPRINTING TOWARDS THE NEW CHEMICAL ENTITY-1 DESIGNATION

New Chemical Entity (NCE) minus 1 filing, also known as a paragraph IV filing, is a type of application submitted to the US Food and Drug Administration (FDA) for a new drug that is a slight variation of an existing drug. The minus 1 in the type of submission refers to the fact that the NCE is one small change away from an existing drug that has already been approved by the FDA and marketed under its surveillance. The Regulatory body approval process for NCE minus 1 filing is generally faster and inexpensive in comparison with entirely new drugs, as the agency can rely on the safety and efficacy data from the original drug. This can be beneficial for companies, as it allows them to bring new drugs into market quickly and efficiently, making the new treatments available for patients sooner.

It is also worth noting that the NCE minus 1 filings are known as Paragraph IV filings because they are filed under the provisions of the Hatch-Waxman Act (1984). The Act was designed to balance the need for innovation with the need for affordable drugs by allowing for a more streamlined and efficient drug approval process for generic drugs. So, the NCE minus 1 filing is done under this Act for the same reason, to bring new drugs to market faster and more efficiently.

If you are a pharmaceutical company, it's important to be prepared for paragraph IV filing, also known as New Chemical Entity (NCE) minus 1 filing. These types of filings are becoming increasingly common in the industry as companies seek to extend their patents and maintain exclusivity in the market.

Here are some tips to help you be ready for a paragraph IV filing:

- **Understand the regulations:** It is important to have a thorough understanding of the regulations and

requirements for paragraph IV filings, as well as the FDA's approval process. This will help you navigate the process and ensure that your application is complete and meets all the necessary requirements.

- **Conduct thorough research:** Before submitting a paragraph IV filing, it is essential to conduct thorough research on the existing drug and the proposed changes to it. This will help you understand the potential benefits and risks of the new drug, as well as its potential impact on the market.
- **Prepare your patent and exclusivity strategy:** A key aspect of a paragraph IV filing is the patent and exclusivity strategy. It is important to have a clear plan in place to protect your patent and maintain exclusivity in the market, as well as a plan for dealing with any potential challenges to your patent.
- **Get legal support:** It is also important to have legal support throughout the process, as paragraph IV filings can be complex and involve significant legal challenges. A good attorney will be able to help you navigate the process and protect your interests.
- **Be ready for the challenges:** Be prepared for the challenges that may arise during the process, such as legal challenges and competition from other companies. It is crucial to deal with these challenges and protect your interests.
- **Keep in mind the patient's well-being:** Above all, keep in mind that the ultimate goal is to bring a new treatment to patients in need, making sure that the new treatment is safe and effective. Make sure that the proposed changes to the existing drug will provide some benefits for the patients.

In conclusion, NCE minus 1 filing can be a useful tool for pharmaceutical companies to bring new and slightly modified drugs into the market quickly and efficiently. However, it is important to consider the potential drawbacks, such as the lack of innovation, higher drug prices for consumers, and the proliferation of similar drugs. The FDA must continue to balance the need for innovation with the need for affordable drugs and ensure that the patient's well-being is at the forefront while approving these applications.

Let Freyr know your take on NCE-1 Filings and evaluate the best practices.




# ABBREVIATED SmPC: A MODERN APPROACH IN THE EU FOR PROMOTIONAL MATERIAL

Summary of Product Characteristics (SmPC) is a medical monograph created and updated by pharmaceutical companies based on product research and knowledge. It offers much more than a structured list of vital information on each drug, such as fixed dosage and potential side effects. Pharmacists, doctors, nurses, and other healthcare professionals rely on this data to appropriately prescribe medications and educate their patients about medicinal product use.

SmPCs are reviewed and approved by the United Kingdom (UK) or European medicines licensing body, the UK Medicines and Healthcare Products Regulatory Agency (MHRA), and the European Medicines Agency (EMA). SmPCs are used by various healthcare providers, including pharmacists, to prescribe and use medication appropriately and safely. As new efficacy or safety data emerges, they are kept up-to-date throughout the medicinal product's lifecycle.

The SmPC information is crucial for the correct and safe use and distribution of medicine. The SmPC consists of qualitative and quantitative information about each drug's benefits and hazards. The following information is required:

- The medication's composition
- Interactions with other medications
- Concomitant disease
- Organ impairment
- Effects on pediatric, geriatric, and pregnant populations
- Genetic variables and more

This life-or-death material is complete with instructions on what to do in emergency scenarios. That is why SmPC updates and accuracy are critical for patient safety.

## What is an Abbreviated SmPC?

An abbreviated SmPC is a shorter/crisper version of the SmPC used to prepare promotional material in Europe. The abbreviated SmPC is usually four (04) - five (05) pages, its template could vary from company to company, and it helps physicians with a quick review instead of the SmPC data. Only the very important data is presented in the abbreviated SmPC, unlike the SmPC. It is critical to maintaining the consistency of claims and the overall meaning of the SmPC or the abbreviated SmPC.

An abbreviated SmPC should contain an important note/ mandatory statement at the top of the document, quoting "Before prescribing, consult/refer to the full prescribing information." The nomenclature could vary between Reduced PI, Basic Succinct Statement (BSS) document, and abbreviated SmPCs from company to company. It also helps in defending legal cases arising due to promotional material. The following picture represents the components of both the SmPC and the abbreviated SmPC.

## Information on SmPC vs Abbreviated SmPC

| | Base Components of SmPC | | Base Components of Abbreviated SmPC |
|---|---|---|---|
| VS | Name of the Medicinal Product | 1 | Name of the Medicinal Product |
| | Qualitative and Quantitative Composition | 2 | Qualitative and Quantitative Composition |
| | Pharmaceutical Form | 3 | Pharmaceutical Form |
| | Therapeutic Indications | 4 | Therapeutic Indications |
| | Posology and Method of Administration | 5 | Posology and Method of Administration |
| | Contraindications | 6 | Contraindications |
| | Special Warnings and Precautions for Use | 7 | Special Warnings and Precautions for Use |
| | Interaction with Other Medicinal Products and Other Forms of Interaction | 8 | Interaction with Other Medicinal Products and Other Forms of Interaction |
| | Fertility, Pregnancy, and Lactation | 9 | Fertility, Pregnancy, and Lactation |
| | Effects on the Ability to Drive and Use machines | 10 | Effects on the Ability to Drive and Use machines |
| | Undesirable Effects | 11 | Undesirable Effects |
| | Overdose | 12 | Overdose |
| | Pharmacodynamic Properties | 13 | Marketing Authorization Holder Information |
| | Pharmacokinetic Properties | 14 | Date of Creation/Revision of the Text |
| | Preclinical Safety Data | 15 | |
| | List of Excipients | 16 | |
| | Incompatibilities | 17 | |
| | Shelf Life | 18 | |
| | Special Precautions for Storage | 19 | |
| | Nature and Contents of a Container | 20 | |
| | Special Precautions for Disposal | 21 | |
| | Marketing Authorization Holder/Numbers | 22 | |
| | Date of First Authorization/Renewal of Authorization | 23 | |
| | Date of Revision of the Text | 24 | |



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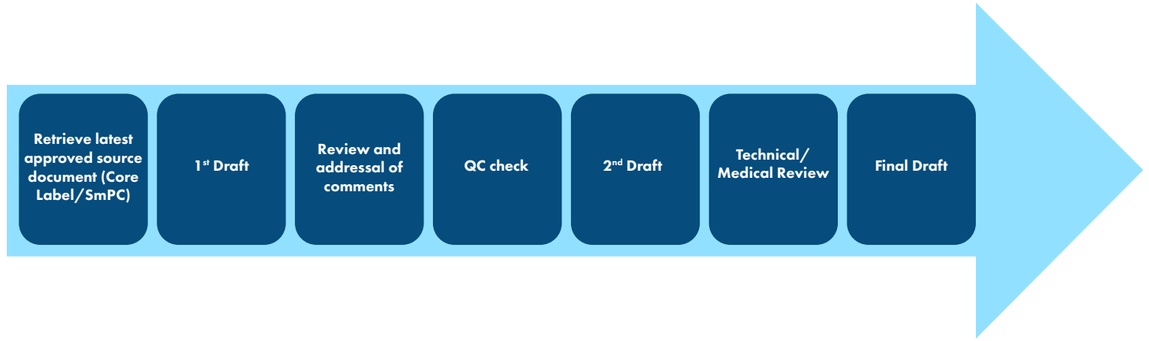
The Abbreviated SmPC preparation process varies from company to company. The source document which is used to prepare the Abbreviated SmPC must be an approved document, core label, or the latest approved SmPC. Post the 2nd draft, the translations are done, if required, before the medical or technical review. The comments are addressed, and then the final draft is rolled out. The diagram below illustrates the process of abbreviated SmPC preparation.

## Abbreviated SmPC Preparation Process Flow




Various conditions can arise that necessitate a change to the SmPC or abbreviated SmPC, resulting in tens of thousands of revisions per year. Adverse drug events and changes in safety communication standards are the two most typical reasons for SmPC/abbreviated SmPC upgrades. Adverse drug events that occur after a product has been released to the market are reported to national Health Authorities (HAs), and the responsible manufacturer is advised that an update is required.

Safety communication updates are regularly conducted to ensure that compliance and patient safety criteria are met. SmPCs and abbreviated SmPCs are updated as compliance criteria change. Because this data is regularly updated during the medicinal product's lifecycle, it can be challenging to track and manage, not to mention time-consuming. As the data represented in the abbreviated SmPC is in a crispier form, the time required to prepare an abbreviated SmPC is shorter, as compared to the SmPC.

Our team of experts at Freyr have experience with products registered under multiple registration types and are experienced with creating and updating the Abbreviated SmPCs. Get in touch with us now!


# PAPERLESS REGULATORY SUBMISSIONS IN CHINA: A BIG MARKET OPPORTUNITY

China's pharmaceutical industry has seen substantial growth since its entry into the World Trade Organization (WTO). As of 2021, China holds a 12% share of the global pharmaceutical market, making it the second-largest contributor. According to Xinhua News Agency, the Chinese pharmaceuticals market generated 708.75 billion yuan in 2021, while the Chinese domestic medicinal companies amassed 502 billion USD in profit.

As you may know, the National Medical Products Administration (NMPA), the Health Authority of China, has started accepting eCTD Marketing Authorization (MA) applications as well as Clinical Trial Applications (CTAs), paving the way for more opportunities. However, it brings its own set of challenges.

In this blog, we examine the world of electronic Common Technical Document (eCTD) submissions, as they are rapidly becoming the go-to method for document submissions in the pharmaceutical industry.

## Challenges Faced by Companies in China for Adapting to Mandatory eCTD Submissions

- **Complexities in the Chinese eCTD Format:** Unlike the universal standard, which is quite simple, the Chinese eCTD format is complicated and can be difficult to pass through for companies that are not familiar with the process. This can lead to setbacks in presenting the essential credentials.
- **Increased Complexity While Compiling eCTD Submissions:** NMPA, has implemented new rules and regulations to support the transition to electronic submissions, but firms are still expected to navigate a complex and dynamic environment. This can be more challenging for those companies that do not have a local presence or thorough understanding of the Regulatory ecosystem of China.
- **Multi-lingual Support in Paper and Electronic Submissions:** The documents need to be submitted in Mandarin with English versions as a reference, which can be a difficult task for companies that do not have affiliations with qualified language translators.

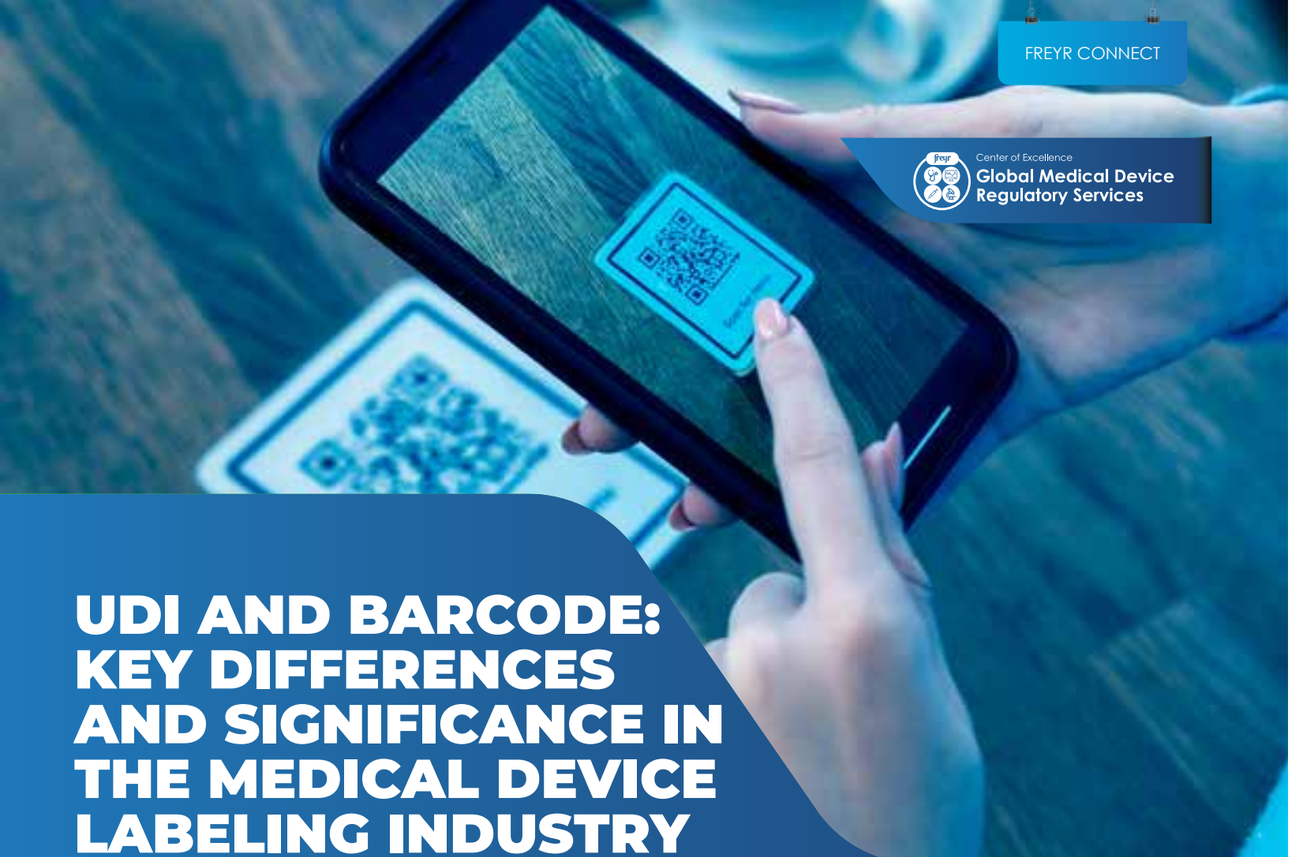
## Opportunities While Transitioning from Paper to Paperless Submissions

- **Well-timed Entry into the Chinese Pharma Market:** Entering the Chinese market has become more convenient, thanks to the transformative reforms and policy upgrades implemented. One of the key changes is the adoption of electronic submissions, which streamlines the process and eliminates many of the challenges that companies once faced. This is a testament to China's commitment to promoting structural adjustments, procedural transformations, and overall market growth.
- **Faster Drug Approval Process:** Now that submissions have become electronic, the drug approval process will be much faster, and hence, the process of bringing medicine to market will be smoother and quicker. This will eventually help big pharmaceutical companies further increase China's share in the global pharmaceutical market.
- **Advantage of Patent Medicine:** Patent medicine is the second-largest product segment, with great profit margins. However, long return periods, soaring research and development (R&D) costs, and prolonged R&D periods are involved in the manufacture of originator drugs. With the implementation of electronic submissions, all of these obstacles can be dealt with. As of 2022, foreign companies are still the main participants in this market, thus making it a niche market to target this segment.

| Opportunities | Challenges |
|---|---|
| 1. Well-timed Entry into the Chinese Pharma Market | 1. Complexities in the Chinese eCTD Format |
| 2. Faster Drug Approval Process | 2. Increased Complexity While Compiling eCTD Submissions |
| 3. Advantage of Patent Medicine | 3. Consistency in Paper and Electronic Submissions |

## How to be Ready for this New Implementation in China?

The transition to mandatory eCTD submissions in China presents a wealth of opportunities for companies looking to remain competitive in the world's largest pharmaceutical market. By partnering with the right expert, companies can navigate the ever-evolving Regulatory landscape with ease and confidence. To stay ahead of the curve, having a subsidiary with a local presence and an understanding of the HA regulations is crucial. Freyr SUBMIT PRO, a publishing and submissions software, helps manufacturers enter the Chinese pharmaceutical market with ease. To learn more about the tool, request a demo.




# UDI AND BARCODE: KEY DIFFERENCES AND SIGNIFICANCE IN THE MEDICAL DEVICE LABELING INDUSTRY

The primary distinction between a Unique Device Identifier (UDI) and a barcode in medical device labeling is that the UDI is a standardized identifying number assigned to each medical device, whereas a barcode is a graphic that can be scanned and read by a barcode reader or a scanner.

Device Identifier (DI) and Product Identifier (PI) are the two parts of UDI. DI is a fixed proportion that helps in identifying a specific device model. Device manufacturers assign the DI. It is distinctive to a particular device model.

DI consists of the following parts:

- **Device Labeler Identifier:** It is a specific code that is assigned by the FDA to manufacturers or labelers.
- **Device Identifier:** This code helps in the recognition of a specific device model.
- **Version or Model Number:** As the name suggests, this helps identify the model or version number of the device.
- **Catalog Number:** This code helps in matching the device in the manufacturer's catalog.

PI, on the other hand, is a variable proportion of UDI. It provides the Identification of a specific production unit or batch of the device. PI is an essential part of UDI, as it helps track specific production units or batches of devices, thus, making sure that the device is being used within its recommended shelf life.

PI consists of the following parts:

- **Serial Number:** A specific number assigned to every individual device within a production unit or batch.
- **Lot Number:** A unit number assigned to a particular batch of devices.
- **Expiration Date:** The date after which the manufacturer no longer guarantees the safety or effectiveness of the medical device, formatted as year, month, and day (YYYY-MM-DD). It is also known as the "use by" date or the "do not use after" date.
- **Manufacturing Date:** The date on which the device was manufactured, formatted as year, month, and day (YYYY-MM-DD).



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- **Other Information**: This includes the manufacturer's date, address, country of manufacture, device version, and model number.

## Barcode

Barcode is an illustration of the data. It can be read using a scanner or a barcode reader. In terms of medical devices, a barcode is a graphical representation of a UDI. The barcode is printed on the labels or packages of the device and enables health professionals and authorized Regulatory personnel to quickly get all the specific information about the device.

The following are the reasons why barcodes have to be implemented:

1. **Identifying and Tracking Devices:** This helps users track not only the device, but also access information regarding its indications and contraindications of use. It reduces the risk of misdiagnosis, medication errors, and adverse effects.
2. **Inventory Management:** Barcodes help identify the location and number of devices available in a healthcare facility's directory. This minimizes the risk of shortage and keeps track of the overstocked items
3. **Quality Control:** Production and distribution of devices can be tracked using barcodes so that any defects or problems with the device can be readily identified. This ensures safety and quality when it is being used in patient care.
4. **Regulatory Compliance:** Some Regulatory bodies, such as the Food and Drug Administration (FDA) and European Union (EU), have mandated the use of barcodes for easy tracking and identification

Barcodes have made it possible for healthcare professionals to quickly identify and access crucial information about the devices they use. This helps to improve patient safety and the standard of care.

## Key Differentiating Points Between Barcode and UDI

| | UDI | Barcode |
|---|---|---|
| **Readability** | Human-readable | Machine-readable |
| **Purpose** | A standardized identification code that is assigned to every medical device | A visual representation of data that can be scanned and read |
| **Components** | As explained above, it has two parts, DI and PI, each having their unique purpose | A graphical representation of UDI |
| **Use** | Used to identify and track a specific device throughout its life cycle | A primary tool used to quickly access UDI and other device-related information |
| **Location** | Appears as a series of codes on the label or package | Represented graphically in the form of lines, with different gradations on the device label or package |
| **Format** | Follows a specific format as mandated by the respective Regulatory bodies | Can be encoded in various forms, such as 1D or 2D |

A barcode will be used in conjunction with a UDI. Through this, healthcare providers can directly access key details about the device, such as its intended use, contraindications, and potential side effects. Barcoding serves to increase patient safety by reducing healthcare-related issues

Overall, while the use of a barcode in conjunction with a UDI on medical equipment is not always mandatory, it is frequently suggested to improve patient safety and the quality of care.

To get accurate barcoding and UDI enabled on your medical device labels, Consult Freyr.


# WHY IS PHARMACEUTICAL AGGREGATION VITAL?

Manufacturing counterfeit and fraudulent items are highly profitable, particularly in the pharmaceutical industry. The illicit market for prescription medication has become a global menace, with patients' lives at risk as it they continue to flood hospitals and pharmacies worldwide.

Counterfeiters have established robust networks for over a decade and exploited the pharmaceutical industry, which desperately needs rules and security. To combat this, many governments worldwide are taking the necessary steps to enact strict rules and new laws to protect their countries, the various factors in the pharmaceutical supply chain, and, most importantly, the patients.

Be it "serialization," "coding," or "track-and-trace," the pharmaceutical sector is rife with terminology indicating a desire for transparency. The most recent is "aggregation," a rising data collection technology aimed at streamlining inventory and the supply chain. While the approach is still in its early stages, it has the potential to assist in counterfeiting, theft, inefficiencies, and confusion.

When working with a large number of products, product aggregation is a highly efficient activity that helps save time and resources. While aggregation provides more security, its utility stretches beyond security, and into various other areas, such as:

- **Data Serialization**: The data can be compared to predecessors by scanning the code at numerous locations along the pharmaceutical supply chain. If the numbers differ in any way, it indicates that the product has been compromised.
- **Enhanced Inventory Management:** During aggregation, the information obtained through screening and serialization is recorded with a central repository, which instantly returns the batch location when searched.



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- **Faster Decommissioning:** Pallets can be decommissioned from bulk shipments without having to be physically there. It can also be accomplished using a mobile platform by looking for the damaged item and eliminating it from the shipment.
- **Operational Flexibility**: The procedure aids in the simplification of other complex medication like those in the export-import (EXIM) chain. Because many countries will be compelled to use aggregation as part of their pharmaceutical supply chain, its widespread adoption will aid in the regularization and screening of shipments across global pharmaceutical manufacturing countries.
- **Quicker Rework**: When you already know where the medicine is, you can easily replace the batch of a vial. You can achieve this by retrieving it from the system and modifying the unique identifiers and batch. Manual box handling is no longer required. You can also acquire information about a "child" while scanning the "parent."
- **Faster and Effective Recalls**: If there are any worries about a particular product, it is simple to recall it. They can be returned quickly and without inflicting any damage.
- **Enhanced Process Security**: The pallets are kept sealed until they reach their destination. There is no need to open the pallet every time to inspect the contents. All the products can be identified by scanning the pallet serial shipping container code (SSCC) label. Because all the products remain inside the pallet, the procedure is more secure, as no products are misplaced or lost.
- **Improved Warehouse Management**: It is simpler to locate the products. The serial number of the goods can be traced back to the SSCC, which will lead to the precise pallet, case, or bundle where the product was packaged.
- **Compliance with Regulations**: Many governments, throughout the world need product aggregation, in addition to serialization. An aggregation solution facilitates "track-and-trace" operations throughout the pharma supply chain. Critical information can be exchanged and validated from producer to wholesaler to distributor. It indicates that if the product emerges somewhere other than where it is scheduled to arrive, it is a counterfeit or stolen product.

So, to round it off, it is essential that pharmaceutical companies start adopting aggregation to combat the issues of counterfeit drugs and medicines. As we have learned above, it comes with various added advantages. Adopting this technology is a one-time investment that will yield results and give benefits in the long run. As a result, outsourcing all artwork-related tasks to an experienced Regulatory partner like Freyr helps pave the way to global compliance. Contact us right now!

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Global Medical Device Regulatory Services

# US FDA APPROVAL PATHWAYS FOR IVDs

In-Vitro diagnostics (IVD) are products that are reagents, instruments, or systems that can detect diseases or other conditions and monitor a person's overall health to help cure, treat, or prevent diseases.

The classification of an IVD determines the appropriate premarket process for approval. The United States (US) Food and Drug Administration (FDA) classifies IVD products into Class I, II, or III, based on the associated risk.

| Classification | Level of Risk | Examples |
|---|---|---|
| Class I | Low to Moderate Risk | Complement Reagent<br>Phosphorous Test Systems<br>E. coli Serological Reagent |
| Class II | Moderate to High Risk | Immunological Test System<br>Glucose Test System<br>Coagulation Instruments |
| Class III | High Risk | Automated PAP Smear Readers<br>Nucleic Acid Amplification Devices for Tuberculosis |

You can determine the classification by searching the FDA database using related search terms or identifying a similar device with the same intended use and technology. The three (03) letter product code and seven (07) digit regulation number can be helpful for identification. If the classification cannot be determined, you can use the 513(g) process by the FDA.

## Approval for Class I IVDs

Most of the Class I IVDs are **exempted** from the FDA requirements for Pre-market Notification (510k) and Pre-market Approval (PMA).

## Approval for Class II IVDs

Most Class II IVDs are approved through the Pre-market Notification or 510(k) process. A 510(k) is a pre-market submission made to the FDA to demonstrate that the diagnostic devices to be marketed are at least as safe and effective, Substantially Equivalent (SE), to a legally marketed one. For IVDs, the review of a 510(k) includes an evaluation of the analytical performance characteristics of the new device, as compared to the predicate, including:

- The bias or inaccuracy of the new device
- The imprecision of the new device
- The analytical specificity and sensitivity of the new device

A step-by-step process for preparing and submitting a 510(k) application is carried out by the manufacturer, and the FDA user fee is paid. If the device is deemed cleared in the 510(k)-review process, the submitter receives an SE letter, and the device will be listed in the 510(k) FDA database. If a non-high-risk IVD with no predicate is shown, it may be reviewed and placed under a Class I or Class II under a De-Novo submission classification.

## Approval for Class III IVDs

Most Class III devices are subject to the Pre-Market Approval (PMA) process, wherein the diagnostic technology to be marketed cannot be considered substantially equivalent to the existing technology. A PMA application is submitted as per FDA guidance, and a user fee is paid. Upon approval, the FDA issues a PMA approval letter and posts it online.

The foreign manufacturer must appoint a US agent representative as a local point of contact with the US FDA, irrespective of the risk class of the device.

## Labeling Requirements

IVDs have additional labeling requirements under 21 CFR 809, Subpart B, In Vitro Diagnostic Products for Human Use. Before a manufacturer obtains marketing authorization for an IVD product, they must label it according to the regulations. After the required clearance, grant, or approval of the IVD, the manufacturer must register the establishment and list the IVD in the FDA Unified Registration and Listing Systems (FURLS). The manufacturer must pay an annual fee to maintain its establishment registration.

## Approval for Companion Diagnostics (CDx)

An IVD companion diagnostic device provides information essential for the safe and effective use of a particular the rapeutic product. A companion diagnostic, or CDx, informs the use of personalized treatment options for advanced cancer patients by identifying FDA-approved treatment options that may be appropriate, based on the unique drivers of their cancer. The US FDA follows a risk-based approach for the approval of companion diagnostics. The level of risk will determine if the IVD companion diagnostic requires a PMA or a 510(k).

The US FDA reviews each CDx device within the context of the corresponding therapeutic product. The CDx manufacturers can opt for any of the following submission and approval scenarios:

- The IVD is already approved and legally marketed, and the IVD manufacturer intends to add a new indication for use as a CDx with a drug or a biological product. The manufacturer must submit an additional pre-market submission for the new intended use.
- Both the CDx and drug or biological products are novel, and CDx is essential for the safe and effective use of the product. The CDx and the therapeutic product should be developed and approved simultaneously.
- If the US FDA determines that the CDx is essential for the safe and effective use of a novel therapeutic product, generally it will not give its approval if the CDx is not approved or cleared for that indication.
- In case of a new biological product intended to treat severe/life-threatening conditions or already approved therapeutic products, the US FDA may approve the **biological product without approval or clearance of companion diagnostic.**

It is recommended that sponsors time their clinical developments and pre-market submissions as they can initiate **early consultations with US FDA** to determine the appropriate Regulatory pathway. The FDA intends to issue approvals for the CDx and the therapeutic product **simultaneously**.

In case of more queries and assistance for approvals of your IVD products and companion diagnostics in the US, feel free to schedule a call with our Regulatory experts.





What is Article?

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# WHAT IS DRUG ADMINISTRATION LAW (DAL)?

The National Medical Products Administration (NMPA) is the primary Regulatory authority in China. It is the supporting agency of the State Administration for Market Regulation (SAMR). SAMR is the super ministry, and NMPA is its subordinate bureau. Further, the NMPA is also divided into various departments such as the Centre for Drug Evaluation (CDE), Centre for Drug Re-Evaluation (CDR), Centre for Medical Device Evaluation (CMDE), etc.

Earlier, the China Food and Drug Administration (CFDA) was the only responsible authority that regulated pharmaceuticals and medical devices, but later in 2018, CFDA was reshaped into smaller segments and called SAMR.

NMPA oversees pre-market approvals, distribution, and manufacturing, and post-marketing activities. It is divided into different departments, and it also has affiliated centres that cover different products in the Regulatory market.

As conventionally observed in the US, there are different laws that regulate different products, such as drugs, devices, foods, and cosmetics. On the contrary, there is entirely a separate law or an administrative regulation overlooking these areas. The directive regulating drugs along with biologics is the Drug Administration Law (DAL). The State Council has approved a general set of implementing rules for the DAL, referred to as the Drug Administration Law Implementing Regulations (DALIR)

A new Drug DAL came into force on December 01, 2019.

This revision is the most significant of all the other amendments. Other revisions were made in 2001, 2013, and 2015, but these were partial revisions.

Major changes included in the new version of the DAL are:

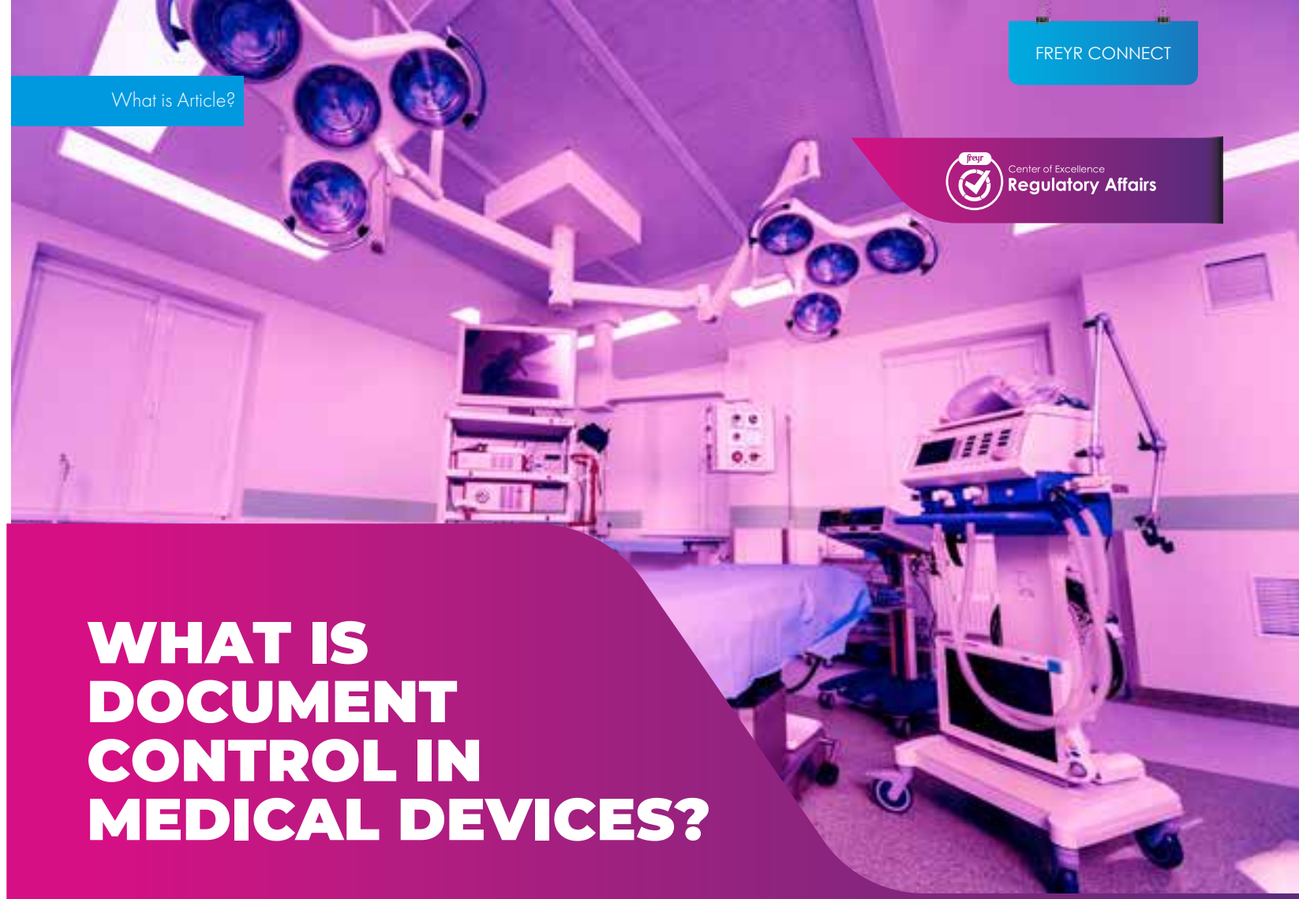
- **60-workday Deadline for Approval by NMPA:** The new system announced that if the applicant does not receive any communication regarding the approval of the clinical trial application by NMPA within 60 working days, the trial will be considered "approved" by default.
- **Legalization of Online Prescription Drug Sales:** Prescription drugs can now be sold online by the marketing authorization holder (MAH), drug distributors, and third-party e-commerce portals. However, vaccines and blood products are not included in this list.
- **Application of the MAH System:** In accordance with the prior system, only regional drug manufacturers could receive the approval to market their products. Later, after the implementation of the new system, the companies were able to outsource their manufacturing to contract manufacturing organizations (CMO). However, there was an exception for high-risk products like vaccines.
- **Increased Penalties:** Violation of the DAL will invite administrative penalties. The penalties have been increased to also impose personal liability on individuals responsible for corporate violations.

China's pharmaceutical market is highly governed by tedious regulations and dynamic laws. We, at Freyr, with a team of highly qualified professionals, can help you with a quick, effective, and smooth drug registration procedure in China.

To know more, consult our Regulatory experts at Freyr!







# WHAT IS DOCUMENT CONTROL IN MEDICAL DEVICES?

## What is Document Control in Medical Devices?

Document control refers to the procedures and methods that an organization has in place to manage the required documents and records during all the stages of the product lifecycle. It includes the processes of creating, approving, sharing, and archiving documents.

## Why is it Important to have Document Control Practices in Place?

Effective document control helps in improving the process of auditing and inspection by making the appropriate versions of documents accessible to the right personnel. It lies at the crux of the Quality Management System(QMS) and is critical to demonstrate compliance with Regulatory requirements. Quality System Requirements (QSR), as per 21 CFR 820 and ISO 13485:2016, both have well-defined requirements for document management.

## What are Document Control Requirements as per QSR (21 CFR 820)?

Subpart 820.40 of 21 CFR 820 describes QMS requirements for document control in detail.

820.40a of 21 CFR 820.40 details requirements related to document approval and distribution, such as:

- Designation of an individual(s) to review for adequacy of documents before issuance
- Documentation of approval, including the date and signature of the approver.
- Availability of documents required for this part at all

locations for which they are designated, used, or necessary, and removal of obsolete documents from all points of use or preventing them from intended use.

820.40b of 21 CFR 820.40 details requirements related to document changes, such as :

- Changes to documents to be reviewed and approved by an individual in the same function or organization that performed the original review, unless specifically designated otherwise
- Communication of changes to appropriate personnel in a timely manner
- Maintenance of records of changes to documents
- The change records to include a description of the change, identification of affected documents, the signature of the approving individual(s), the approval date, and starting when the change will become effective

## What are Document Control Requirements as per ISO 13485:2016?

ISO 13485:2016 details the control of documents in 4.2.4. The documented procedures are developed to:

- Review and approve documents for adequacy prior to issuance
- Review, update as necessary, and re-approve documents
- Ensure that the current revision status of and changes to documents are identified
- Ensure that relevant versions of applicable documents are available at points of use
- Ensure that documents remain legible and readily identifiable
- Ensure that documents of external origin, determined by the organization to be necessary for the planning and operation of the QMS, are identified and their distribution controlled
- Prevent deterioration or loss of documents
- Prevent the unintended use of obsolete documents and apply suitable identification to them

It is evident that both standards have quite a few key similarities, such as:

- Standardization of documents across the organization
- Maintenance and availability of updated documents at points of use
- Appointment of relevant personnel by management for review and approval

## What are Some of the Common Errors?

Some of the common errors that medical device organizations make, as evidenced in the FDA inspection reports, are:

- Documents were not reviewed and approved by the designated individual(s) prior to issuance.
- Document control procedures have not been adequately established.
- Records of changes to documents were not adequately maintained.
- Documents were not available at all locations for which they are designated, used, or otherwise necessary.
- Documents that were obsolete were observed at a location where they are being used.

## How Can an Organization Minimize Errors?

- Having Standard Operating Procedures (SOPs) for document control with detailed and non-ambiguous instructions
- Training of the personnel involved in the SOPs
- Staying up to date with changing Regulatory requirements
- Traceability and quick retrieval of documents
- Removing obsolete documents from points of use

It is apparent from the discussion that document control is one of the crucial aspects of the QMS(Quality Management System), and efficient document control practices serve as proof that the devices are safe and efficacious for use.

For more information and insights regarding document control and other aspects of quality management, consult or schedule a call with our Regulatory experts.



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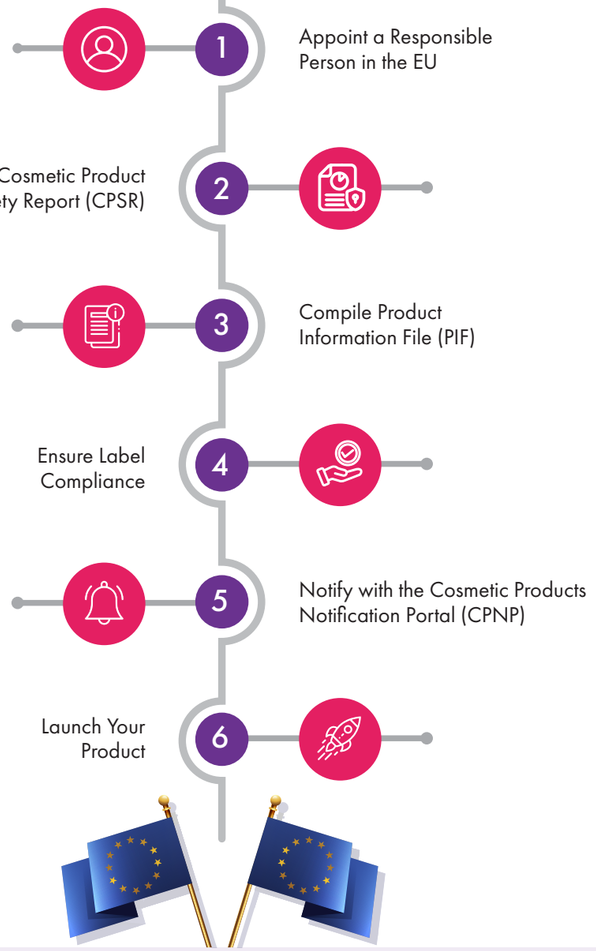
Global Cosmetics Regulatory Services

Infographic 1

# Cosmetic Product Notification in the EU

The European Union (EU) cosmetic market has experienced steady growth over the years and has been considered one of the most lucrative markets for cosmetics in the world. In the region, cosmetic product notification is monitored by the European Commission (EC) under Regulation EC No. 1223/2009. The regulation harmonizes the notification process of cosmetic products across the EU, covering all 27 EU member-states along with Norway, Iceland, and Lichtenstein.

**Here is a quick outline of the Cosmetic Product Notification process in the EU market:**




Decode the cosmetic product notification process in detail and comply with the regional Regulatory standards

**Consult Freyr**

Center of Excellence
Global Food and Food Supplements Regulatory Services

FREYR CONNECT

Infographic 2

# Dietary Supplements Labeling and Claims Review in the US

## Importance of Labeling

Food supplement labels provide information to the consumers to help them make a rational choice. It helps to ensure public safety by providing information like manufacturing date, expiry date, ingredients, storage instructions, declarations, cautions, and many other factors.

## Regulatory Authority

The United States (US) Food and Drug Administration (FDA) regulates dietary supplements in the US.

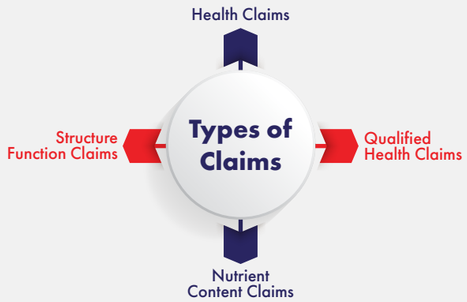
## What are Claims?

Claims are established regulations and scientific standards to ensure that food label claims are correctly expressed and scientifically substantiated.

These regulations and scientific requirements can differ based on various factors like the type of label claims, the product of interest, intended use, etc.

## Why are these Claims Required?

1. In the US, dietary supplement manufacturers are required to comply with the regulations set by the FDA.
2. To demonstrate the product's safety by providing the required information on the labels.




For more details Consult Freyr

Case Study 1

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Center of Excellence
Regulatory Affairs

# SUCCESSFUL FILING OF NDA-PADER, CMC AND GENERALCORRESPONDENCE SUBMISSIONS

**Client**
USA-focused, Growth-oriented, Specialty Pharmaceutical Company

**Health Authority**
USFDA

**Freyr CoE/Products**
Publishing and Submissions

**Service Offering**
Filing of NDA-PADER, CMC, and General Correspondence

**Industry**
Pharmaceuticals

**Service Region**
US

**Client Location**
US

**Therapeutic Area/Indication**
Epilepsy

**BENEFIT HIGHLIGHTS**

- Ensuring 100% Accuracy
- Quick Turnaround Time

## Business Imperatives

- Client was looking for quality submissions to be delivered within swift timelines
- Filing of Change in Contact, PADER, Annual Report, and CMC
- Maintaining lifecycles of all the products
- Ad-hoc submission requests
- Coordinating with the CMC team for publishing documents
- As a new player in the generic market, the client was looking for 100% quality submissions to be delivered within swift timelines for a fast approval process

## Challenges

- Tracking versions of frequently changed documents and replacing the same in eCTD
- Delivering submissions within very stringent timelines
- Freyr's team was challenged to work on large volumes of documents over a defined period
- Last-minute submissions were prepared and submitted to the FDA within the given time limits, and with good quality

## Freyr Solutions and Services

- Granular Document Level Publishing (DLP)
- Detailed tracker creation to track all the version changes made throughout the publishing cycle
- Successfully handling all the ad hoc submissions and delivering them on time
- Validation using industry-accepted/agency-recommended tools
- Rigorous quality checks performed at every step of the process

## Client Benefits

- Provided valid submissions with zero errors and warnings
- Maintained transparency throughout the process
- Played an important role in accelerating ahead of the competition with swift submission approvals





Center of Excellence
**Global Pharmaceutical Regulatory Services**

# AN INNOVATIVE DOCUMENT MANAGEMENT TOOL FOR A CHINA-BASED, HIGH-TECH BIOPHARMACEUTICAL COMPANY

**Client**
China-based Pharmaceutical Company

**Health Authority**
NMPA

**Freyr CoE/Products**
Freyr rDMS

**Service Offering**
Co-authoring, Co-Reviewing of Regulatory Documents

**Industry**
Pharma and Medical Devices

**Service Region**
China and US

**Client Location**
China (Beijing), US (Bridgewater)

**Therapeutic Area/Indication**
NA

**BENEFIT HIGHLIGHTS**

- Better document management
- Seamless third-party integration
- No limitations to number of documents.
- Concurrent authoring and reviewing of documents
- Enhanced agility

## Business Imperatives

- Document authoring and reviewing tool. They had moved away from a contract vendor for BLA submission writing. The vendor used another document review tool. The replacement tool would require single as well as collaborative authoring and reviewing capabilities.
- The client wanted to use the tool for authoring and reviewing regulatory submissions, which included BLA,IND,MAA.

## Challenges

- Collaborative authoring and reviewing of documents across geographies
- Keeping track of changes made to documents by authors and reviewers
- Ensuring that latest versions of documents in progress are available to authors and reviewers
- After moving away from the previously used tool, clients were using OneDrive for document sharing and review.
- Access, version and folder maintenance were beginning to become cumbersome to keep track of

## Freyr Solutions & Services

- Freyr's rDMS integrated with the client's Office 365 served as a document authoring tool with the document repository under the client's domain. The tool allowed for secure and online accessibility from any location, with control over individual access, permissions, and rights.
- Freyr rDMS was integrated with the client's Office 365, which allowed for collaborative authoring and reviewing of documents. Users could now work on the same document concurrently.
- Traceability and audit log features ensured that the client could track all changes made to the document.
- Trainings on the use of the tool were provided to the team. Minor customizations were also made for the client.

## Client Benefits

- Better management and indexing of documents.
- Concurrent authoring and reviewing of documents by multiple users across geographies.
- Secure cloud storage and access to documents, which could be manged by the tool.
- Microsoft Login, allowed the client to utilise their own security requirements for application login





Webinars

Freyr Webinar Series

In a view to making the industry understand the most recent updates on the Health Authorities (HAs) and to ensure that they follow the best compliance practices, Freyr has conducted on-demand webinar sessions on the following topics:

**Indian Medical Device Regulatory Landscape - Current Dynamics**

February 22, 2023

**Strategic Regulatory Partnerships How to Evaluate and Engage with a Regulatory Partner?**

February 28, 2023

Know More

# Client **Testimonials**





I am sure you have heard by now that we have received our first-ever approval from the FDA for our Brands division. This is a major milestone for us as well as for my team here in Reg Ops. I would be remiss if I didn't point out that we would not have been able to do this without the help of your dedicated team. From the original filing, to the following year of responses, all helped get us to final approval.

Thank you, Freyr team, for a job well done!

**Sr. Director, Head of Regulatory Operations**
Ireland-based, Global Specialty Pharmaceutical Company

A big thanks to Freyr team for the support they have provided to us on priority. We really appreciate the extra effort that the Freyr team has put into providing the reports on time. We are looking forward for a continuous business association with Freyr.

**Head of Quality Assurance**

You have exceeded our expectations as a team and as individuals! Special thanks for all the added prepared technical documentation!! What an effort, team! Again, many thanks for all the work and effort put into this, Moving forward positively.

**Regulatory Affairs Officer**
UK-based Global Medical Device Design and Manufacturing company

I think these reports were very detailed, and generally either confirmed some of our assumptions or provided some new context around claims or administrative practices that helped complement our understanding. Thank you so much for the diligence towards these.

**Global Regulatory Director**
UK-based Top Multinational Consumer Goods Company

Thank you for the timely support over the weekend, which allowed us to resubmit quickly after being notified. This continues to demonstrates Freyr's commitment towards our company's milestones.

**Director, Global Regulatory Affairs, Operations**
India-based, Global Top Generic Pharma Company

*A Glance at Medtech with*

# SATISH CHANDRA BEHARA

DIRECTOR, AMERICAS MEDICAL DEVICES SALES

## HELLO SATISH.

**A warm welcome and good wishes to you!**

Thank you so much for having me here! Glad to share my thoughts.





**In 2022, the global medical devices market reached a value of nearly $495.46 billion, and the number is projected to double in the next ten (10) years. Amidst these projections, how can Medtech firms stay intact and cash on the growth opportunities?**

Yes, you are correct. There is humongous growth happening in the medical devices industry, both in developed and emerging markets. There was a slight decline in the demand for medical devices during the COVID-19 period because people were not opting for procedures that were not life life-threatening, like dental procedures or orthopedic treatments. But that has not stopped Medtech companies from investinvesting in their research and development (R&D) activities. On the other hand, the pandemic has rapidly increased the demand for wearable devices, despite some security concerns attached to them. There is an increasing number of players entering into this segment, offering a variety of features and options to the consumers along with extremely affordable pricing.

In my opinion, Medtech companies have a lot of growth potential, taking into account that the consumers are opting for more portable & wearable devices, and homecare settings, in the post post-pandemic era. Also, the rising number of geriatric population and the prevalence of chronic diseases due to sedentary lifestyles have only multiplied this demand. Medtech companies should scale up to leverage these conditions and come up with solutions that cater to these demands.

**Year after year, we witnessed Freyr winning medical device customers by a multifold. It takes a great deal to sustain such growth. What, according to you, has been a breakthrough for us in this journey?**

Freyr's biggest strength is its expertise. We have played to our forte and expanded our service spectrum, catering to the end-to-end Rregulatory needs of our customers. Freyr has always aligned itself to the ever-evolving market demands, whether it is in the Software as a Medical Device (SAMD) or digital space, which gives us an edge over our competition. As per my understanding, our growth has been very organic, and the main reason for this is our DNA, which is a confluence of adaptability, scalability, and resilience.

**Artificial Intelligence (AI) is redefining the medtech industry. At the same time, HAs worldwide are updating their regulations to govern this move to protect patient safety. As a service provider, what competitive advantages or framework do we offer to companies to stay compliant with the advancements?**

American journalist and author of "Hit Makers: How Things Become Popular," Derek Thompson, said that people prefer to choose something that they are familiar with. What makes it interesting is adding a surprise factor to it. The familiar surprise can be in the form of a chatbot or deep tech, or Natural Language Processing (NLP) that comes with our regular products and services. Freyr is making great strides in the digital space with its chatbots and AI integrations to provide a better experience to its customers. We are in the process of automating our processes and service in this space, whether it is in Rregulatory intelligence or submissions or artwork and labelling, or the Regulatory Information Management System (RIMS) platforms, thus targeting to enhance the customer delight index and creating an edge over our competition.

**Should we be cautious of the idea that someday, advanced technologies will also hit the Regulatory service provision? Is there any technology that the service providers must adapt to?**

It is imperative that Rregulatory companies understand the global megatrends and get aligned with itthem. Climatic changes and geopolitical uncertainties are also affecting Regulatory processes across the globe. Freyr is leveraging technologies like AI, Machine Learning (ML), and BIG DATA to facilitate real-time regulation and intelligence. Now, Rregulatory companies and agencies are also leveraging real-world evidence to collaborate with and assess the

benefits and risks associated with medical devices. Rather than being cautiousn, we are getting into a mode of proactive approach, where we are training our Rregulatory professionals to upskill in digital technologies, as the future is all about data rather than documents.

## Exploring, Experimenting, and Expanding. If we could relate it to Freyr, where exactly do we stand in each phase with Respect to the medical devices segment?

It perfectly fits the phases that the medical devices segment is going through at Freyr now.

> **We are exploring some of the most unchartered markets across the globe, experimenting with new technologies in the digital space, and expanding our services spectrum into areas like technical writing, change assessments, SaMD, etc.**

## Medtech App you regularly use.

Practo.  It had proved to be a blessing in disguise for me, especially during the COVID-19 period.

## Team moment for a lifetime.

Henry Ford said, "Coming together is a beginning, staying together is progress, and WORKING TOGETHER is a success."

> **If we are working together towards a single goal, every moment is a teammoment, and fortunately, I am experiencing that every day here at Freyr.**



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Complying with the General Data Protection Regulations (GDPR), we have changed how we collect, store, process, and transfer data. We hope you understand Freyr's efforts in complying with mandatory GDPR requirements. Let us be compliant together.

Kindly note that the Regulatory scenarios and mandatory deadlines discussed in this issue may be altered in the near future. It might be due to the current pandemic outbreak or the periodic Health Authority (HA) updates. Hence, it is probable to find different perspectives/opinions in comparison. Kindly be aware.

# Globally, Freyr is a Strategic **Regulatory Solutions** and **Services** Partner to

**8** Product Labeling and Artwork Management

**5** Forbes Global Top 10 Health Care Equipment and Services

**3** Forbes Global Top 10 Household and Personal Product Companie

**3** Forbes Global Top 10 Chemicals Companies

**2** Forbes Global Top 10 Food and Drink Companies

## 1200+ Customers

**135+** Innovator Pharma Companies

**55+** Bio-Tech/Bio-Similar Companies

**135+** CROs/Consulting Companies

**290+** Medical Device Companies

**400+** Consumer Companies (Cosmetics/Food and Food Supplements/ Chemicals)

**185+** Generic Companies/API Manufacturers

USA | UK | Germany | UAE | India | Canada | Mexico | Malaysia | South Africa | Singapore

Slovenia | Sri Lanka | Australia | Poland | France | Switzerland | China | Japan | Brazil | Columbia

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