freyr
GLOBAL REGULATORY SOLUTIONS & SERVICES
AN ISO 9001 & 27001 COMPANY

VOL 4 ISSUE 3
2016

CONNECT

Dynamics of eCTD Submissions influencing the Industry

freyr CPhI Pharma Awards 2016
FINALIST - 2016
Excellence in Pharma:
Regulatory Procedures and Compliance

LEAD STORY
eCTD Current Trends and Landscape

WHAT'S INSIDE ?

Content Contributors

Nanda Kumar Gollapalli
Vishal Chaudhary
Sudeep Kolluri
Mohammed Abdul Irfan
Kush Mukherjee
Venu Gopal

FOREWORD

Hello Everyone,

Welcome to another episode of Freyr Connect!!!

It's a great pleasure to present another insightful edition of our quarterly newsletter. It gives us great sense of satisfaction to know that we continue to be favorites for our clients. Our partner ecosystem continues to thrive with a renewed and focused effort to build a strong partner network, in all global regions.

Every quarter we see remarkable transformations in terms of business prospects that help us deliver excellence to our customers. This quarter, we are pleased to announce one such remarkable achievement that **Freyr has won a finalist spot along others like Merck in CPhi Pharma Awards 2016 for Excellence in Pharma: Regulatory Procedures and Compliance.** On this occasion, we don't want to miss a chance to thank our committed employees for their unrelenting support to the company.

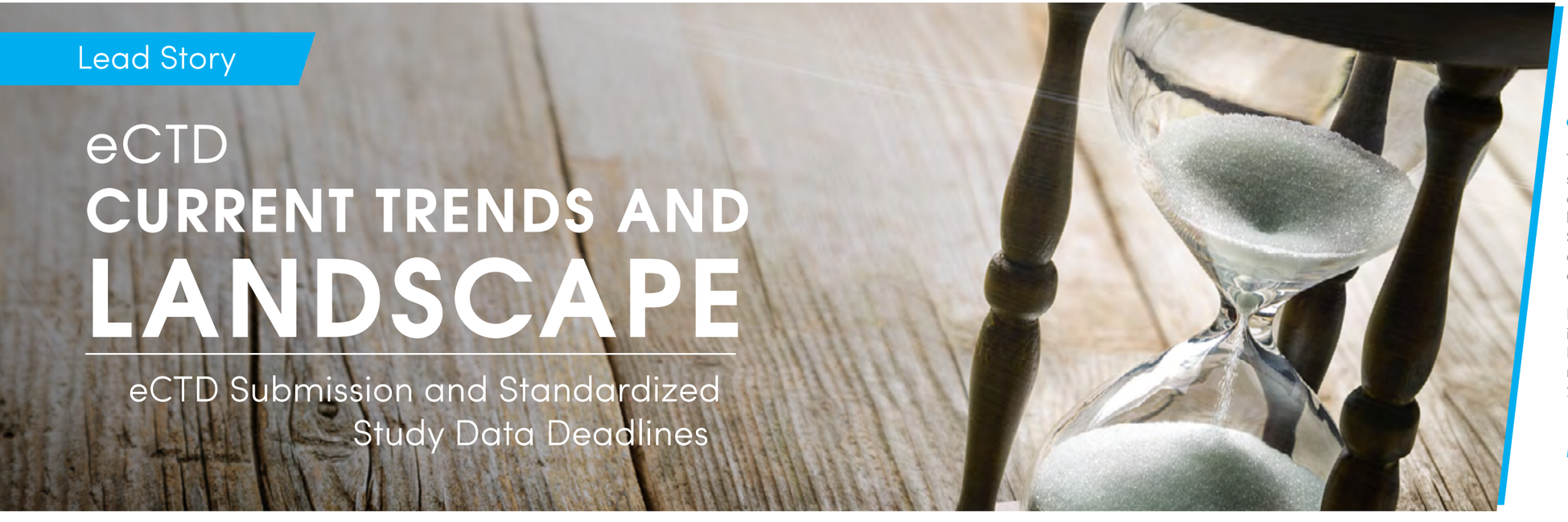
What's inside this time? We begin with our lead story, "eCTD Current Trends and Landscape" that emphasize on the immediate requirements of eCTD submissions in the industry. Reading through this issue, you'll get latest insights on industry updates and best practices to win-over the competition in a streamlined regulatory landscape. Make sure you check out the issue for 360° overview of all the fun and development happened in house.

Lastly, we would like to thank everyone who contributed to this edition of Freyr Connect. We hope this copy will enlighten your day.

Happy Reading!!!

Rajiv Rangan
Co-CEO

Suren Dheenandayalan
Co-CEO



Lead Story

eCTD CURRENT TRENDS AND LANDSCAPE

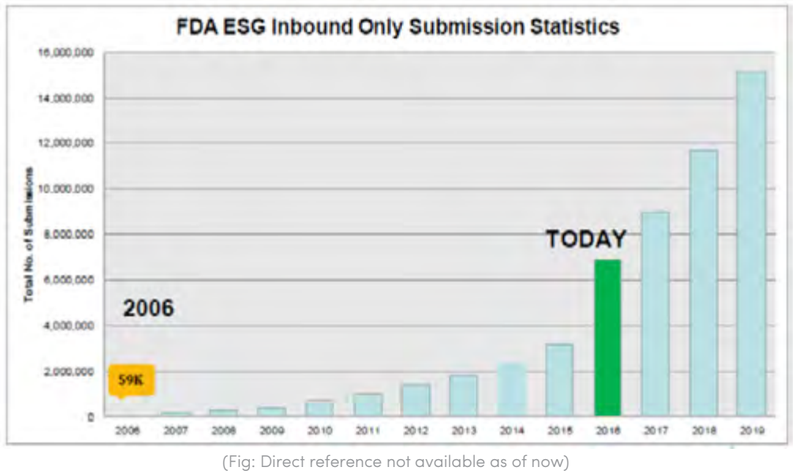
eCTD Submission and Standardized Study Data Deadlines

Ever since the electronic common technical document (eCTD) submissions are made mandatory by the FDA in 2008, the life sciences industry has been facing certain difficulties in regulatory processes. Even though the eCTD has been of great help in managing huge volumes of important documentation, there are a few glitches that complicates the submission process for the organizations. In this segment, we'll be discussing about those stumbling blocks faced by life sciences companies during the eCTD submissions.

The role of eCTD is to help pharmaceutical companies streamline the submission process by reducing the time to market while minimizing overall cost. However, a recent analysis made by the Open Text™ Corp (a leading company in enterprise content management), it's found that most of the pharmaceutical companies are facing difficulties to meet the deadline created by the FDA to comply with the standards using eCTD format.

Present-day Picture

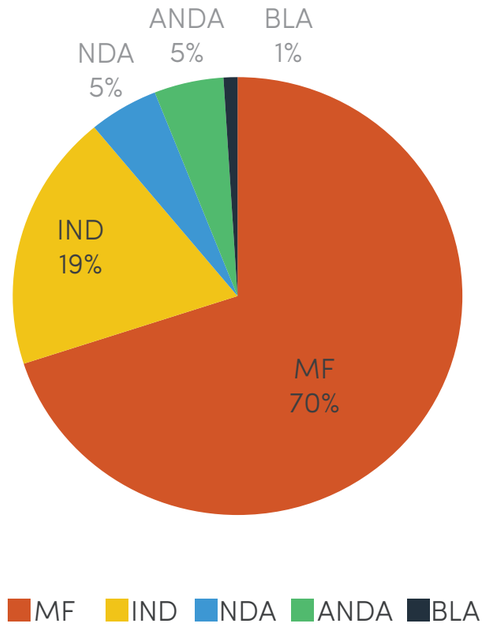
According to the reports, 2017 is expected to mark Electronic Submissions Gateway (ESG) submissions with a huge number of 9,000,000 submissions. By the end of 2016, the industry is expected to witness an increase in ESG submissions by approximately 5,000,000.



(Fig: Direct reference not available as of now)

Although it seems that the progress rate is worth a talk, the numbers say otherwise. Out of all the DMF holders, only **27%** have made it to submissions through ESG.

PAPER SUMBISSIONS TO FDA



freyr Regulatory Centers of Excellence

Submissions 360
Global Electronic Submission and Publishing Services

eCTD Essentials

The central role of eCTD in pharmaceutical industry is to streamline all the regulatory submissions. And it is carried out by coordinating the outline and module-based set-up for pharmaceutical submission requests. Such submissions ratifies convenient and quicker application filing. This interface is elevated by the ICH at even intervals in order to make it more user-friendly.

For instance, in February 2015, there was a draft implementation guide for ICH eCTD v4.0 released by ICH's M8 expert working group (EWG). It was the first major version update after the announcement of v3.0 in 2003.

More on the eCTD

- eCTD is built on acknowledged standards aligning to the ICH requirements that didn't witness major modifications in past few years
- Regulatory tools used to evaluate the submissions have been upgraded and henceforth deliver robust performance
- It uses a common format with relatively simple deviations (Module 1 and STF acceptance)
- The development lifecycle offers comprehensive submission history with easy knowledge sharing for product
- Unified development ensures transparency in the submissions lifecycle
- Simple tools are used for Publishing and Submissions
- Conversion and development process aligns to the paper-based methods
- Sharing the changes with local affiliates involved in the submission procedures
- Affordable implementation

Major Stumbling Blocks in the Process

In spite of all the advantages, there are still a few impediments that makes eCTD implementation quite a challenge for the life sciences and pharmaceutical companies. The foremost bottleneck here is to identify the best-suited regulatory software that abides by the eCTD submission requisites, in addition to the following hitches:

- Requires cutting-edge technology and seasoned staff
- Standardization can not be implemented to the entire content
- Regional differences seen in bookmarking, hyperlinking and PDF version
- Demanding to implement last-minute modifications
- Product knowledge is lost if the concerned subject matter expert leaves the processes in between
- Limited access for creation or customization for local affiliates
- Region specific validation and approval rules
- Expensive baseline submissions
- Strenuous lifecycle management

How should Companies Deal with eCTD Challenges?

"Always listen to experts. They'll tell you what can't be done, and why. Then do it."

Robert A. Heinlein

As eCTD format has become mandatory in the key markets, it has become essential for the companies to conceive a unified environment that aids the lifecycle of every kind of inherent submission. In this way, they can effortlessly manage the exhaustive system of accumulating, acclaiming, releasing and documenting new drug/medical device applications.

However, in most of the cases, companies lack such an integrated platform. Even though some pharmaceutical companies have some of the components, there are still many fields where key functionality is integrated. There are firms, who still follow the traditional paper-based methods, thus wasting both considerable amount of time and money. In order to successfully carry out eCTD submissions, pharmaceutical companies must grasp all documents, including assortments, responses to questions, modifications, and restorations in a consistent electronic format.

The primary component of eCTD submission is XML "backbone" file that provides metadata info for the submission files and provides lifecycle guidelines for each document within the submission. Pharmaceutical and life science companies should use this data structure, as it helps effective submissions at a faster rate. It is advisable for the pharmaceutical companies to use a robust software product to manage the integrated regulatory data and regulatory submissions process.

-End of Article

UNIQUE FEATURES THAT SIMPLIFY DOCUMENT MANAGEMENT

- Flexible, simple, efficient and centralized platform
- Covers end-to-end TMF process
- Supports DIA TMF reference model V 3.0
- Secure and Cloud-hosted
- Configurable to existing eTMF model
- Pay-as-you-go application

Freyr eTMF

GO AUDIT-READY FOR GLOBAL CLINICAL TRIALS

Integrate a Global TMF Document Management System

It takes five phases and many years to experiment a new drug to bring it to the market. Working through the grueling clinical trial processes at many individual sites across the globe, you may wish to get to the market with a clean chit from the respective Health Authorities. But have you thought of inspection-readiness of your clinical data? Is it properly tracked, compiled and documented? A single compilation, documentation or validation error may put down all your compliance efforts. **Act Now!!!**

Integrate a centralized global TMF document management system, **Freyr eTMF**, to collaborate the data with ease, to validate it in real-time and ensure the audit-readiness for successful global Clinical Trials.

FOR MORE, VISIT

REACH US AT

+1 908 483 7958/ +44 2037 012379
+49 6181 707 9007 /+91 040 4848 0999
sales@freyrsolutions.com

Label 360
GLOBAL AND REGIONAL Label Content and Process Services (CCSD/LPD/RSI)

FDA PUTS THE GENERIC LABELING RULE ON HOLD UNTIL APRIL 2017

Generic Drug Labeling and the Dilemma Prevailed over Updating the Safety

We explained in our last edition that how FDA's announcement for rolling out the much-anticipated labeling rule for generic drug manufacturers created a momentous buzz in the industry. With the new announcement, the generic drug companies may still have to wait till April 2017 to update the labels like their brand name counterparts. This is the third time since 2013 that the FDA has put off this particular rule for generic drug manufacturers.

Back in time, the US FDA had proposed a rule that was expected to allow generic labelers/companies to update their labels as soon as they found new safety events.The main purpose of this proposed rule is to take care of the patient safety at a more granular level.

The risk factors, the right direction, the fear of improved costs, and why the FDA can't take the responsibility: the dilemma prevails.

Are there any risk factors that can be triggered with this delay? Should generic drug manufacturers be worried about it? Well to some extent, yes. The cost implications and timeline delays directly put the manufacturers under the risk of failure to warn cases. Manufacturers with a prevalent product line across globe will face even bigger possibilities of risk since they will be obliged to sustain the complex labeling requirements for same product in different countries. The delayed rule may also affect the precision of safety label changes because of the distributed and partial safety information available for generic manufacturers, which otherwise is accessible either by the innovator or the FDA.

Even though the branded and generic labels should be similar, the recommendations for generic drugs may get affected if information on the label is different. The healthcare providers and the patients may further be driven into the confusion caused because of multiple versions of labels. In the current scenario, Generic drug labelers, even if they have found new safety events, cannot update the safety labels but to mirror the labels of Reference Listed Drugs (RLD). As a result, the scope of updating the new safety information on labels for generic drug manufactures would be very less. This could push them for being accountable for the unexpected adverse events that might affect patient's health condition and thus might risk generic manufacturers to legal liabilities Meanwhile, there are even suggestions that the FDA should take up the responsibility of updating the old generic drug labels in order to leave it for manufacturers which in a way will increase the costs.

In Conclusion

There is no doubt to the fact that this labeling rule might have a huge impact on the generic industry. This can be one of the key reasons that the FDA is taking time to ensure persistence and evaluate if there is a more efficient approach of guaranteeing patient safety and perhaps confiscating the associated concerns. Meanwhile, we suggest all holders of NDAs, and ANDAs put in force the robust Regulatory intelligence systems and keep track of post-marketing reports to ensure the information on their product labeling is accurate, and not false or misleading.

-End of Article

CMC 360
Global CMC and Change Management Services

TYPE IV DMF

DRUG MASTER FILE

Drug Master File (DMF) holds great importance in terms of information associated with several medical products regarding their chemical specifications, and manufacturing. The type IV DMF is associated with the material used in their preparation or as we call them excipients. Excipient DMF is submitted to FDA to support IND, NDA, ANDA, BLA, and other DMF. Let's take a tour of the general guidance to prepare Excipient DMF as stated by "The International Pharmaceutical Excipient Council (IPEC) of the Americas".

- Excipients should follow ICH CTD format
- Excipient: Other than API which are tested for safety, functionality and included in the formulation
- There can be a single DMF for single ingredient excipient / for mixtures formulated to one excipient
- Excipient DMF submission is not a law, it is up to the DMF holder
- Excipient DMF will not be approved/rejected
- The main purpose of filing excipient DMF is to maintain confidentiality of the information containing manufacturing, controls and technical data to support safety and quality
- DMF should be in English / translated to English (if in other language)
- DMF should contain
  - US Agent appointment letter (If agent appointed)
  - Statement of commitment (stating that DMF is current)

Maintaining the DMF

- If DMF holder adds/deletes/changes any significant information from the DMF, then he/she should intimate changes to authorized persons to use DMF in writing
- Two types of submissions may occur once DMF is filed
  - Significant change reports to FDA (refer IPEC significant change guide for the classification of the changes like Level 1 changes and Level 2 changes)
  - Annual reports to FDA
- Both the submissions should contain transmittal letter regarding the submission type and complete Letter Of Authorization (LOA) list
- If no annual report is filed for 2 consecutive years then the FDA will consider DMF as Inactive .

DMF - New Submission

1. **Transmittal Letter**
   - Contains Type of DMF, US agent address, manufacturer name, manufacturing facility address, holder
2. **Statement of Commitment**
   - To ensure that the DMF is current and will comply with the statements made, conditions and procedures described herein shall be strictly followed
3. **Content according to ICH CTD - Explained**

Amendment to Original Submission

1. **Transmittal Letter**
   - Must contain, type of DMF, US agent address, manufacturer name, manufacturing facility address and holder
2. **Statement of Commitment**
   - To ensure that DMF is current and will comply with the statement made. Conditions and procedures described herein shall be strictly followed
3. **US Agent Appointment Letter**
4. **Changes Description**

Annual Report

1. **Transmittal Letter**
   - Contains type of DMF, US agent address, manufacturer name, manufacturing facility address and holder
2. **Statement of Commitment**
   - To ensure that DMF is current and will comply with the statement made. Conditions and procedures described herein shall be strictly followed
3. **US Agent Appointment Letter**
4. **List of changes during one year period, with dates**
5. **List of authorized parties to refer the DMF, dates of LOAs**
6. **List of parties whose authorization has been withdrawn to use the DMF**

Technical content of the DMF

Recommendations from FDA

- A4 size
- 8.5×11 size paper
- Times new roman font 12 size

Is recommended and any required binders should be used as per the DMF specified by FDA.

Description & Characterization

Physicochemical characterization of the excipient (if it is a mixture – composition of the mixture)

Intended Use

Maximum daily dose, functionality, human/veterinary use etc.

Characterization of the Excipient

- **Physical characters:** Color, MP, BP, Refractive index, Pk, Optical rotation
- **Chemical structure:** proof of structure (IR, NMR, UV, optical rotation, MS etc.,)
- If the excipient is USP/NF grade then no need to further characterize the excipient. If not, detailed methodology and validation data should be provided
- **If the excipient is not official**
  - Qualitative and quantitative description, proof of structure (IR, NMR, UV, optical rotation, MS etc.,), chemical attributes like – M.P, structural formula, empirical formula, molecular formula etc.,
  - Any recordings like chromatograms / graphs etc.,
  - Purity tests like HPLC/GC/TLC/ appropriate analytical procedures

Facilities Description

Address and contact details of the manufacturing site

Manufacturing

Origin of materials, flow chart of manufacturing process, identify critical steps, key equipments, controls and packaging

Process Controls during Manufacturing and Packaging

- Controls during manufacturing and packaging
- Acceptance criteria and results

Specifications

- Based on the developmental data, manufacturer should propose specifications
- If any monograph controls the excipient, and reference to monograph should be provided and all the tests in the monograph should be included and additional test methods should be validated.
- If the excipient is of non-compendia excipient then minimum specification should include description, identification assay, impurities, water content (if applicable), physicochemical characters (pH, viscosity, particle size etc.,) of the excipient

Reference Standards for Materials

Details regarding used reference material

Batch Analysis

- Size, date, batch number
- Minimum of 1 COA should be provided

Stability

- Most of the excipients are stable but some excipients which are liable to change with respect to time – manufacturer should conduct stability studies on 3 batches (minimum of pilot scale)
- Refer IPEC guideline for further information.

In Conclusion

In order to ensure quality, safety, and efficacy of the medicines it is critical to maintain quality of the excipients. The drug formulations are influenced by excipients to a great extent due to which the API (active product ingredient) and drug products falling under categories of cosmetics also get impacted. For that reason, implementing GMP (Good Manufacturing Practice) standards and maintaining smooth CMC operations for the excipients becomes necessary.

-End of Article

Regulatory
Dossier 360
Global Regulatory Dossier Services

Medical Device Registrations in Saudi Arabia

An overview of Challenges Vs Solutions

The Saudi Food and Drugs Authority (SFDA) ensures safety, quality, effectiveness and performance of the medical devices according to their intended purpose. The SFDA regulates all the medical devices manufactured or marketed for selling within the Kingdom of Saudi Arabia through the medical devices Interim Regulation (IR) and Saudi Arabian Medical Devices Marketing Authorisation System (MDMA). However the process leads to several technical challenges and poses a great difficulty for companies to get along with device registration requirements. To make you better understand the scenarios, we are presenting you majority of those challenges and the possible appropriate solutions.

Technical Challenges & Possible Solutions

If the SFDA recalls manufacturer's devices due to the violations according to Saudi Food and Drug Authority (SFDA) law?

Solution: Authority may recall devices if they are either defective or pose a risk to health, or both. But a medical device recall doesn't always mean that the customer must stop using that device or return it to the company. A recall sometimes means that the flaws in the medical device needs to be adjusted, or fixed.

Possible actions to consider in case of device recalls:

a. Inspecting the device for problems
b. Taking appropriate corrective actions to identify the defect and repair the device
c. Rectifying and correcting settings on the device
d. Re-labeling the device with appropriate instructions
e. Notifying patients about the problem to avoid any future health risks

If the SFDA rejects one of the accessories for medical device?

Solution: According to the SFDA, accessories are devices specifically intended by its legal manufacturer to be used in combination with the corresponding medical device to accomplish its intended purpose. If the accessory can be used as a stand-alone medical device, then the SFDA does not consider it as an accessory.

In such cases accessories must be listed as a medical device.

If the SFDA rejected label due to an issue with a/c power supply?

Solution: If a device uses an a/c power supply, the manufacturer needs to provide accurate information "operate with a 60 Hertz supply at nominal values of either 230 or 400 volts" on the label. If the voltage or Hz values on the label submitted in label section are outside the range, then a justification is required from the manufacturer. It is advisable not to alter the text of the template.

If the SFDA is not accepting the Audit Report (more than 1 year old) of the manufacturer, issued by the Europe based notified body?

Solution: The audit report is required to verify that the certificates issued by the notified body are current and valid. If the most recent audit report is more than a year old, the applicant must provide a justification issued by the notified body. A common error, generally observed is the certificates & audit reports are submitted on behalf of the makers of the device (subcontractors) and not the manufacturer. There must be at least one month validity remaining on the certificates for the SFDA to process the application.

If two sub-manufacturers make the same product for the same legal manufacturer, then how to apply for the MDMA?

Solution: The MDMA will be issued to the legal manufacturer based on the name & address mentioned in the original approval and must match with all the related documents. For example, Label & Instruction for Use (IFU).

If a manufacturer has a device which is approved by the US FDA and the European notified body, which jurisdictions information/documents would be useful for processing the SFDA approvals?

Solution: It is advisable for a manufacturer to undergo CE Mark approach because, the SFDA review process for the CE Mark method tends to be smoother and faster, so in general the applicants /Manufacturers are advised to extend the dossier approved in EU to Saudi Arabia. Nevertheless, the manufacturer must consider the license validity in both the US and Europe, as it speeds up the process to get the SFDA license. Here we can find interesting strategy; for example, if a manufacturer has obtained the CE Mark from one of the EU notified body, that will expire in 1 year, and a 510(k) certificate from the US FDA, that will expire in three years, then the manufacturer should take the US FDA route to get compliant with SFDA rather than the EU route since they will get 3 years of validity for device license in the SFDA too.

In Conclusion

It is very important to know the market value and market entry strategy of products. Successful registration of manufacturer's medical devices with the SFDA is based on how the manufacturer is providing the entire documentation, mandatory fields, certificates, and AR (Authorised Representative) accessibility with the SFDA. Successful maintenance and renewal of registrations further depends on how the AR monitors, reports and maintains the surveillance records during the post-marketing phase for the continuation of marketing.

-End of Article

Artwork 360
Global Artwork Design and Process Management

Quintessential Rudiments for

Dynamic Artwork Management System

What makes AMS a must-have enterprise solution for driving artwork processes?

Most often companies consider labeling as one of the key practices in pharma regulatory lifecycle and tend to neglect the importance of artwork in the due course. The process is complex, since it involves several team members and sponsors to coordinate, with that it ultimately affects the supply chain to a great extent. More the number of people involved in the process, more are the chances of errors in the final artwork. The risks that come along can lead to:

- Risk to Patient's Health
- Negative Brand Reputation
- Product Recalls and Delays

While most of the companies all over the world have their own AMS (Artwork Management System) in place, in most of the cases either it is still driven in paper format or isn't competent enough. In such scenarios where a variation needs to be executed, paper or manual based AMS (Artwork Management System) can make it challenging to implement the change through different platforms. Collating and translating inputs from technical, marketing, regulatory and local market content further becomes challenging. Ineffectual AMS can lead to several challenges such as:

- Incomplete/missing translation
- Manual QC dialed to detect detailed errors
- Approvals for huge capacities
- Duplicated information led by multiple revisions
- No transparency
- Incorrect source copy

These challenges directly or indirectly affect different stakeholders associated with the process. Let's explore how erroneous Artwork management impacts different stakeholders in the regulatory lifecycle.

Regulatory Authorities

When the products get into the hands of regulators, most of the recalls are triggered due to labeling errors which may or may not be an outcome of poor coordination of the artwork management. Repeated incidents have made regulatory authorities less tolerant towards inefficient practices and therefore tend to take retributive action against the companies who fail to stick to anticipated GMP criteria.

Pharmaceutical Companies

Warning letters or product recalls due to artwork errors affect the company's brand repute, revenue, and assets. Recalls straightaway drives the company to rework which not only wastes resources but also costs of tens of thousands.

Patients/End Users

Patient safety is the most important aspect in the regulatory space. All these regulations ultimately make sure that the patient's health is never jeopardized. It is manufacturer's eventual accountability to display accurate information on the drug package, so that the data is not misled or does not pose any risk to patient's health due to incomplete information. The harm may not be severe but the patient's trust definitely gets undermined.

AMS (Artwork Management System) besides being an automated system needs to be aligned with key activities to deliver industrial results. Let us explore the vital undertakings that is critical in the whole picture.

- Assessing functional groups involved in the current artwork review and approval process
- Considering the number of artwork studios involved in the artwork creation
- Evaluating current arrangements, applications and tools used in artwork process
- Assessing current artwork repository
- Identifying the number of SKU's and brands or product line
- Analyzing opportunities in terms of manufacturing sites, markets, print dealers, third party companies and third party markets
- Defining scope and success criteria

PERKS OF ARTWORK MANAGEMENT SYSTEM

What is so good about an AMS (Artwork Management System)? How can it help an organization? Is it worth? These are few questions, which companies often stumble upon to make a decision for implementing AMS in their labeling and package lifecycle. Let's have an quick look on how AMS can impact the overall lifecycle:

Agility: It becomes easy to manage intricate needs of translation in different local languages as per the regulatory requirements. This further helps companies to increase the scope of global business and eventually time to market. It becomes easy to understand the triggers of artwork changes and business dynamics around it.

Compliance Ready: Being compliance ready is a demanding task for companies. Artwork management system helps to quickly retort to the ever-evolving regulatory requirements resourcefully and meritoriously. Single process followed across the globe reduces the compliance driven penalties.

Traceability: Comprehensive audit trail allows companies to track down the information even at granular levels, thereby keeping the data flow transparent.

Automated: AMS is an automated system which does not require any specific technical skill. The system keeps the contextual information and content in a segregated format, provided by multiple departments such as design, compliance, trademarks, sales, etc.,

Effective Monitoring: Centralized control system to manage and store regulated translations and content that can be pulled for programmed labeling and packaging requirements. Increased quality due to drop in product recalls or critical cases & product launch as a result of no artwork errors.

Business Case

Business Challenge

The client witnessed product recalls for a couple of products that ultimately lead to delay in artwork release and additional overheads. There were a number of rework iterations ranging between 7 to 8 cycles due to lack of process standardization.

Freyr Solution

Analyzing the status quo, Freyr consolidated and centralized various artwork studios and set up an FDA compliant and validated environment. Electronic proofreading solution and centralized common repository was implimented for artwork files. To streamline instructions for different functional groups, Freyr team created global standard operating procedure for the end-to-end artwork review and approval process. Our experts created an automated reviewer list so that none of the functional groups could have missed in the review and approval process. This in turn helped the client to measure the performance of the overall process.

Client Benefits

As the outcome of these implementations, the client received **(zero recalls, 99%** of proof reading accuracy, improvement in productivity by **75%**, zero compliance issues) for almost 2 years and multi lingual support.

In Conclusion

It is important to understand that implementing and deploying a robust artwork management system is a complex arrangement that demands strategic decisions to be made. Enterprise solutions for Artwork are advisable for companies in order to avail a centralized and standardized end-to-end pharmaceutical artwork creation process leading to improved accuracy mitigating product recalls or critical incidents.

freyr Regulatory Centers of Excellence

Content360
Medical regulatory, safety and clinical writing services

Narrative Writing Project Management, Made Easy

In the previous edition of Freyr Connect, we discussed about various challenges in the Narrative Writing Project in the article, "An Introduction to Safety Narratives for CSR". Going forward, in this article will discuss some of the tips to successfully manage the narrative writing projects. With different teams/members involved in the entire process, let us explore how each one of these can support managing the narrative writing projects.

Clinical Research Organization (CRO)

Careful management of narrative writing projects is a time consuming and tricky task! Excellent project management skills are required for tracking projects to ensure accuracy and consistency across a large number of narratives. Equipped with the following capabilities a CRO can help to efficiently manage and streamline the entire process.

- Assigning Lead/Key Medical Writer (MW), who can be a single point of contact between the CROs Medical Writing team and Clinical team /Reviewers at Sponsor
- Creating agreed work-flow to execute the project
- Defining realistic timelines
- Assigning adequate resources to complete the project
- Equipping Medical Writing team with the adequate facilities such as proper IT systems and other communication channels
- Having a risk mitigation plan

Lead/Key Medical Writer (MW)

A narrative writing project of greater volumes is complex as it involves several medical writers, and managing all of them becomes equally difficult. In such scenarios, a lead/key medical writer is required not only to act as a bridge between the medical writing team and Sponsor's clincial study team/ reviewers, but also to align the team on the same page with regular meetings, particularly to discuss changes requested based on the client review. Thus, it would be easy to maintain the consistency across all the narratives by different teams. The following are some of the crucial steps a Lead MW should consider and implement for the successful delivery of the narrative writing projects:

- Design a narrative template with the Sponsor's approval
- Writing sample narratives as a pilot inclusive of all categories and getting it reviewed and approved
- Request the Sponsor/study team to provide all the required source documents
- Update the team about time-to-time global comments
- Assigning the narrative batches for drafting and reviewing within the timeframe
- Reminding the reviewers to provide their comments in agreed timeframes

Based on Freyr's experience, the anticipated number of subjects, which would require narratives to be written for the studies in different therapeutic areas, are presented in the following table:

Therapeutic Area	Percentage of subjects who qualify for safety narrative in a clinical study
Immunology/Transplants	60% to 70%
Oncology/ Critical Care/ Hematology	50% to 60%
Infectious disease	30% to 50%
Metabolic disorders/ Respiratory/Gastrointestinal	20% to 30%

-End of Article

The Sponsor

The Sponsor has a key role to play in the narrative writing project just like in other clinical trial projects. With a clear view on the requirements and expectations, a sponsor should

- Provide a clear picture about the projects and timelines to the CRO
- Involve and approve the narrative writing project planning, process flow designing and planning timelines for the draft, review and quality check
- Assign key stakeholders such as Clinician, Sponsor's investigator, Clinical Trials lead, Therapeutic lead to review and approve the narratives
- Provide inputs and approve narrative templates to fulfill their requirements before starting the project
- Review the sample narrative and provide necessary comments on-time

The Narrative Template and Sample Narratives

Having a flexible narrative template that meets both the client requirements and the style guide requirements is very important. In order to avoid hassles at a later stage for discussions about the style and format, the Sponsor/study team should confirm the template criteria for narratives and the format/presentation style, at first. Having reviewed and agreed on the sample narratives in all narrative criteria will help the medical writers to draft their narratives in similar format/style.

Auto populated text in the form of SAS output per subject can be a good kick off point to start writing narratives. This automates the process, reduces the time, increase the quality, and standardize some of the text in the narratives.

Important aspects regarding the style/format needs to be discussed are:

- Sentence framing (e.g., some clients prefer to start a sentence with a date, while others prefer to have subject demographic details, etc.)
- Date formats
- Criteria to decide the relevancy of medical history and concomitant medications
- Inclusion/exclusion criteria of normal ranges for laboratory results
- Trade/generic names to be used for drugs

Drafting and Reviewing Narratives in Batches

The narrative writing projects are carried out in batches (about 20 to 30 narratives in one batch) during the drafting and reviewing stage, to avoid the rework and to:

- Gives enough time for the reviewers to review and provide their comments
- Standardize the process, and to incorporate the feedback comments in the upcoming batches
- Manage project issues, if any, then and there instead of keeping it for the prolonged time

Peer Review and Quality Check (QC) of Narratives

The peer review and QC is a critical activity in the narrative writing project. The lead or key medical writer should review all the first drafts with respect to scientific, event flow, template, and formatting aspects. The respective medical writers should address the peer review comments before sending the narratives for the Sponsor review.

The narrative QC will be usually performed at the last stage of the project. This QC activity should be properly planned and allocated to medical writers with enough time to review with utmost accuracy.

Tracking Narratives

Tracking huge volume of narratives is critical and it plays a very crucial role in narrative writing projects. The lead medical writer and fellow writers involved in the authoring are usually in charge for the tracker update (with dates or other data required).

Well defined trackers (Microsoft Office Excel) with the key milestone dates, subject identification numbers, narrative events, medical writer who is authoring the narrative, first draft date; review dates, QC, and finalization/approval date is necessary. It gives exact count and status of the narratives in different stages and helps to trace out the history of development of particular narrative.

In Conclusion

The key behind a successful narrative writing project is to have all the processes streamlined with information collaborated from different sources within the timelines. The teams working on all the projects should be on the same page in terms of the style, format and content of the narratives. Lack of communication among the team members generally results in delays thus may leads to project failure. Therefore, it is recommended to opt for expert medical writing services to drive the project lifecycle efficiently, without any gaps.

-End of Article

freyr
Regulatory Centers of Excellence

PV 360
Global Regulatory PV and Safety Services

A Comprehensive Outlook

Medical Dictionary for Regulatory Activities (MedDRA)

In the later phases of 1990s, the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) developed MedDRA (Medical Dictionary for Regulatory Activities), which is highly standardised medical terminology to facilitate the sharing of regulatory data globally for medical products used by humans.

The documentation, registration, and safety monitoring of information for medicinal products, before and after approvals for distribution, is now available for everyone through MedDRA. Products covered under MedDRA include pharmaceuticals, biologics, vaccines and drug-device combination products. At present, MedDRA's implementation by regulatory authorities, pharmaceutical companies, clinical research organisations and healthcare professionals in countries like the United States, European Union, and Japan helps in attaining better global protection of patient health. The use of MedDRA is currently mandated in Europe and Japan for safety reporting.

MedDRA includes Standardised Terms for

- Symptoms, signs, diseases, syndromes and diagnoses
- Medication errors
- Medical device malfunctions
- Medical, social and family history information
- Sites (e.g. application, implant and injection sites)
- Medical, social and family history information
- Medical and surgical procedures
- Recognized medical devices and prescription practices
- Sites (e.g. application, implant and injection sites)
- Types of investigations (e.g. liver function analyses, metabolism tests).

Kindly Note: The names of drugs or devices are not included in MedDRA.

Organization of the Dictionary

Hierarchy of MedDRA dictionary is organized in the following way i.e. System Organ Class (SOC), which is divided into High-Level Group Terms (HLGT), High-Level Terms (HLT), Preferred Terms (PT) and ultimately into Lowest Level Terms (LLT). The MedDRA dictionary also includes Standardized MedDRA Queries (SMQs). SMQs are groupings of terms that relate to a defined medical condition or area of interest.

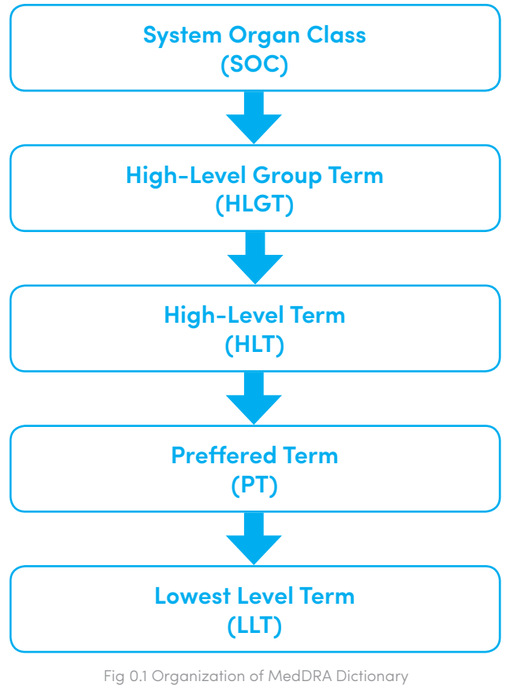


Fig 0.1 Organization of MedDRA Dictionary

MedDRA Term Level Definitions

- **LLT -** Lowest level of the terminology, related to a single PT as a synonym
- **PT -** Represents a single medical concept
- **HLT -** Subordinate to HLGT, superordinate descriptor for one or more PTs
- **HLGT -** Subordinate to SOC, superordinate descriptor for one or more HLTs
- **SOC -** Highest level of the terminology, and distinguished by anatomical or physiological system, etiology, or purpose.

There are 26 MedDRA System Organ Classes

1. Blood and lymphatic system disorders
2. Cardiac disorders
3. Congenital, familial and genetic disorders
4. Ear and labyrinth disorders
5. Endocrine disorders
6. Eye disorders
7. Gastrointestinal disorders
8. General disorders and administration site conditions
9. Hepatobiliary disorders
10. Immune system disorders
11. Infections and infestations
12. Injury, poisoning and procedural complications
13. Investigations
14. Metabolism and nutrition disorders
15. Musculoskeletal and connective tissue disorders
16. Neoplasms benign, malignant and undetermined (incl cysts and polyps)
17. Nervous system disorders
18. Pregnancy, puerperium and perinatal conditions
19. Psychiatric disorders
20. Renal and urinary disorders
21. Reproductive system and breast disorders
22. Surgical and medical processes
23. Respiratory, thoracic and mediastinal disorders
24. Skin and subcutaneous tissue disorders
25. Social circumstances
26. Vascular disorders

MedDRA Terminology Incorporates Terminology from the:

- Japanese Adverse Reaction Terminology (J-ART)
- Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART)
- Medicines and Healthcare Products Regulatory Agency (MHRA)
- World Health Organization Adverse Reaction Terminology (WHO-ART)
- International Classification of Diseases and Clinical Modification (ICD-CM)
- International Classification of Diseases (ICD)

Let us look into an example i.e. Nausea in the hierarchal organization of MedDRA

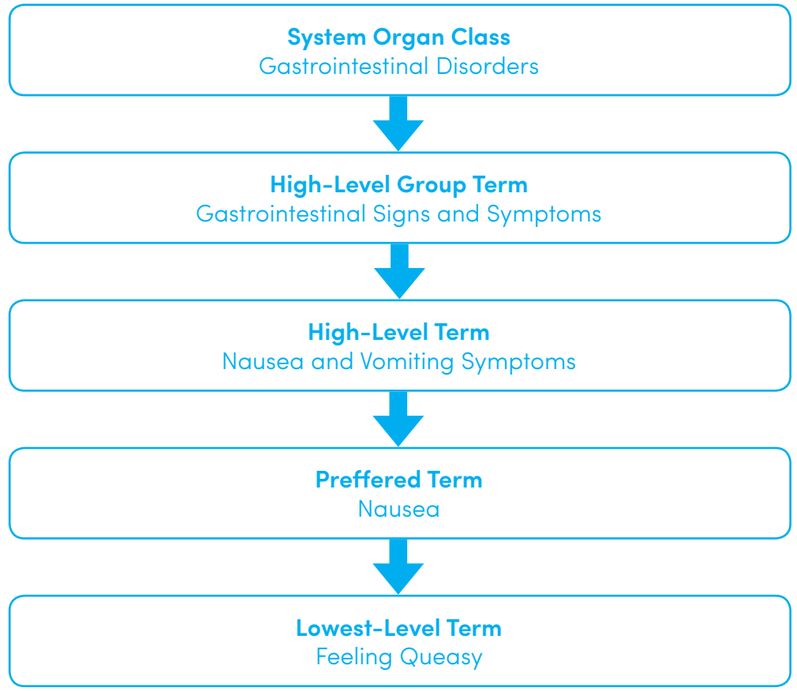


Fig 0.2 MedDRA hierarchal Organization for Nausea[5]

Maintenance of MedDRA

MedDRA is managed by the MSSO (Maintenance and Support Services Organization) under the supervision of the ICH MedDRA Management Board. The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) is the Trustee of the International Conference on Harmonisation (ICH) Steering Committee and sustain the intellectual property rights (ownership) of MedDRA. The Northrop Grumman (American global aerospace and defense technology company) - has been contracted by the ICH to act as the MSSO. MedDRA provide free access to regulators and is priced according to the company revenue for the industry. MSSO updates the MedDRA according to the changes entreated by the subscriber, for example to add a new medical concept that is yet to be introduced in MedDRA or to change an existing model. The verdicts are concluded by international medical officers on how to map the terminology within the grouping classes conferring to an overall agreement grounded on the language contemplations across different countries.

Updated MedDRA versions are released by the MSSO twice a year i.e. in March and September. The main annual release is released in March and contains changes at the HLT level and above, along with LLT and PT changes. The release which takes place in September typically contains changes only at the LLT and PT level.

Version 19.0 is the most recent one.

In Conclusion

MedDRA is a tool which allows for uncomplicated and easy analyses as well as advanced analyses. Appropriate coding of the term through MedDRA would be very helpful in analyzing the aggregate data during signal detection and PBRER. And also, SMQs (Standardized MedDRA Queries) is a unique and powerful tool which is used to understand the safety of a drug during pre and post marketing period.

-End of Article

Intelligence360
Medical regulatory, safety and clinical writing services

REGULATION OF DIETARY SUPPLEMENTS IN EUROPE

Placing dietary supplement in the European market can be an exigent task; having an understanding on the EU Food supplements regulations is the need of the hour for the food industry to beat the heavy competition.

Introduction

Dietary supplements, otherwise known as food supplements, in Europe are considered as the concentrated nutrients such as vitamins and minerals, which are marketed under the category of pharmaceutical dosage forms like tablets, pills, capsules, liquid ampoules, powders etc. These supplements are used along with normal diet either as the nutritional source or for physiological benefits. The dietary supplements majorly include vitamins, minerals (nutrients) and other elements such as:

- Essential fatty acids
- Amino acids
- Enzymes
- Pre and probiotics
- Botanicals and herbal extracts
- Other bioactive substances

It has been confirmed scientifically that dietary supplements are beneficial for maintaining overall health and assist in managing critical health conditions. The dietary supplement market in Europe is steadily on the rise due to increasing aging population, rising lifestyle diseases and exclusive healthcare facilities. There is no single well laid-out path for the commercialization of food products in Europe, owing to non-compliance issues that may arise across different member states. There have been continuous efforts to introduce new regulations and amend and revoke the redundant laws in order to achieve the harmonized control over different facets of supplements across the European Union.

European Food Supplements Directive

Dietary supplements, similar to food in general, follow the requirements and the general principles of the food law (178/2002/EC). In addition, the supplements are further regulated under the directive 2002/46/EC which came into force in August 2005. The objective of the directive is to make sure that the safety of the consumers is not compromised and promote the free movement of products across the member states of Europe and maintain a fair competition. The directive majorly focuses on quality of manufacturing, maximum daily allowances of vitamins and minerals, labelling requirements, health claims and market access. Currently, only vitamins and mineral supplements are subjected to this directive, though in future it may also regulate amino acids and other food supplements. Vitamins and minerals which are approved for manufacturing and their nutrient reference values (Recommended Daily Intake[RDI]) are given in annex I and II of this directive. The maximum amounts of vitamins and minerals are established based on the scientific risk assessment studies conducted by the European Responsible Nutrition Alliance (ERNA) taking into account the sensitivity of various consumer groups. As per this directive, introducing the product in the market requires notifying the competent authority by forwarding a model label of the product.

Labeling

Regulation (EC) No 2000/13 provides recommendations on labeling for the food products. As a part of the advertisement, the label should not indicate prevention, treatment and alleviation or cure of human diseases, and neither should the label bear the statement declaring that the balanced diet cannot normally supply the required nutrients. As per the regulations, the label should:

- display the name of the class of nutrients or the substances and their quantities (units as specified in the directive)
- possess the warning statement to prevent the consumption beyond the recommended daily allowance
- not give false notion that the dietary supplements substitute the normal balanced diet
- include the statement instructing that the product be stored properly to prevent the reach of young children

Health Claims

The health claims of the dietary supplements to be advertised are outlined in the regulation (EC) No 1924/2006. Scientific substantiation supporting the health claims is required to be submitted to European Food Safety Authority (EFSA) by the manufacturer or the business operator. The claims should not

- be misleading ambiguous or false
- cause suspicion on consumption of other foods
- give impression that the normal diet can lead to nutritional inadequacy
- condone or encourage over consumption of food
- induce fear in the consumers by using symbolic, pictorial and textual representations referring to changes in functions of the body

Novel Foods

Novel food is defined as the food or food ingredient that has not been consumed by humans at significant degree in the EU prior to 1997.The novel foods are generally developed by employing the latest production processes and technologies. EU directive considers the following as the novel foods

- Food with new or modified primary molecular structure
- Foods produced from genetically modified organisms & food containing genetically modified organisms (currently, these are regulated by the implementation of a separate regulation No 1829/2003)
- Food elements produced from algae, fungi and other micro organisms
- Foods produced from plants and animals that neither have a history of safe use nor did they originate from traditional propagation and breeding practices

Novel foods receive authorization in two ways; the first procedure is the notification system which requires the submission of evidence to the European Commission (EC) that the novel food is substantially equivalent to an already existing food product in terms of nutritional or physiological benefits, composition, and nutrient value, plant or animal source and type of propagation and breeding. Three months after the submission, the European Commission communicates about the dossier to the member states and the approval is based on its acceptance of the substantial equivalence. In case of lack of sufficient evidence, full authorization procedure is the subsequent step. The applicant can approach any of the desired member states and submit the dossier. The member state authority appoints the assessing body after verifying the submitted dossier which is followed by deliverance of the report

Mutual Recognition

Mutual recognition (764/2008/EC) allows the commercialization of food products that are not harmonized by the EU guidelines. Through this agreement, any product sold lawfully in any one of the member state of the European Union can be marketed in another state irrespective of the technical rules (any provision of a regulation, law of a member state not in compliance at EU level) which are specific to the national competent authority. The mutual recognition regulation require the following conditions to be met:

- THE FOOD PRODUCTS SHOULD BE LAWFULLY MARKETED IN AT LEAST ONE MEMBER STATE
- THIS REGULATION APPLIES ONLY WHEN THE PRODUCT IS NOT HARMONIZED AS PER THE EU LAW
- THE ADMINISTRATIVE DECISION MUST BE FORWARDED SOLELY TO THE AUTHORIZED ECONOMIC OPERATOR
- THE ADMINISTRATIVE DECISION SHOULD RELY ON THE TECHNICAL RULES OF THE CORRESPONDING MEMBER STATE
- THIS REGULATION IS APPLICABLE WHEN THE RESULT OF THE ADMINISTRATIVE DECISION POINTS, THE PROHIBITION FOR MARKETING OF THE FOOD PRODUCT, WHICH IS PREVIOUSLY MARKETED LAWFULLY IN ANOTHER MEMBER STATE

Important EU Regulations on Food Supplements

CATEGORY	REGULATION
Food supplements directive	2002/46/EC
Labeling	2000/13
Claims	(EC)No 1924/2006
Novel foods	(EC)No 258/97
Genetically modified food	(EC)No 1829/2003
Food for particular Nutritional uses	89/398/EEC
Infant Formulae	91/321/EEC
Energy restricted food for weight reduction	96/8/EC
Foods for special medical purposes	1999/21/EC
Mutual recognition	764/2008/EC

In Conclusion

In spite of extensive regulations on food supplements, complete harmonization to facilitate streamlined market access across the European Union is still a formidable task. There is non conformity among the member states on the following issues:

- List of vitamins and minerals in the annexes of the directive 2002/46/EC
- Health claims
- Maximum and minimum levels of dietary supplements
- Labeling issues (nutrient reference values, tolerance levels)
- Products other than vitamins and minerals

Therefore, companies intending to market the dietary supplements should beforehand evaluate the specifications and limits set by each member state in order to avoid the disapproval. In this aspect, companies should partner with regulatory intelligence experts who are proficient to gather and analyze publicly available regulatory information and help companies modify current practices, regulatory strategies, opinions or recommendations etc. based on the new information.

-End of Article

freyr
Regulatory Centers of Excellence

IDMP 360
IDMP Strategy Process Information and Technology Management

IDMP TASK FORCE DEVELOPMENTS IN THE BACKGROUND

As discussed in the previous edition, the logical approach to ISO IDMP lies with your compliance readiness. Enroute, being enabled with high-end technology isn't just enough to be compliant, but keeping abreast with the recent developments in the area like updated data transition requirements, creating the needed code sets and a little bit knowledge on why VedDRA instead of MedDRA would suffice your goal of comprehensive compliance.

From the recently concluded ISO IDMP Task Force meeting, held on June 30 and July 1, 2016, under the purview of European Medicines Agency (EMA), some of the key takeaways which we think that you must know are:

- For the proposed Veterinary medicinal products' IDMP implementation in 2019, the EU legislation is expected to be signed in 2017. The major difference comes with using VedDRA in place of MedDRA, which doesn't require MedDRA kind of licensing.
- Data transition from XEVMPD to IDMP was one of the key action items that have been discussed in Task Force. Migration path for Article 57 data is the sorts of action items which suggests that there will be certain kind of instructions provided on how to approach XEVMPD to IDMP data migration.
- Addressing the complexities of hard-to-use implementation guides from ISO and EMA, which were targeted towards programmers and didn't provide what data needs to be collected, there was comprehensive discussion about bringing in real user guides which can provide detailed inputs on fields to be filled while submitting or updating new application, for various variations, etc.
- Aligning with updated requirements – MedDRA's need for additional terms to support interactions; and ATC codes which do not include herbal medications, there is a need to create new code sets. The Task Force meeting on June 30 and July 1 2016, has seen some movement towards the code creation.
- Referentials Management System (RMS) to include a lot more information on associated attributes, and related codes etc. Apart from current codes, provisional and deprecated codes are expected to be included.
- The Organization Management System (OMS) is expected to be the basis for creating user registration system for IDMP submissions. Having similar programming interface as that of the RMS, OMS initially is expected to have Market Authorization Holders (MAHs) which later expected to include Sponsors and manufacturers and clinical sites. However, only national Regulatory agencies can make the changes initially to assess every registered medicinal product has an MAH. Later on, even MAHs can start submitting the changes.
- Substances are expected to be managed in the Global Ingredient Archive System (GInAS).
- In the IDMP data submission, the GTIN (barcode number) is expected to be included as a "Data Carrier Identifier" for the packaging information to form the connecting data elements between IDMP and Falsified Medicines Directive (FMD).

Given the complexities, implementing IDMP is a critical process which involves not only decoding the regulations but also impeccably mapping them with your internal processes for successful compliance. As the systems and processes are being steadily fine-tuned through Task Force meetings, risk-free your XEVMPD to IDMP data transition approach with ever evolving updates. Stay tuned for more.

CASE STUDY

Clinical Cosmetic Safety Assessment

CLIENT
Global Top 5 Pharma & Consumer Health Company

GEOGRAPHY / LOCATION(S)
Asia Pacific

FUNCTION(S)
Regulatory Affairs

SERVICE(S) / SOLUTION(S)
Clinical Cosmetic Safety Assessment

THERAPEUTIC AREA(S) / INDICATION(S)
Skin Care, Baby Care, Wound Care, Oral Care

PRODUCT(S)
OTC

BENEFIT HIGHLIGHTS

- Assessed **40+** products across diverse global brands
- Submission of fast track assessment reports within a week
- Significant cost benefits with strategic advice on claim support for "To-be" marketed products

Business Imperatives

- The project required performing a benefit and risk assessment report on the product and regulatory filing strategy
- The focus was to **provide consultation** in terms of the **clinical safety** tests required based on its available data, exposure and intended population.

Challenges

- Providing rational and scientifically sound clinical safety assessment in a **time-bound frame ensuring cost effective solutions**
- **Effective communication** with the formulators from different countries
- Helping client to s**treamline and harmonize clinical safety assessment** across all the business regions.
- **No clear information** about the safety and efficacy of the product

Freyr Solutions & Services

- Provide highly rational and scientifically sound clinical safety assessment to determine the **clinical safety of the client products**
- **Minimize redundant testing** for similar formulations
- **Conduct literature search** and compile the scientific data to enable client to design strategy to **elevate their efficacy** and **safety standards** of their products

Client Benefits

- Rationale, sound and scientific assessment enabling client to place the products confidently in market
- Fast-track assessment report delivery timeline within **6 working days**
- Strategic advice on claim support for to-be marketed products
- **Significant cost-reduction** by providing technical justification to support the safety of the product
- Freyr has assessed over **40 products** across diverse global brands

CASE STUDY

Robust Program Management

CLIENT
Global Top 5 Pharma Company

GEOGRAPHY / LOCATION(S)
Europe Middle-East and Africa

FUNCTION(S)
Regulatory Affairs

SERVICE(S) / SOLUTION(S)
Program Management Office

BENEFIT HIGHLIGHTS

- Successfully establishing a centralized PMO
- Defined processes and streamlined metrics
- Substantial savings on cost of compliance

Business Imperatives

- The client needed to set up a robust Program Management Office (PMO) for EMEA
- The PMO is responsible for defining, planning and scheduling the program goals, milestones and deliverables in consonance with the client's requirements.
- Freyr needed to deliver the EMEA centralization program within the agreed quality, costs, resources, and scope and time parameters.

Challenges

- The PMO was expected to function in a complex environment such as multiple stakeholders, diverse geographically distributed teams and multiple business units
- No single platform to identify the synergies between the various projects being executed by different teams.

Freyr Solutions & Services

- Freyr developed a centralization strategy to provide both strategic and operational oversight to all the projects
- Delivery of program within the agreed quality, costs, resources, and scope and time parameters
- Predictive cost tracking to ensure optimal utilization of allocated budgets

Client Benefits

- **Substantial savings** due to reduction of onsite contractors
- **Cost avoidance** on several critical compliance mandates
- **Ongoing compliance** to health authority mandates
- Development of metrics resulted in identification and **elimination of inefficiencies**

KRANTHI REDDY

VP-Product Engineering

With an extensive experience over 12 years in product engineering, Kranthi is responsible for the structuring and operation of the product development and managing business strategies and user needs into intuitive and functional interfaces for mobile, web and emerging technologies. He has been providing end-to-end management of development lifecycle with his strategic planning for the direction and control of product development activities. He holds extensive experience in UI, UX, User Experience, SDLC, Software Projects, Web services, Oracle, SharePoint etc. and conceptualized & designed new interfaces from wireframe to final concept ensuring to deliver a good user experience. Prior to Freyr, he was associated with Sameva Inc. and TAKE Enterprises Services.

The Startup Scoop

The First Lap

I was working as an Associate Project Manager and my immediate manager was Rajiv Rangan. It was during the first quarter that the company we were working for was acquired by a company bigger than we were. I also knew a little about Suren by then, we worked together in putting together a website for one of the products. One fine evening my complete team including myself were busy capturing live baseball games using the in-house built technology and suddenly my phone rings and I see Srini calling on the screen.

I answered the call after few rings, we spoke about some general updates, and then he asked if I had any one around who can overhear the conversation which he is going to have with me. I found a quiet place but a series of questions were knocking in my head about the conversation we were about to have.

And then Srini started talking and I was all the ears. "A new venture" he started the conversation with. Developing a product which would cater the needs of Life sciences domain and he wanted me to join and start the prototype. The project was going to be huge & I had to quit the current job and dedicate all my time for this prototype.

I was skeptical at the beginning. I told Srini that I will have to check with Rajiv since he was my reporting manager and the next moment Srini passed over the call to someone else. To my surprise, it was Rajiv on the line. It took a moment for me to realize that Rajiv was already in and then I took no longer to say Yes. The next thing was, I flying to New Jersey to work on the prototype with Suren and in parallel, we were trying to establish a team that could execute the project and build the product.

The Identity

It really took a month for me to design a logo for the company. Most of the times, I used to work out of Srini's place and rarely I used to get into the nearby Barnes and Nobles and work. It was fun , and there was only one charging point and my laptop would be dead if I didn't charge it every 15 mins.

By the end of October, some circumstances led us to take a turn from the prototype of Regulatory information management to a different service project.

The first Big Slam

Our First Client

After all the days and nights we worked, it was time to get some taste of our first success story. We had our first two clients on the bus and the good part is we still have these guys with us. We received the first cut of payment. We did develop a web application for their business and a business card as a freebie.

The Life Sciences Shift 2012

Where The World Was Supposed To End, We Just Started!

2012 The EVMPD - The shift

Things were going well with multiple projects in our hands but amidst all this, the prototype which we built initially was dusting in a folder in my computer. It was last week of October, when we met to develop a product to cater the needs of EVMPD. The deadlines seemed to be no picnic for us.

We all then rolled up our sleeves, formed a team with couple of developers, a shared UI expert, a tester and myself. This was how the EVMPD team and eventually the first team of Freyr was established.

There were many iteration until first week of December and chain of events happened as follows:

- Product Launch on Dec 17th 2011
- Website launch on Dec 20th 2011
- First email campaign Dec 22nd 2011
- First list of responses from the email campaign: Jan 11th 2012

The First Demo

So we wrapped the development for Freyr EVMPD solution; the product was ready and now was the time to display our masterpiece. The first demo was then scheduled on Feb 9th and there was no looking back. As more and more demo requests were coming in, the product undertook many iterations. For us, every demo was as important as the first one. We were curious to know the feedback which was later on converted into requirements and features.

The Big Win in Life Sciences

We signed-off with our first client in 2012. This time we had to deliver a robust document management system – Freyr rDMS. The development went on in full swings and we were able to put the product on the table by end of the second quarter. In the meanwhile, Freyr also got ISO certified on March 12th 2013.

The Journey So Far....

2011

DEC: Developed the first App EVMPD

DEC: Freyr was titled and the website went live within 2 days

2012

APRIL: Freyr was listed in top 10 Technology and Service Providers for EVMPD by an independent consultancy in Europe

JUNE: Freyr got its first customer for EVMPD product

2013

APRIL: Freyr got the ISO 9001 and 27001 certification

Grabbed a project from a Global Top 5, $70+ Bn, Pharma & Consumer Healthcare Company in the same month

Freyr gets its 100th employee

2014 2015

Freyr expanded its Consultant Network in 120 countries

Signed up by 6 of top 10 consumer healthcare and 3 top of the 10 Biopharma companies

2016

Freyr expands to UK & Global

TRAVELOGUE

COORG TRAILS

Do you remember those art classes back in school when you were asked to 'draw whatever you wish'? And you would swiftly pick up the stubby crayons and draw a half rising sun neatly placed between perfectly scaled triangular hills, a row of gently swaying trees, a zigzagging clear stream lined with pebbles, and a brown thatched hut with a gleaming yellow window. The 'scenery' we all thought just existed in our dog eared art books. What if I tell you this is for real? What if I say you can happily fly your big red kite in those blue skies or dip your feet in the icy cold rivulet skipping stones? Coorg in southwest Karnataka is thoughtfully weaved right out of your colorful childhood yarns.

Pepper trees standing tall amidst ginger plantation

Tibetan Monastery at Kushalnagar

As the sun broke through the heavy hanging raincloud, the man sitting right next to me in the local bus at the Madikeri bus stand pointed out "You're lucky, you know. The endless downpour has come to a halt only today." This man was a 'schoolmaster' at the town government high school. Yes, in this part of the world, a teacher is still called so. As we trudged along the unsullied south, waving to school children in gumboots splashing through muddy puddles in the sleepy villages, he spun many a magic tale. How this land was infested with the fiery tigers once upon a time; how when a man shot a tigress, he was entitled to marry her in a ceremony called 'nari mangala'; how the original martial class highlanders, the Kodavas' population has shrunk to less than one-third today; how they're exempt from the India Arms Act and are allowed to own and carry arms without license till date; how coffee became the leading crop relegating rice to the third position, even after pepper; how the smell of coffee blossoms is often mistaken for that of jasmine. A sudden sharp shower filled the evening air with petrichor, mingled with a distant waft of freshly brewed coffee as I blissfully dwelled in that rare moment of perfect time and space.

I was repeatedly told to come here in the monsoon to safely escape the wrath of tourists, topped with a creamy bonus of an unutterably beautiful panorama dressed to kill in the finest colors. A smooth 5-6 hours drive in a KSRTC Volvo from the Bangalore Satellite bus depot that halts only for the 'Kamat special' extra crispy dosas, you'll know you've entered this tiny slice of heaven when you see the well tarred roads lined with towering sandalwood, rosewood, teak, and thickets of bamboo slowly paving way to the endless rows of neatly trimmed coffee bushes. The sinewy silver oak trees entwined with pepper vines, sown for the sole purpose of protecting coffee bushes from the glaring sun is another common sight. The undulating topography is strewn with every shade of rain-washed green, teeming streams spurring from the Cauvery (Kaveri), waterfalls well hidden in the thick, lush paddy fields spread as far as the eyes can see, deep valleys and grassy downs. Where else do fairies live, if not here?

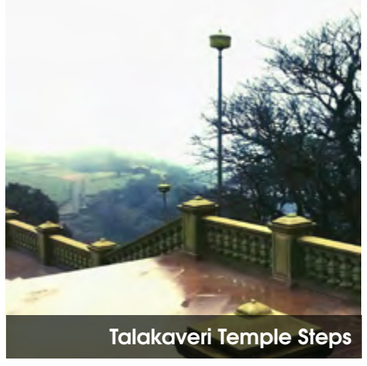
Plantation at Upper Coorg

Tumbling down the seemingly endless rabbit hole, we reached Kabbinakad junction; from this point a 3.5 kms uphill ride in a 4X4 sturdy jeep to our home stay, peacefully perched 4250 ft above sea level. What the host failed to mention over the phone is the three amiable miniature donkeys-in-residence that led the wet mossy path picking up scents all along while we gaped in amazement at the forest canopy view. Lily, the mother donkey and her two doting lads also have a score of mountain dogs in random hues of black and beige to keep them company. A hot water bath heated through solar power was followed by a traditional Kodava meal; pandi (pork) curry, kadambuttu (rice dumplings), wild mango (kaddu manga) curry, and fresh cucumber chutney in the cozy dining hall overlooking the mist hung Western Ghat tranquility. A quick glance at the polished wooden cupboards neatly stacked with tasteful books and we would return back to this heavenly realm after a blissful night's sleep listening to the soft murmurs of a nearby stream beyond the green plastered wall.

That night I dreamed of wandering the enchanted woods in search of a slumbering Totoro, riding on a grinning catbus past midnight, gaping at the great forest spirit, chasing unicorns. And soaking in the mild sun over a cup of strong Robustica coffee the next morning at our balcony, I smiled long and hard. Miyazaki was here to stay; in such divine spaces of blurred reality.

Evening bath at Dubare Elephant Camp

Igguthappa Hindu Temple



Talakaveri Temple Steps

freyr | CLUB

Freyr Brings

ECSTASY TO WORKPLACE

We are delighted to introduce Freyr Clubs to have our Freyrians, row their boats through intriguing ports of romp, recreation, and learning.

LOL

Some stress busters will come your way every now and then.

Garage

Get inside the iron machines and explore what these beasts are made of. May be one day you can build yours.

Game of Talks

Put right words to put your thoughts on the table. Communicate with confidence.

I Workout

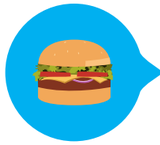
It's not about the number on the scale, but a lifestyle to feel awesome about your body.

Event-ually Yours

Create magical events in-house that blows everyone's mind.

Forum I

Enrich the business pipeline and strengthen the culture of innovation.



Being Hungry

Life's too short to count calories. Let the lip-smacking dishes destroy everyone's diet plans

The Eco Minions

Leonardo's Oscar winning speech talked a lot about our nature. Why not start doing about it something? Think Green, Go Green.

Keep Calm

We don't want to become the monks who sell their Ferrari. But getting that peace won't hurt anyone.

SEIZE THE MOMENT

For some, photography is a passion; for some a profession; and for the rest, a way to capture a moment to be cherished all their lives. Heading with the idea of seizing the moment, Freyrians have shared some of the breathtaking moments captured in their cameras with us.

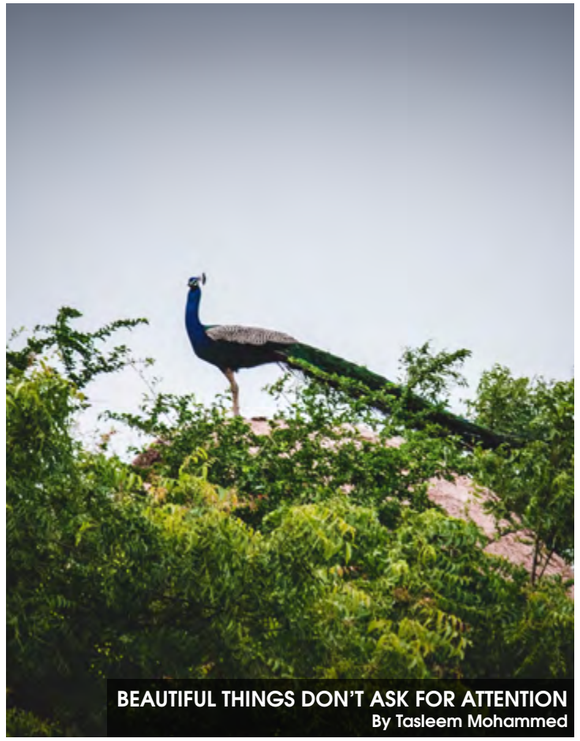
ENJOY THE SNAPSHOTS.

Light Escape By Raj Vinesh

Kranthi Reddy

Monsoon love By Srujana Penthakamsetty

Thirsty By Arun Nallanagula

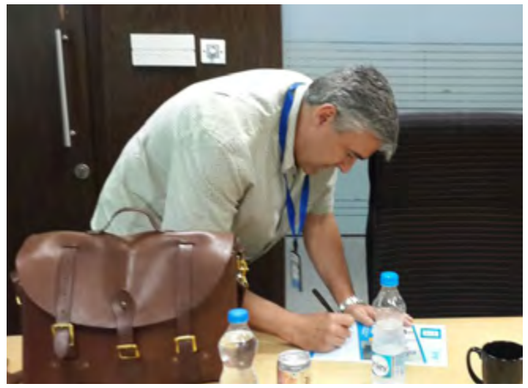


BEAUTIFUL THINGS DON'T ASK FOR ATTENTION
By Tasleem Mohammed

CLIENT VISITS

It was a great honor to welcome a multi-million pharmaceutical company at Freyr to oversee the ongoing projects for Labeling and discuss the future perspectives for medical writing services.

Client delegation meets Freyr core group to discuss business aspects aligning with ANDA dossier preparation & publishing. The client also explored other capabilities on artwork and labeling during the visit.



CLIENT TESTIMONIALS

"Under the EMA's tight timelines, your resource has successfully delivered on commitments with overwhelming speed and decisiveness ensuring we met the requirements on time. We just wanted to recognize their hard work and diligence on the product information update for a drug. Within just few weeks of their stint at our organization, they successfully navigated our processes and integrated them into the product team. Quite impressive! We must reiterate!"

Senior Regulatory Associate,

Worldwide Regulatory Strategy
A leading research-based global Biopharmaceutical Company

"Freyr was a great find indeed. The Freyr Publishing team catered excellent Study Report publishing services. The icing on the cake was their proper coordination, flexibility, dedicated study team, timely and constant communication and subject matter expertise that added to the ease of doing business and towards successfully accomplishing the end goal. This, as well as the fair pricing, is what sets Freyr apart from their competitors. As always, I would recommend Freyr again with no hesitation and should the opportunity arise, we absolutely approach Freyr."

Project Manager,

A full-service Clinical Research Organization (CRO)
Based in Florida

CLIENT WINS

Freyr to provide Regulatory Intelligence and Ingredient Analysis Services to help a client, a fast growing India- based Pharma and Healthcare products company, gauge the regulatory readiness of its products for US.

Freyr bags a strategic submission and publishing project implementing it's robust tool: Freyr SUBMIT to a Denmark-based Specialty Pharmaceutical company.

Freyr to provide end-to-end Submission & Publishing services focused on IND submission Project Management to a leading biotechnology company.

Freyr to deliver strategic Non-clinical overview Writing services to an integrated pharmaceutical company focusing on API, Formulations, and Clinical Research.

Freyr to deliver its paramount Submission & Publishing services to a US-based healthcare company.

REWARDS & RECOGNITIONS

Freyr has conducted Rewards and Recognitions for Quarter 1 to acknowledge employee efforts towards accomplishment and implementation of projects successfully. The rewards were handed over to employees who went an extra mile in different categories like Target Oriented Performance, Critical Incident Performance, Deadline Meeting Performance, Innovative Performance, and Client Appreciated Performance.















At Freyr, we recognize the practical potential of your products and create a strategy for a smooth ride through the drug development and drug approval lifecycle.

NEWSLETTER DISCLAIMER

The Freyr (Freyr Inc , Freyr Software Services Pvt. Ltd.) Newsletter(s) ("Freyr Connect") is a free electronic publication strictly for information purposes only and shall not be relied upon by any party for whatever purpose. The Newsletter(s) is not an offer, recommendation, solicitation or advice to buy or sell any product. Nothing in the Newsletter(s) is intended to be or should be considered as legal, regulatory, tax, financial or other advice.

The "Freyr Connect" Newsletter(s) is not responsible or liable for any actions taken from the use of content and opinions expressed within the publication. The materials and information included in the Newsletter(s) are provided as information and do not reflect endorsement by Freyr or its employees.

The information contained in the Newsletter(s), including any data or content, projections and underlying assumptions, are subject to be based on certain assumptions, management forecasts & analysis or information from publicly available sources on the internet and may be subject to change at any time without notice. While reasonable care has been taken to maintain the accuracy and objectivity of the information contained in the Newsletter(s), Freyr and its employees make no representation or warranty, whether expressed or implied, and accept no responsibility for its completeness or accuracy. As such, Freyr and its employees do not accept liability for any errors, inaccuracies, omissions or any consequences or any losses/damages howsoever suffered by any person or party, arising from any reliance by any person or party on the data, content, views expressed or information in the Newsletter(s).

Freyr does not make any claim on nor accepts any responsibility for the images, pictures or logos used in the Newsletter(s). All images, pictures and logos are property of their respective legal owners used by fair means for illustrative purposes only by expressed or implied permission provided in written or verbal communication form.

Any copying, redistribution or republication of Freyr Newsletter(s) ("Freyr Connect"), or the content thereof, for commercial gain is strictly prohibited. Freyr hereby disclaims all liability to the maximum extent permitted by law in relation to the "Freyr Connect" Newsletter(s) and does not give any warranties (including any statutory ones) in relation to the content/articles. The Newsletter(s) is a free electronic publication service and therefore any person or party agrees by downloading the "Freyr Connect" Newsletter(s) that this disclaimer is reasonable and applicable to the downloading person or party.

Freyr Worldwide

US

Headquarters
North America Operations Center
150 College Road West, Ste 102 Princeton, NJ 08540
Phone: +1 908 483 7958

UK

1 Bell Street, Maidenhead
Berkshire, SL6 1BU
Phone: +44 2037 012379

Germany

Consultinghouse Campus
Office Kurt Blaum Platz 8
63450 Hanau – Frankfurt
Phone: +49 6181 707 9007

India

Level 4, Building No. H-08
Phoenix SEZ
HITEC City 2, Gachibowli
Hyderabad – 500081
India
Phone: +91 40 4848 0999

About Freyr

Headquartered in New Jersey, USA, Freyr is a specialized full-service global Regulatory Solutions and Services Company and a specialist Consulting, Operations & Technology Services provider, exclusively focusing on the entire Regulatory value chain of Bio-Pharma (Innovators/Generics), Consumer Healthcare and Medical Device organizations, globally.

Freyr is a Strategic Regulatory Solutions & Services Partner to 6 of the Forbes Global Top 10 Pharma, 3 of the Forbes Global Top 7 Healthcare, 2 of the Forbes Global Top 6 Biotech and many $1 Million to $10 Billion Fast growing global Life Sciences, CROs and Standards Companies.

Exclusively focusing on the entire Regulatory value-chain, Freyr leverages its Regulatory healthcare domain expertise and technology innovations to evolve hi-end next generation regulatory solutions and services that enable accelerated performance, operations excellence and significant cost of compliance bene ts to clients while approaching for successful complaince

Freyr is one of the few global companies to have pioneered specialized Centers of Excellence (CoEs) exclusively focusing on the entire Regulatory value-chain which are supported by rapidly growing global teams of 400+ Regulatory Professionals. Freyr's Global Operations, Delivery and Development Centers are ISO 9001 Certi ed for Quality Management and ISO 27001 for Information Security Management. Freyr has an extensive global Regulatory A liate Network spanning 120 countries to offer best-in-class local and regional Regulatory support services to global companies.

www.freyrsolutions.com

Follow Us

www.linkedin.com/company/freyr-solutions
www.twitter.com/FreyrSolutions
www.facebook.com/FreyrSolutions
www.plus.google.com/+Freyrsolutions-services

Contact Us for Queries

Sales: sales@freyrsolutions.com

Alliance: alliance@freyrsolutions.com