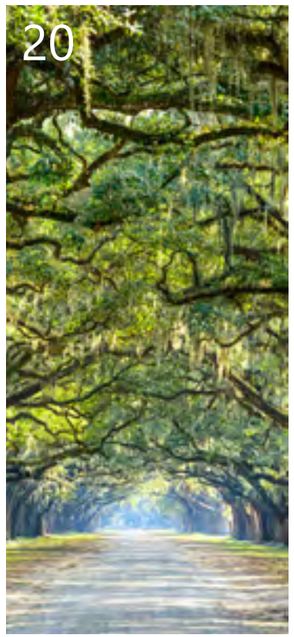
freyr
GLOBAL REGULATORY
SOLUTIONS & SERVICES
AN ISO 9001 & 27001 COMPANY

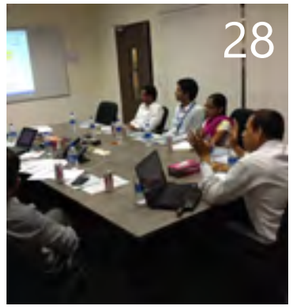
Vol 3 Issue 4
2015

CONNECT

INSIDE

WHAT'S INSIDE





FROM THE EDITOR'S DESK

Bonjour Freyrians!!! It's time to reconnect with the latest edition of Freyr Connect.

As my first newsletter for Freyr, I am thrilled to be a part of this. This edition is mixed bag of insights from regulatory sphere, talking about **trends in emerging markets and few other areas like UDI and Cosmetic Legislations.**

This quarter was filled with lots of client wins, new appreciations, and new perspectives. We met folks who went an extra mile and explored all avenues to get optimal results and were rewarded as a symbol of Thank You.

Lastly, the editorial team would like to take this opportunity to thank everyone who contributed to this edition of Freyr Connect. We wish you to see more.

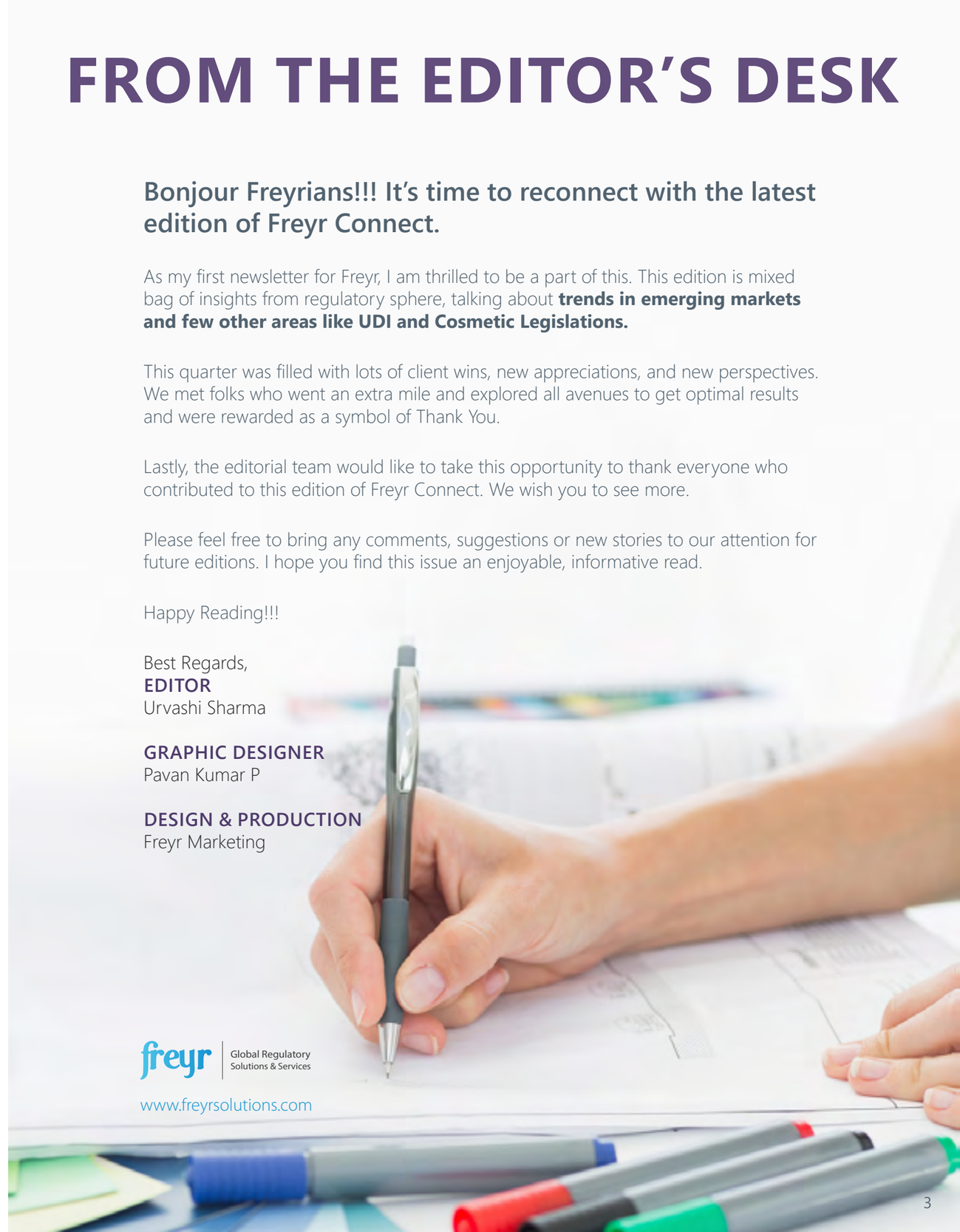
Please feel free to bring any comments, suggestions or new stories to our attention for future editions. I hope you find this issue an enjoyable, informative read.

Happy Reading!!!

Best Regards,
EDITOR
Urvashi Sharma

GRAPHIC DESIGNER
Pavan Kumar P

DESIGN & PRODUCTION
Freyr Marketing



freyr | Global Regulatory Solutions & Services

www.freyrsolutions.com

THE CHANGING MOMENTUM & REGULATORY CHALLENGES IN EMERGING MARKETS

As per studies, emerging pharmaceutical markets will account for 30% of global spending in 2016. These are defined as countries such as Brazil, Russia, India, China (collectively known as the BRIC countries), South Africa, Turkey and Mexico, as well as some Asia-Pacific markets, including Thailand, Malaysia and Indonesia.

With growing economies, big patient pools, growing numbers of patients with chronic ailments and regulatory bodies motivated to bring new medicines to market, these countries could be the future destination of pharmaceutical giants because of drugs going off-patent and rising generic competition in established markets like the US and Europe.

Opportunities

Economic and Demographic Growth

In terms of population using chronic drugs there is a marked growth in these emerging markets with rapid growing GDP and elevated lifestyles. For instance there is an increase of 20% diabetic patients in Mexico making it a probable destination for core diabetic specialist BIGPHARMA.

Growing Middle Class and Destination of Generic Drugs

As far as the economic aspects are concerned there is a noticeable growth in the volume of middle class population in these nations. Because of the limited economic conditions cost effective medicine is opted by the population making it potential place for Generic companies.

Regulatory Challenges

Lack of Professionals

There is a lack of professionals in healthcare sector in these nations when compared to the developed nations. As pharma always relies upon the support of professionals it is evident that over the last decade the clinical trials data is delayed at the submission time or there are instances that the clinical trial data was proven to be manipulated.

Regional Disparities

In the emerging markets there is a distinct disparity between the Rich and poor when compared with the mature markets. This also is quite marked in the case of the insurance regarding healthcare. At this aspect the innovator companies are facing a major hurdle regarding the marketing of the drug.

The FDI Policy

There is a lot of uncertainty regarding FDI policies of the emerging markets. For instance, India has a pharma FDI in pharma of 100% but in recent times there are proposals from the health ministry to reduce the FDI because of the fear of lacking low cost generics.

This aspect is of at most interest in revenue aspects when innovators are at the time of losing the patent period.

The NPPP

The National Pharmaceutical Pricing Policy has been put forward by many nations as per the WHO guidelines. Whenever this comes in the case of the innovators, the foreign exchange of the market influences the drug price. As a result the innovators face problems in the generic competitive market which is one of the major drawback for MNC's.

Uniform Code of Pharmaceuticals Marketing

This is a part of ethical knowledge acquisition by the Government imposed on the pharmaceutical firms in the recent era. As the promotional specs of the companies keeps on increasing to rocket the sales this provides the restricted data on the marketing facts. Complaints and claims keep on increasing from the open market and might affect the sale of the medicine.

Strategies to Overcome Challenges

Innovation Driven Vs Market Driven

The time has arrived for the pharma giants to decide their way and prioritize the market strategy as the Generic companies rocketing in sales over the expired patents the BIG pharma needs to check whether the scope of the Research is beneficial over the Revenue aspects. Proper balance must be maintained and plan should be applied to prevent future disturbances.

Improvised Product Design

Improvised product design is needed as the local companies are competing heavily with innovators. For instance, In Indian market there is a heavy competition for orthopaedic joint reconstruction medical devices. Here even the MNC's are facing the heat. To overcome this better Product design and affordability have to be kept insight.

Adapt to Updated Technology

In the changing scenario need for the technology augmentation is essential. For instance, Mobile hand held devices are being developed in India where a device can check blood sugar level, pulse rate, blood pressure, oxygen level of a patient in remote area and can transmit the same to the healthcare service provider or practitioner to facilitate quick treatment support.

Region Specific Strategies and Business Models

As per the demographic responses of the current market Region specific strategies have to be developed as per the understanding norms with the local entities. This provides accurate revenue to the company thereby can resist against cheap based local firms. Best example is in the case of MSD and Sun pharma venture for Sitagliptin drug in Indian market. Roche's dual version strategy: Roche launched their new dual-target HIV-1 qualitative test that works with both plasma and dried blood spot (DBS) collection cards to facilitate PCR testing, sample collection and transportation easy, even from the smallest infant in the most rural area. This is not possible for local companies to imitate.

Pooling of Resources

Data integrity is a major hurdle for every company to face the regulatory audits. Also equally important is the pooling of resources. Hence it is better that the Pharma giants themselves bring all the healthcare requirements under a single roof to avoid such discrepancies as a part of their business expansion.

Branded Generics

The evolved form of the innovator drug is a branded generic. Off patented innovator medicines are released into the market on behalf of the subsidiaries making it a reliable drug of choice with its similarity to the innovator drug. These have been generally put forward to reduce the share of local drug firms in generic market. As in the case of MSD and Sun pharma venture for Sitagliptin drug in Indian market.

CONCLUSION

It is evident that the emerging markets are full of opportunities tied up with challenges ahead.

Hence it won't be wrong to conclude that upgradation of technology, tailor made strategies and quality play a major role in the future pharma industry.

This is the need of the hour and the balanced strategies prove the potential of innovators in this critical period.

Contributed By
Sainath Kari
Trainee – Regulatory Operations

REGULATED PRODUCT SUBMISSIONS

-(RPS) An Update

RPS at a Glance

Regulated Product Submissions (RPS) is the Health Level Seven XML message standard for submitting product information to regulatory authorities.

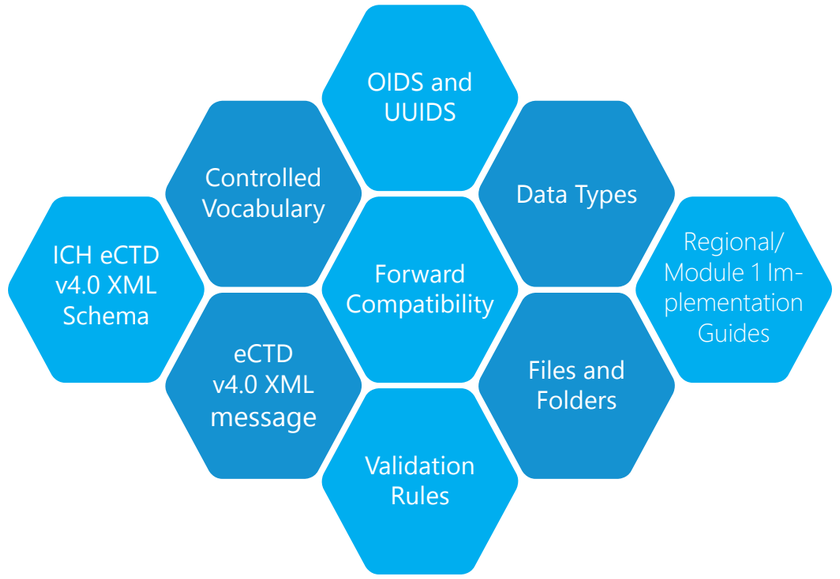
RPS is being developed in response to performance goals that the US Food and Drug Administration (FDA) is to achieve, as outlined in the Prescription Drug User Fee Act (PDUFA).

Along with US, regulatory agencies of Europe, Canada & Japan are at varying levels of interest & participation.

Two obvious advantages over eCTD are two way communication and cross reference. Now it was headed by ICH to have more international requirements.

ICH Electronic Common Technical Document (eCTD) v4.0

Components of RPS



OIDS & UIDS

There are 2 types of unique identifiers, Object Identifiers (OIDs) and Universally Unique Identifiers (UUIDs).

Object Identifiers

- An OID is a sequence of numbers that uniquely identify an object and represent a hierarchically-assigned namespace, defined using the International Telecommunications Union
- OIDS are represented as follows:
  - **String of digits separated by periods: 2.16.840.1.113883 582**
- In ICH eCTD v4.0, OIDs will be used to provide the code system value for each element defined by ICH that requires a code.

Universally Unique Identifiers

- A UUID is a hexadecimal number in the form of 8-4-4-4-12, including 32 digits and 4 hyphens.
- UUIDs are formally defined by ISO/IEC and ITU-T. UUIDs are represented as follows:
  - **String of digits separated by hyphens: 25635f23-a3a4-4ce0-9994-99c5f074960f596**
- In ICH eCTD v4.0, UUIDs will be used for any identifier root attribute value.

Data Types

- In order to provide all of the information required in the XML message, the data types are represented as elements and attributes.
- The data type for the elements and attributes are as follows:

Alpha	Allowing only alpha characters to be used (e.g; language-en,jp, etc.)
Alpha Numerics	Allowing alpha, numeric and special characters to be used in a string. XML should follow W3C standards for alpha numeric values.
Numerics	Only allows numeric characters (e.g; 0 through 9. E+-)to be used in a string for integers and real numbers.
Boolean	Allows a true or false value to be provided.
Null Flavors	These are used when required values need to be left blank. Null flavors are based on HL7 Messaging standard and constraints will be mentioned for each XML element. Currently, null flavors are not used in eCTD v4.0.

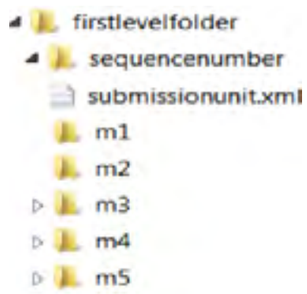
Regional/Module 1 Implementation Guides

- Regional/Module 1 Implementation Guides play a key role in providing the administrative information about the submission.
- The information in ICH eCTD v4.0 Implementation Guide is necessary, but not sufficient for creating the complete XML message for transmission. The Regional/Module 1 Implementation Guides are required to send a complete XML message.

Submission Contents, Folder and File Structure

Submission Unit Contents

- When submitting the contents of a Submission Unit, the following structure should be used:



- First Level Folder will be determined by Region/ Country
- Second Level Folder should be the same for all regions and named with the "sequence number" of the submission unit i.e., the actual value of the sequence number
- Following contents should be included in the Second Level: ICH eCTD v4.0 XML Message for an individual Submission Unit, named "submissionunit.xml".
- Note: the sender should not send the schema files – i.e., the util folder is no longer required, the XML should reference the interaction schema being used.

Naming Conventions

- Folder and file names should be written in lower case only
- All files should have one and only one file extension
- The file extension should be used to indicate the format of the file
- The First Level Folder should follow details of the respective Regional/Module 1 Implementation Guide

Allowable Characters

$	Dollar sign, Peso sign
-	Hyphen, Dash
_	Underscore, understrike, low line, low dash
+	Plus sign
!	Exclamation mark
'	Apostrophe, Single quotation mark
(	Left parentheses, Left bracket (UK)
)	Right parentheses, Right bracket (UK)

Length

- Maximum document (i.e., file) name length: 64 (including file name extension)
- Maximum folder name length: 64
- Maximum path length including first level folder: 180

Note: this allows the folder structure to exist under a logical drive with high level folder that is applicable to the submitter's environment

- File name extension = 3 or 4 characters

Path Name Conventions and Best Practices

- The pathname convention should reference the relative folder path using the forward slash (/) character to separate the folders.
- For example, the following pathname indicates the location of the file relative to the submissionunit.xml file e.g.,"m2/23-qos/introduction.pdf".

Folder Hierarchy: Sample files and folders for modules 2-5

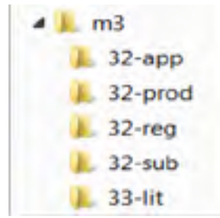
Sub-folders within a folder should not exceed 25 folders and there should be no more than seven (7) levels of folders (i.e., nesting greater than 6 levels is not acceptable) within the Second-Level Folder.

Module 2 Summaries

- The files in this module should be provided as PDF text with the exception of a few embedded images, when needed.
- The name of the folder for module 2 should be m2. No additional folders are necessary in this module.

Module 3 Quality

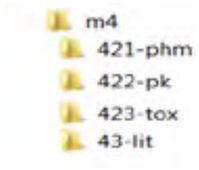
- The name of the folder for module 3 should be m3.
- The folders in module 3 should be named as follows but can be further reduced or omitted to minimize path length issues.
- Additional folders should only be provided to organize files with the same name.



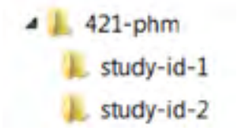
Section in CTD	Description	Folder Name
3.2. A	Appendices	32-app
3.2.P	Drug Product (name, dosage form)	32-prod
3.2.R	Regional Information	32-reg
3.2.S	Drug Substance	32-sub
3.3	Literature References	33-lit

Module 4 Nonclinical Study Reports

- The name of the folder for module 4 should be m4.
- The folders in module 4 should be named as follows but can be further reduced or omitted to minimize path length issues.
- Additional folders may be added to organize study files, which may be required to allow multiple files with the same name.
- The folders should be named with the study identifier number (e.g., study-id-1) as depicted in Figure



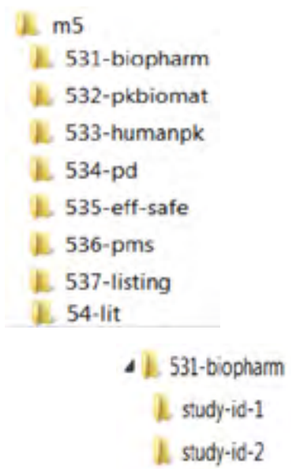
Section in CTD	Description	Folder Name
4.2.1	Pharmacology	421-phm
4.2.2	Pharmacokinetics	422-pk
4.2.3	Toxicology	423-tox
4. 3	Literature References	43-lit
3.3	Literature References	33-lit



Module 5 Clinical Study Reports

- The name of the folder for module 5 should be m5.
- The folders in module 5 should be named as follows but can be further reduced or omitted to minimize path length issues.
- The CTD organization provides locations for case report forms and individual patient data listings in Module 5.3.7.
  - In the eCTD v4.0, files for publications and literature references should be located in the folder for Module 5.4.
  - Additional folders may be added to organize study files, which may be required to allow multiple files with the same name.
  - The folders should be named with the study identifier number (e.g., study- id-1)

Section in CTD	Description	Folder Name
5.3.1	Reports of Biopharmaceutic Studies	531-biopharm
5.3.2	Reports of studies pertinent to Pharmacokinetics using Human Biomaterials	532-pkbiomat
5.3.3	Reports of Human Pharmacokinetic (PK) Studies	533-humanpk
5.3.4	Reports of Human Pharmacodynamic (PD) Studies	534-pd
5.3.5	Reports of Efficacy and Safety Studies	535-eff-safe
5.3.6	Reports of Postmarketing Experience	536-pms
5.3.7	Case report forms and individual patient listings	537-listing
5.4	Literature References	54-lit



File Formats

- In the eCTD v4.0 message, file formats are not specified.
- Regional/Module 1 Implementation Guides gives us additional information about what file formats will be accepted.

Checksums

- The eCTD v4.0 XML message will contain checksums for all Document.text.integrityCheck elements.
- The SHA-256 integrity check algorithm should be applied to obtain a checksum for all files referenced in a document element within a given submission unit.

Controlled Vocabularies

- Controlled vocabularies are one of the essential components of the eCTD v4.0, which enable interoperability – i.e., clear, unambiguous communications between systems sending and receiving XML messages.
- Controlled vocabularies are defined external to the message; a code is used as the identifier to convert the code value into the meaningful terms that will be used in any system that implements the viewing of the information sent in the XML message.

Overview of Forward Compatibility

- There will be one way to transition from v3.2.2 to v4.0 messages to meet the objectives of forward compatibility.
- The applicant needs to submit a "Current View" message that will transition all current content to v4.0 in one message.
- The forward compatibility transition mapping message will be based on the Current View, which is defined as follows:
  - Only submission content that has been submitted to the Regulator should be included in the transition mapping
  - All current submission contents(Excludes any leaf elements that were deleted or replaced) should be transitioned regardless of whether or not the content will undergo life cycle
  - Any sequences under development should be submitted after the transition mapping submission
- Once the applicant submits the forward compatibility transition message the following actions may be taken:
  - Perform any submission content life cycle thereafter on any of the content in a v4.0 message; or
  - Use of the transition mapping message when selling the product and transferring application content to the new owner.

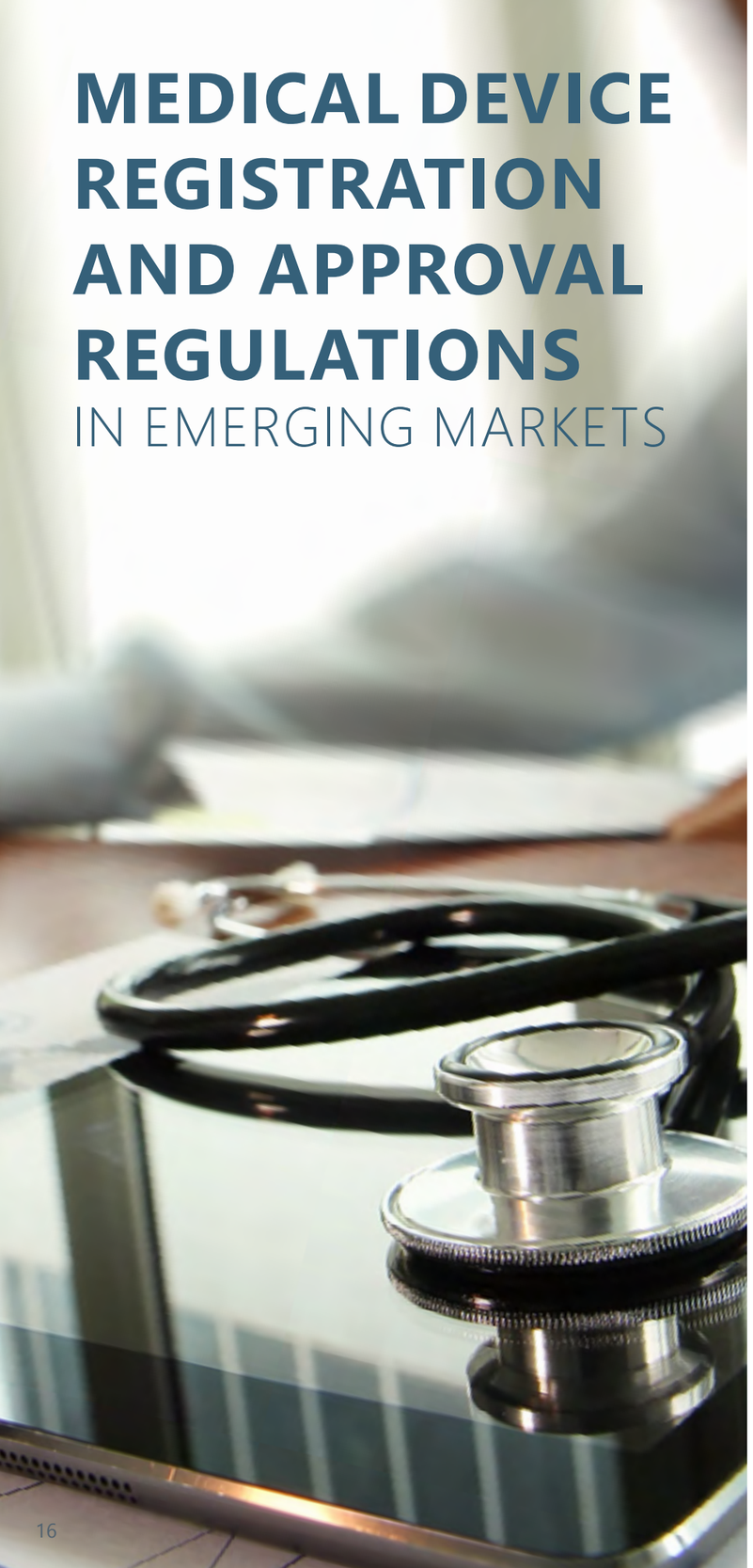
Schema

- RPS Schema used for transition message and all required elements will be included.
- Since the schema does not include additional constraints or machine readable validations, the same schema can be used for both the transition mapping message as well as the v4.0 message.

No/Unique ID	Category	Validation Criteria	Issue Description	Corrective Action
eCTD 4-054	Business Rule	Submission File Name	The submission file name is not submissionunit.xml	The filename should be corected to the specified naming convention required foe eCTDv4.x
eCTD 4-055	Business Rule	Submission File quantity	There is more than one submissionunit.xml file included in the submission package.	The submission unit needs to b resubmitted with just one submissionunit.xml
eCTD 4-056	Business Rule	Submission File Location	The submission xml file is not placed at the correct location at the folder structure to be detected by receiving systems.	The submission unit needs to be resubmitted with the submissionunit. xml placed in the top-level of the directory of the submission contents package.
eCTD 4-057	Business Rule	File Name format	The file does not follow the naming convention instructions i.e; lower case is not used	The submission unit needs to be resubmitted with the correct file naming convention for all documents.
eCTD 4-058	Business Rule	Document checksum is validated against the documents calculated checksum	The document checksum(s) of eCTD XML (see validation rules for message-specifically the text element (it is not the same as checksum of the file in the folder.	The submission unit needs to be resubmitted with the correct checksum for the submitted document.
eCTD 4-059	Business Rule	File name length	The file name length exceeds the allowable no of characters. Note- 64 characters allowed.	The submission unit needs to be resubmitted with the file name that meet the 64 character limit.
eCTD 4-060	Business Rule	Folder name length	The folder name length exceeds the allowable no of characters. Note- 64 characters allowed.	The submission unit needs to be resubmitted with the folder names that meet the 64 character limit.
eCTD 4-061	Business Rule	Folder path length	The folder path length exceeds the allowable no of characters. Note- 180 characters allowed.	The submission unit needs to be resubmitted with the folder path within the 180-characters allowed.

Regulated Product Submission (RPS) is a Health Level Seven (HL7) standard designed to facilitate the processing and review of regulated product information.

MEDICAL DEVICE REGISTRATION AND APPROVAL REGULATIONS
IN EMERGING MARKETS



The emerging markets like Japan, China, India, Singapore, Australia and others are thriving for expansion and retailing of medical devices in their markets. There seem to be virtuous opportunities for growth for medical device manufacturers in these countries to benefit accessibility, awareness and contextual clinical procedures.

In addition to these factors, these countries are ready to move ahead with distribution of medical devices that covers a wider spectrum of healthcare industry. Concluding to which they plan to generating more revenue and providing superior health aids to the patients at the same time.

However companies face a big challenge to coordinate with countless regulatory agencies, as each agency will have its own requirements, regulations and guidance.

MEDICAL DEVICE REGULATORY PROSPECTS IN JAPAN

For medical device manufacturing companies to trade their products in the Japanese market, they must comply with Pharmaceutical and Medical Device Law (PMDL) of Japan. The registration system is generally called as "Toroku" under PMDL. The local manufacturers are required to register relevant information about their medical devices and equipment in terms of manufacturing procedure, designing, sterilization, safety measures and warehouse of finished product in Japan with the local authorities. A similar data about manufacturing facilities of medical devices needs to be submitted by foreign manufacturers when they register with PMDA.

The growing life expectancy in Japan has led to rising older population in need of more and superior medical care, thereby proving to be a potential market for medical device manufacturers for years to come. However a recent update in laws governing the medical device registration process has influenced several aspects of the approval process, making it less challenging. Japanese regulatory council has replaced the traditional Pharmaceutical Affairs Law (PAL) with its new Pharmaceutical and Medical Device Law (PMDL). The new PMDL introduces some stringent regulations for labeling of the medical devices for which manufacturers will need to update their CCDS as per the new guidelines.

A pre-consultation program for manufacturers who are yet to enter the Japanese market for medical devices has been introduced that intends to ensure that quality management system requirements are met. This program is planned to help the new manufacturers with queries related to matters like submission material requirements, classification of medical devices based on their risk impacts, clinical data specifications and registration process. Since this program aims to provide the manufacturers with a better insight of the requirements and processes, it can turn out to be a valuable resource for foreign companies who are new to Japanese market. According to the new PMDL, the registrants can use third party certifications from Registered Certification Bodies as a replacement for getting it from PMDA.

The registration process is broadly classified into three stages namely: Pre-market submission, Pre-market certification and Pre-market Approval. To market medical devices in Japan, the MAH must register the device through the following procedures:

Pre-market Submission – Class I Medical Devices To register and market General Medical Devices (Class I devices), the MAH only need to file Pre-Market Submission to the Pharmaceuticals and Medical Devices Agency (PMDA) with no assessment by the PMDA.

Pre-market Certification– Class II Medical Devices Class II devices which are described as Specified Controlled Devices are subject to Pre-Market Certification. To register and market a Specified Controlled Medical Device, the MAH needs to file a Pre-Market Certification application with a registered certification body (third party) and obtain their certification.

Pre-market Approval– Classes II, III & IV Medical Devices To register and market a Highly Controlled Medical Device,[102] the MAH needs to file a Pre-Market Approval Application with the PMDA[103] and obtain an approval from the Minister of Health, Labor and Welfare. Class II devices that are not Specified Controlled Devices are also subject to Pre-Market Approval.

Japan is one of the most rigorous and challenging market to enter for medical equipment manufacturers due to huge language barriers and intricate registration process. However it is worth a shot for manufacturers since Japan owns the third largest medical device market after US and Europe beating China in the game.

SOUTH AFRICA MARCHING TOWARDS
A SUPERIOR MEDICAL DEVICE REGULATORY STRUCTURE

In South Africa, there is no chief regulatory structure that oversees the approval and registration of medical devices. There is no such law or regulation as of now that states an explicit timeline for the completing the registration process or provides a method to fast track the process.

Little what South Africa medical device regulatory system has is, that it mandates for companies to register listed electronic products such as electromagnetic medical devices or radiation emitting devices before making them available in market for selling, leasing, operating or using in South Africa.

This process is commenced by applying for approval by Director General of the National Health and Population Development (the Director General), failing to which, the next application is submitted to the Minister of National Health.

It is required from the companies to submit the data confirming quality, safety and performance throughout the lifecycle of medical devices while submitting application to the Council for authorization and registration of the medical devices to be used in South Africa. Post market vigilance and regulations are also monitored by the council which is intended to maintain high level of patient safety.

The assessment for approval process is based on the potential risk of the medical device which generally varies from low risk to substantial potential risks to patient health. If the medical devices fail to get approval, the council undertakes other evaluation methods such as:

- Authorized importers and prescribers
- Clinical research and evaluations

ENHANCED MEDICAL DEVICE APPROVAL PROCESSES
IN MEXICO

The registration assessment process for medical devices to be sold, manufactured, distributed or used in Mexico is governed by Mexico's Federal Commission for the Protection against Sanitary Risks (COFEPRIS). The medical devices are categorized on a key factor that other countries also adhere to, is the potential risk a medical device possess to the public health.

Class I:
For devices that are well identified, safe and effective in the medical practice and are not introduced in the human body

Class II:
Devices that are generally introduced in human body in a medical practice for less than 30 days.

Class III:
Devices that have been introduced in medical practice recently and are introduced in human body for more than 30 days.

In order to go through the registration process, companies are required to submit supporting documents that must include the following information/ documents:

- Description of manufacturing lifecycle of the medical device
- Relevant technical and scientific medical device data to ensure the safety and efficacy
- Label proposal in Spanish language adhering to pertinent labeling regulations
- Instruction booklet describing the use of the medical device in Spanish Language if applicable
- Description about laboratory tests conducted
- Details about stricture, materials used, functions, parts of the medical device
- References for bibliography

For medical devices that have been already approved by the US Food and Drug Administration (FDA) or by Health Canada, the Mexican government has declared a Directive that intends to streamline the medical device approval process. According to this Directive, the medical device process undertaken in US and Canada is equivalent to the ones followed as per Mexican regulations. If relevant confirmations adhering to this Directive are provided, it generally takes up to 30 days for companies to get approval for medical devices in Mexico.

REST OF THE WORLD

Where on the one hand the emerging markets are building their ways towards a superior and streamlined regulatory state for registration and approval of the medical devices, the other hand has witnessed the mature nations like the US and Europe which have implemented the regulation in an effective way and are now touching more milestones by introduction of technology driven monitoring systems such as UDI to keep a an absolute track record of medical devices in the most operative manner.

SUBMITTING UDI RECORDS TO GUDID:

THE ROAD TO ACHIEVING SEAMLESS COMPLIANCE

The Unique Device Identifier (UDI) is expected to facilitate the storage, exchange and integration of data and systems between suppliers and providers. The UDI mandate is designed to increase a) visibility and b) to improve the quality of information in medical device adverse event reports. It is also expected to improve traceability and security within the supply chain.

Compliance is a time-consuming process and if done ineptly can cause a severe setback to organizations. Consistent, unambiguous, harmonized data will reduce the potential for medical errors as well. The need of the hour is to guarantee UDI readiness for device manufacturers without derailing production.

Compliance Date for Submission of Implantable, Life-Supporting and Life-Sustaining Device UDI Records

The FDA's Center for Devices and Radiological Health (CDRH) has summarized the next two compliance dates for UDI requirements.

- September 24, 2015 for non-class III implantable, life-supporting, and life-sustaining (I/LS/LS) devices
- September 24, 2016 for class II devices

The original compliance date, Sep. 24, 2015 applied to four activities for Life sustaining, life supporting, and implantable devices.

- Labels and packages have a UDI
- Dates must have the correct format
- Permanent marking on applicable devices
- Loading the data into Global Unique Device Identification Database (GUDID)

The only changed date is "Loading the data into GUDID" which has moved from Sep. 24, 2015 to Oct. 24, 2015.

If a company markets I/LS/LS devices in the US, it must have a solid plan to achieve full compliance through submission of the UDI records to the GUDID.

Restoration of Full Functionality for GUDID

Due to security vulnerability, the FDA had earlier announced it was taking the GUDID production and pre-production environments offline. But as of 19 Aug 2015, the FDA announced today that it has restored full functionality for GUDID. The pre-production and production environments of the FDA web interface are available for use.

Due to the unexpected downtime of the system, the FDA has announced it will extend the 2015 compliance date one month to October 24, 2015. Previously, the FDA restored SPL functionality to the GUDID, which allowed labelers to make submissions of UDI records to the database in HL7 SPL format while other issues were being addressed.

Non Compliance
To Prove Costly

Failing to comply with the deadline stated about the new labeling and data submissions requirements will give the device manufacturers a severe setback. The device manufacturers must run the risk of their products being considered by the FDA as misbranded. Under FDA guidelines, non-compliant labels are treated the same as labels that may contain "false or misleading" information. Apart from the risk of financial and legal penalties, misbranded devices cannot be sold anywhere.

UDI Data Errors
Most Common Issues with Records Submitted to GUDID

FDA's Unique Device Identification initiative relies heavily on the high-quality data being submitted to the FDA's GUDID by medical device companies. Companies must keep a close eye to detect common errors that go undetected into GUDID data records.

Some Common Errors and Explanations

D-U-N-S Number
The D-U-N-S Number of the device labeler organization is one of the 55 required fields of data submitted to the FDA for each device record. D-U-N-S, contains nine digits, and is to be associated with the company name and address printed on the device label itself.

Primary DI
UDI has two parts; a Device Identifier, (DI) submitted to the GUDID and can be up to 23 characters long, and a Production Identifier (PI). Approved DI Issuing Agency-GS1, HIBCC, and ICCBBA each have different data format and check digit rules, and submitted data is not same as the human readable or bar code values printed on the product label.

Package DI Entry Errors
The Primary and Package DIs must be entered correctly in their respective fields and that Package DIs must not be mistakenly associated with an incorrect Primary DI record.

Size Entry
Size information must be entered in the Clinically Relevant Size section and use the size list of values where possible, in place of the size text field.

Version/Model Entry
Enter the Device Version or Model value in these fields and remember to omit the word "Version" or "Model."

UDI in Europe
Complications in Regulatory Landscape

Other countries are in the midst of creating UDI systems similar to the US, in a bid to better identify medical devices from the manufacturer, through the supply chain, to the patient. Implementation of a globally harmonized, consistent approach to medical device identification is expected to increase patient safety and optimize healthcare across the industry. The International Medical Device Regulators Forum (IMDRF), the European Commission and the U.S. Food and Drug Administration (FDA) are working in cohesion with other regulatory agencies across the world toward reaching this goal.

Currently, the European Union (EU) is actively formulating its own UDI regulations. Some of the European device manufacturers that distribute in the US must be familiar of FDA's final rule on UDI.

EU Regulatory Body
Independent Policy Makers

The EU is an economic and political affiliation of sovereign nations covering most of Europe as such there is no centralized regulatory body. Each nation has its own regulatory body to oversee products that are sold within that individual country. Therefor EU's UDI system may take a longer path towards reach consensus in order to reach its final stages.

EU Politics and Impacts on Policy
The European Parliament, the Council of the European Union, and the European Commission (EC) are the major role players in creation of any policy. The EC, comprises of representative from each member country, proposes new policy which is debated and voted on by the Parliament and the Council. The EU UDI initiative is currently under discussion following the election of new members in 2014. The UDI initiative has been under development for a lengthy period of time.

EU Regulatory Policy
During the drafting phase, the EC works to build a consensus, post which the policy is presented for legislation to the European Parliament and then seeks approval from the Council of the European Union. The EC had issued a recommendation for a UDI system on April 5 2013 and provided a high level description. A binding regulation is expected to be approved in the 2016 to launch the UDI system throughout Europe.

The EC then may release detailed guidance documents which will define an implementation schedule based on device class and type (device, implantable device, or diagnostic device). The guidance documents will specify the device data reporting details and expansion of the current medical device database, EUDAMED, for information storage.

US Regulatory Policy
The FDA has a different path toward policy finalization, that includes publishing of a proposed rule, and waiting for public comment (for a certain period) then publishing the final rule with changes incorporated. The FDA also releases draft and final non-binding Guidance documents to clarify the specifications as and when necessary.

The FDA requires medical device manufacturers to submit device data to the Global Unique Device Identification Database (GUDID) but there are multiple methods by which manufacturers can accomplish those submissions and three different standards a company can choose from for their Device Identifier.

CELEBRATING NEW CLIENT WINS

As an organization, we at Freyr, have always placed the highest value on our business associations and partnerships.

It has been our guiding principle to identify newer opportunities and create exceptional engagement excellence for our clients that transform into long-term relationships.

As always, it is a great pleasure to announce the New Wins of this quarter.

STRATEGIC AND TIME-CRITICAL ARTWORK AND LABELLING CONTRACT WITH A SWISS BASED PHARMA

- Provide end-to-end regulatory artwork and labelling services covering graphic designing, proof reading and publishing ready documents
- Focusing to create solutions to help clients leverage a globally scalable and efficient labelling and artwork management ecosystem to effectively meet the needs of the global life sciences industry

REPORT WRITING CONTRACT FOR A US BASED COSMETICS MANUFACTURING CO.

- Support Cosmetic Product Safety Reports (CPSR)
- Delivering comprehensive CPSRs providing information about the global acceptability of two ingredients that are being used by the client in their cosmetic products
- Deploying strategic and innovative offshore models with 24x7 project assistance to the client

REGULATORY INTELLIGENCE SERVICES FOR A US BASED COMPANY

- Assist the client for one year aiming to improve distribution of client's food products across 13 countries
- Provide comprehensive, and in-depth quarterly reports along with a geo-specific customized tool for effective decision making in terms of regulatory strategy and new market expansion
- Enabling access to authoritative and real-time standards-based regulatory information across multiple market segments, and product categories

REGULATORY PARTNER TO PROVIDE REGULATORY ECTD SUBMISSION AND PUBLISHING SERVICES FOR US BASED CRO

- Provide eCTD submissions and publishing services to the client leveraging its deep capabilities and skills to drive improvements in the planning and delivery of critical submissions, and to generate process efficiencies
- Improve the regulatory function strategy, processes and operations to accelerate superior submissions and reduce operational costs

STRATEGIC REGULATORY SUBMISSION SERVICES FOR A US BASED BIOTECH COMPANY

- Provide end-to-end support for submission of a New Drug Application (NDA) that will require conversion of 3000+ pages of Module I, II, III non-electronic documents to eCTD format in very strict timelines.

FREYR EXPANDS ITS GLOBAL SERVICES AND DELIVERY FOOTPRINT WITH A NEW OFFSHORE DELIVERY FACILITY IN INDIA.

New Facility Enhancing Company's Regulatory Service and Solution Offerings

Freyr recently commenced operations at its new offshore delivery facility in India that enables the company to broaden its regulatory services portfolio and global delivery capabilities. Exclusively focusing on the entire Regulatory value-chain the new facility augments Freyr's professional regulatory talent pool and complement the strategic expansion plans into new emerging regulatory markets to provide a full range of technology-driven services in the areas of Global Regulatory Pathway Strategy, Centralization, Regulatory Intelligence, Information Management and Process Consulting besides the full spectrum of Regulatory solutions and services.

Freyr's new facility is part of Freyr's Business Acceleration Program as it consolidates its position in providing value-added market entry services tied to R&D and IT services centers aimed at improving global operations. As an integral part of Freyr's global expansion strategy the facility enables gaining a strategic foothold in new markets transforming the regulatory outsourcing operations into a partnership engagement model focused on new market entry program for global clients.

Equipped with state-of-the-art infrastructure, the new facility is compliant with global Quality and Process Standards and deploys hi-end data & information security systems. The facility accommodates over 300 professionals from the Regulatory Operations and Regulatory Affairs domain and also host dedicated offshore delivery centers (ODC) for large global engagements.

Managing Dynamic Regulations, Providing Continuous Compliance by Combining High-Quality Service with Lower Delivery Costs

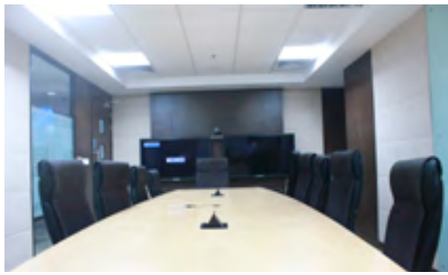
In particular, the addition of the new delivery center helps Freyr to aggregate and leverage its Center of Excellence (CoE) engagement model and aggressively expand its core offerings for enhanced business performance, program management and global service delivery.

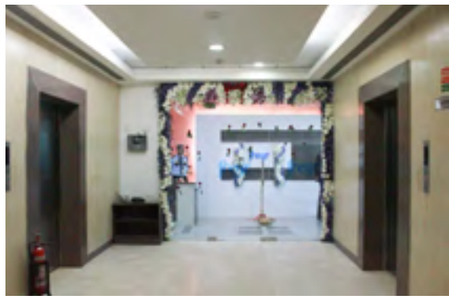
"The new facility operations in India is allowing us to combine Freyr's deep range of regulatory CoE and technology resources with lower cost of service delivery. This is a significant differentiator for us. Freyr offers pioneering, low-cost & innovative, global regulatory affairs service models – right combination of localized & offshore-based functions – offering significant value & faster time-to-approval,"

-Suren Dheenadayalan, Co-CEO, Freyr.

Freyr's strategy is to create a global network of specialized Centers of Excellence to cater to a wide range of critical regulatory functions of large multinational companies and provide end-to-end centralized multi-client, multi-geography program support for large and complex projects.

The facility complements and reinforces Freyr's differentiated, multi-tiered global delivery model comprising onshore, offshore and near-shore capabilities offering measureable business impact and collaboration with clients worldwide.





CLIENT VISIT

In September, we were honored by the visit from **Korea based, $600+ Million Pharmaceutical company.** Freyr helped them in providing details with respect to ANDA filing work plan. The visit turned out to be fruitful as client was happy with proposed future plans for documentation and publishing approach for ANDA.

GOING GREEN AT

GANESH CHATURTHI

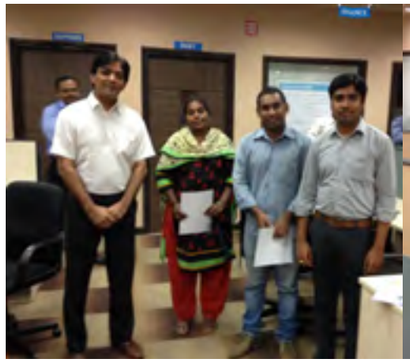
The Celebrations filled the air with spirit of traditional shades across Freyr Family.

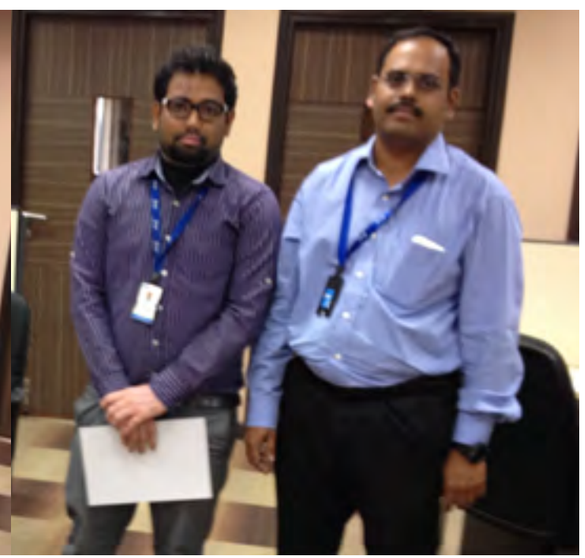
Publishing team bagged a remarkable win with their eco-friendly Ganapati. Well their Ganapati seems to be a real Foodie!!!

Congratulations to the entire team.

REWARDS & RECOGNITION

Celebrating employee accomplishment and excellence for: **Target Oriented Performance**, **Critical Incident Performance**, **Deadline Meeting Performance**, **Innovative Performance**, and **Client Appreciated Performance**.





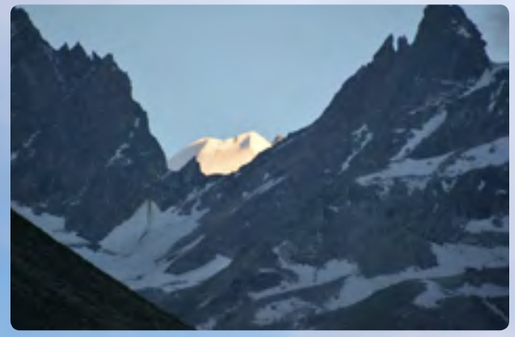
TRAVELOGUE

WHEN I GIFTED MYSELF MY FIRST TREK

A JOURNEY FROM **NOWHERE** TO **EVERYWHERE**

"It's never too late to get started on a journey"

"You have no idea of what you are capable of until you do it"



"The mountains are always calling, you just need to listen"

"The cozy tents were far more comforting than luxurious king size beds"

"You share moments and make many more friends for life"

"This one sight from the top was far more satisfying than a spa"

"At the end you realize that now you want even more!"

Multi-product Challenges?

Multi-site Global and Local Label Challenges?

Multi-language and Translation Challenges?

Artwork Misbranding Challenges?

Are you completely de-risked against regulatory non-compliance challenges?

Freyr supports global top 10 fortune pharma and consumer healthcare companies to completely de-risk and efficiently manage their Labeling & Artwork Lifecycles and to successfully mitigate all non-compliance and misbranding instances.

Visit **www.freyrsolutions.com/labelling-services/** to know more or contact us on **sales@freyrsolutions.com**

Freyr Worldwide

US

Headquarters
103 Carnegie Centre, STE 300
Princeton, NJ – 08540

North America Operations Center
150 College Road West, Suite 102,
Princeton, NJ 08540

USA Contact Numbers:
Phone: +1 908 483 7958

UK

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

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 companies, 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 benefits to clients.

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 350+ Regulatory Professionals.

Freyr's Global Operations, Delivery and Development Centers are ISO 9001 Certified for Quality Management and ISO 27001 for Information Security Management. Freyr has an extensive global Regulatory Affiliate Network spanning 120 countries to offer best-in-class local and regional Regulatory support services to global companies.

www.freyrsolutions.com

Contact Us for Queries:

Sales: sales@freyrsolutions.com

Alliance: alliance@freyrsolutions.com