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BREXIT

LEAD STORY

BREXIT & Its Reflection
On the Pharmaceutical Industry

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What's INSIDE ?

Freyr 360°

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FOREWORD

Dear Patrons,

The pleasure is all ours to bring to you another Issue of Freyr CONNECT - Volume 7, Issue 2.

Since the last Quarterly release, Freyr has been on a roller coaster ride; not only for back-to-back business wins, but also for:

- Sponsoring the IQPC's Cosmetic Compliance Spring 2019
- Launching Freyr SPL – a Dedicated Platform for Structured Product Labeling Submissions
- Been Recognized As One of The 10 Most Innovative Pharma & Life Sciences Solutions Providers 2019
- Launching Freyr iREADY – a Ready-to-use Ingredients Database
- Adding one more global business operational center in Lorrach, Germany

Not to carry away with rapid advancements, Freyr, as always, aims at empowering organizations with exclusive insights on Life Sciences Regulatory landscape. To keep organizations informed, in this Issue we have articulated the most discussed "Brexit" as our lead story with a new perspective on how it will impact the Pharmaceutical industry, Regulatory uncertainties, difficulties, and risks along with the contingency plans for post-Brexit scenarios.

In addition, Freyr CONNECT Volume 7, Issue 2 is built on insights with respect to the Health Canada's Medical Device's action plan, USFDA's Nutrition Labeling Mandate, EU Registration Procedures, and some of the Freyr's proven cases regarding SPL submissions and Artwork Management.

With the end-to-end coverage of Life Sciences Regulatory aspects, we do hope that this Issue will enlighten the Regulatory quotient in you for better and successful global expansion strategies.

Thanking all the efforts gone into publishing this edition, we look forward for your valuable feedback.

Happy Reading!

Suren Dheenadayalan

CEO

BREXIT AND ITS REFLECTION
On The Pharmaceutical Industry

Brexit has been one of the most widely discussed topics across the globe since 2016. With Britain (UK) exiting the European Union (EU), the event is said to influence some of the most important decisions for the UK in the near future. While the entire world was bracing itself for the Brexit's mandatory timeframe in the month of March 2019, both the governments (UK and EU) have decided to push the deadline until October 31st, 2019. Though it is certain that the UK will leave the EU, it is yet to be decided if it will do so with a "deal" or a "no-deal" (if the UK decides to leave the EU without any agreement about future trade). If both the governments manage to agree upon a deal before the set date, the United Kingdom may leave the European Union prior to the estimated date.

While the UK and the EU are adamant about parting ways, it might leave a heavy impact on both the sides. In the aftermath of Brexit, all the sectors, be it regulated or unregulated, in both regions are expected to get affected. The Pharmaceutical industry is not an exception. However, being one of the most affected regulated sectors, the pharma industry is trying to balance the Regulatory affairs between the UK and the EU with utmost dedication.

Pharmaceutical Industry - Current Scenario in the EU and the UK

In the prevalent Regulatory framework, there are two Regulatory bodies, the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA), which together oversee the regulation of medicines in the UK to ensure supply of safe medicinal products. With both the Regulatory authorities still working in collaboration, the current scenario of the pharma industry is elucidated below.

- **Distribution of Medicines** – To sell a medicinal product in the UK, a manufacturer must obtain a market authorization from either the MHRA or the EMA.
- **Production** – To manufacture a product in the UK, manufacturing licenses are required that are granted by the MHRA. The guidelines for manufacturing are set out in the European Commission Directive 91/356/EEC. The MHRA is responsible to ensure that the companies meet the Good Manufacturing Practices (GMP) and Good Distribution Practices (GDP) standards.
- **Clinical Trials** – The UK government is required to align with the Clinical Trial Regulations of the EU to ensure the safety and efficacy of medicines.
- **Pharmacovigilance** – Post-market monitoring of the medicines is undertaken by the EMA for the EU Regulatory network. The Pharmacovigilance Risk Assessment Committee (PRAC) is set up by the EMA to ensure the safety of medicines after the market-entry. The committee is made up of representatives of the EMA as well as the MHRA.

What Does Brexit Mean for Pharmaceutical Industry?

Being a setback in Regulatory affairs of the UK and the EU, Brexit poses a lot of threat to Pharmaceuticals, especially in the UK. Right now, some of the major challenges pharmaceutical companies are facing include:

- Monetary Issues – With the UK exiting the EU, the manufacturing cost for the EU pharmaceutical companies is likely to shoot up along with a decrease in future investments.
- Supply Chain – In case of a no-deal Brexit, it will be difficult to manage the medicinal supplies.
- Regulatory Affairs – In case of a no-deal Brexit, the UK will not have any transition period to discuss and align with the Regulatory arrangements with the EU health authorities.
- Loss of Expertise – With the EMA shifted to Amsterdam, it is expected that there may be a lack of expertize and loss of jobs.

While the industry is still finding a way around these challenges, the companies are trying to minimize the Brexit damages beforehand by taking certain measures. For example, as per reports, many UK-based pharma manufacturing companies have frozen their investments until the terms of Brexit are finalized. On the other hand, major EU drug manufacturers are said to be closing their UK manufacturing and packaging units by 2020. Similarly, one of the UK's leading drug manufacturers has planned to build new laboratories for parallel product testing to ensure that the products can still be sold in the EU. Even though companies are taking measures to prepare themselves for Brexit, the impact is expected to be certain. But how?

Impact of Brexit on the Pharmaceutical Industry

The outcome of Brexit will have both, direct and indirect impact on the future of the pharmaceutical industry in the UK and the EU. More broadly, post-Brexit impact really depends upon what model the UK adopts to maintain its relationship with the EU. The models can be 'No Deal', 'Soft Brexit', 'Hard Brexit,' etc. The multiple exit scenarios will determine the factors that will affect the industry.

Some key opinion leaders acknowledging the potential negative impacts of Brexit have opined that independence from the EU is an opportunity for the UK to leverage its full potential of the pharmaceutical sector. Conversely, some scientists take a more positive view, arguing that Brexit provides an opportunity for more liberal Regulatory rules that will permit the quick launch of drugs in the UK.

Depending on the above-discussed exit scenarios, the industry can decide upon European Economic Area (EEA), Free Trade Agreement (FTA), bilateral agreement or World Trade Organization (WTO) scenarios and how they will affect a broad range of Pharmaceutical functional areas; right from product development to market approval to the shipping of medicinal products. In such a scenario, the most immediate and direct impact will be the level of Regulatory alignment between the UK and the EU. Having said that, below are the list of some of the specific key areas which can be referred to as possible issues:

- **Uncertainty About R&D Funding**

In any of the Brexit scenarios, the UK pharma companies

will have limited access or no access at all to the EU's Research and Innovation programs. Under an EEA or bilateral 'Swiss style' scenario, the UK could become an associated country or a third country in order to be eligible for funding. As negotiating the status of the UK may take time, UK-based multinationals might transfer key research projects outside the country to ensure that they can continue to participate in international research programs. Other European pharmaceutical companies may prefer to put their research teams in other EU countries in the lead.

The UK's exit from the EU – especially under the FTA or WTO scenario – would mean decreased contribution to the EU budget, that regards to research funds.

- **Difficulties in Clinical Trials**

The current clinical trial regime in the EU is due for revamp under the new EU Clinical Trials Regulation (No 536/2014). The new regulation is expected to modernize the current framework for clinical trials and is likely to ensure a greater level of harmonization of the rules for conducting clinical trials throughout the EU. This new regulation is aimed at reducing administrative burdens on applicants allowing a simplified process.

If the UK is not seen within this system, then this could pose extra administrative burdens on companies planning to conduct clinical trials in the EU and the UK. For the same, separate centralized and national clinical trial authorization procedures are expected to be followed and practiced. However, mutual recognition agreements (MRAs) may be arranged to minimize any such inefficiencies brought by the Brexit.

- **Obtaining Marketing Authorizations**

So far, all medicinal products are authorized before they are marketed and made available to patients in the EEA. Following the Brexit, if the UK is out of the EEA then a separate national authorization would need to be obtained for the UK. There could be an increased administrative burden in terms of preparing and submitting exclusive dossiers and applications for the EU and the UK. However, European systems for marketing authorizations are expected to align with that of the UK.

- **Uncertainties Regarding the IP Rights**

The pharmaceutical industry relies heavily on intellectual property (IP) rights, in particular, patent rights. But the Brexit is expected to bring uncertainties regarding the geographical validity of patents. With that decoded, there are some obvious queries such as: will national UK patents automatically be enforceable in the EU and vice versa? The answer is obviously dependent on which form the Brexit will take and, on the changes, that the UK and the EU will make to IP legislation. Also, it is expected that with respect to patents, the EU is close to creating a 'Unitary Patent' (UP) and a 'Unitary Patent Court' (UPC), which is dedicated to protecting patents across the EU.

Depending on the form that Brexit will take, there may be a need to apply for separate UK/EU national IP registrations. This would mean an increased administrative burden. IP license agreements should also be reviewed for their geographical cover and for clauses like 'material adverse change.'

- **Health Authority Review and Approval**

Health Authority (HA) reviews will be one of the foremost areas affected by the events following the final agreement between the UK and the EU. Delving further into post-Brexit situation, companies must study the impact of various scenarios, here on.

If the UK meets a no-deal scenario, it shall come up with an MHRA-centric regulation. The UK will then be considered as a third country by the EU. In such a case, the effects will be dynamic as manufacturers based in the EU will have to restart the process of aligning with new regulations. The UK manufacturers marketing their products in the EU will have to abide by the EMA's rules that are applicable to an entity outside the EU. Since the UK is yet to finalize many of the new regulations, no clear Regulatory framework is laid out until now and with that, the uncertainty for manufacturers is expected to increase. The UK will also have to transfer the documentation related to ongoing assessments of all new medicinal products' progress currently overseen by the MHRA as per the EU regulations.

On the contrary, if the Brexit negotiations conclude with a bilateral agreement – an MRA (similar to the one the EU has with United States of America, Canada, and Switzerland), it shall promote trade and facilitate market access for medicinal products. The MRA will allow both parties to continue trade with an agreed set of rules. The number of changes to be made to existing regulations for HA reviews and approvals would be limited. Thus, the impact on core activities of manufacturers such as market authorization applications, publishing and submissions, license renewals, etc. would be minimal.

- **GxP Regulations**

Similar to the regulations for HA reviews and approvals, GxPs enforced on manufacturing facilities might differ depending on the status of the agreement between the EU and the UK. If agreed, Pharmaceutical products of the EU countries may continue to run their facilities in the UK as per existing GxP standards. If not, the MHRA shall proceed to mandate its own set of GxPs. The same is true for UK manufacturers

based in the EU member nations. Even if the MHRA decides to keep the Regulatory changes minimal, new audits will have to be conducted. The result could be increased administrative activity, which in turn extends the products' time-to-market.

- **Risks to the Supply Chain**

Post the Brexit, the EU Marketing Authorizations (MAs) will no longer be held by the UK-entities. Therefore, companies should be transferring the MAs to other EU entities or should opt for Authorized Representatives in the Europe to manage them. This may lead to fundamental changes to supply chain and at the very least will require a review of the licenses held, to keep the appropriate Manufacturer's / Importer's Authorizations and wholesale dealer's licenses in place.

Irrespective of the Brexit outcome, pharmaceutical companies must be flexible and ready to adapt to the changes to overcome the ongoing economic uncertainties.

- **Pharmacovigilance**

The EU pharmacovigilance (PV) system is regulated by the EMA which ensures effective and coordinated analysis, evaluation of risk, information sharing and periodic checks on market-authorization holders throughout the EU.

Following the Brexit, the UK competent authority is expected to have smaller data sets than those in the EU, and the EU is expected to be deprived of data from the UK. If Brexit results in less co-operation, the amount of post-authorization efficacy data and adverse event reports may drastically be reduced resulting in a PV that is inefficient and costlier.

Contingency Plan for Post-Brexit Scenarios

Among the possible post-Brexit scenarios discussed, the event in which the EU and the UK agree upon common terms is expected to trigger fewer changes. But it is also advisable to be prepared for the worst, i.e., a No-deal Brexit. An area of immediate concern is, without any mutual agreement in place the trade between the EU and the UK might come to a standstill for a brief period once the Brexit is enforced. To ensure a continued supply of medicines, Pharmaceutical organizations of the EU and the UK are being informed by the HAs to stockpile the medicinal products. To enable the same, companies must put in efforts to drive the supply chain more rigorously as it plays a pivotal role in collecting and storing the drug products.

Organizations must also be prepared for different Regulatory scenarios possible in the post-Brexit environment. By being prepared for such scenarios, companies can proceed for further actions, once the final guidelines are published. Here is a list of some common ways in which the companies might stay prepared for No-deal Brexit:

- To conduct drug clinical trials in the EU, companies based in the UK must find a sponsor and a local representative based out of the EU and vice versa
- Avoid duplication of drug testing until an MRA on batch testing and inspections can be agreed between the EU and the UK
- Strategize for new EMA authorizations, for Pharmaceutical products marketed in the EU via MHRA approved authorizations
- Set up alternative freight services for the supply chain to continue import/export of medicines between the EU and the UK

As we focus on individual cases, multiple Regulatory scenarios may arise. But preparing for a situation that is highly probable should be the pharma industry's focus.

Conclusion:

Post the Brexit announcement, addressing all the Regulatory aspects of drug discovery, clinical trials, drug development, HA submission, and Pharmacovigilance has become an uphill task with no proper clarity and information on the updates. In such a scenario, the ability to understand the changes and the capability to quickly align with them decides an organization's market place in the EU and the UK.

As the current situation is predicted to be uncertain, keeping a continuous track of HA guidelines and updates can help Pharmaceutical companies to be vigilant about the Brexit and possible scenarios and Regulatory requirements. What could be more worrying aspect in the current situation is that the companies are lacking local presence. With a solid grip on the Brexit and Pharmaceutical Regulatory prospects, a regional expert can streamline and expedite your compliance efforts. If you would like to know more about compliance best practices in the post-Brexit scenarios, reach out to *sales@freyrsolutions.com*.

Stay informed to be compliant.

Infographic

BREXIT
& THE POSSIBLE SCENARIOS

As the UK is headed for Brexit, there exists 3 possible scenarios that are capable to define a product's market-entry.

POST-BREXIT, THE CHANGES THAT LIFE SCIENCES INDUSTRY SHOULD ANTICIPATE:

01 Appoint new Responsible Persons for the UK market

02 Make changes to supply chain management (E.g. Packaging)

03 Redesign artwork and labels as per MHRA regulations

WHAT MIGHT NOT CHANGE AFTER BREXIT?

01 CE Marking accepted throughout the EU and the UK

02 For device manufacturers, program similar to EU MDR/IVDR is being planned by the UK

Either No Deal or Extension, Brexit seems to be inevitable. The need of the hour is to sustain and adapt to the changes compliantly. Define your Regulatory pathways accordingly.

KEEP ABREAST AND ALIGN WITH THE UPDATED BREXIT SCENARIOS

Contact Us: sales@freyrsolutions.com

Center of Excellence
Global Cosmetics Regulatory Services

KOREA: BOOMING TEEN COSMETICS

Markets | Why are cosmetics gaining the heart of teenagers in Korea? And what do you need to know if you want to enter this thriving market?

Today, teenagers are attracted more than ever to novel products which promise ground-breaking beauty experiences. They have become more conscious than ever of their appearance. Because they have grown up in the world of internet and mobile phones and being exposed to global connectivity, their lives have become transparent to an audience over various social media channels. Given South Korea's long-term experience with smartphone usage combined with continued internet access for a substantial percentage of the population, online marketing, especially targeting teenagers, has the potential to grow. After all, teenagers constitute a large community of digitally connected internet users and they are far more likely to stay attuned to current lifestyle, fashion, and trends. A recent external survey related to online shopping trends projected that cosmetics is one of the leading product categories and the most sought-after product by online shoppers in South Korea. With South Korea being one of the top 10 cosmetics markets in the world, this comes as no surprise. Moreover, beauty being an essential part of South Korean's culture makes Koreans have a natural inclination for cosmetics. The most surprising fact is that cosmetics targeting teenagers are thriving with their sales value rising almost one-third, year-on-year.

A Colour Conscious Generation

With K-beauty taking the world by storm, this recent Korean beauty phenomenon which emphasizes a healthy approach towards beautification has significantly elevated the beauty goals to forward-thinking skin care. This has led to a situation in which nine out of every ten teenage girls in South Korea use make-up. From another recent report on the South Korean cosmetics market, the value for the teen market and those in their early 20s is noted to be worth hundreds of billions South Korean Won. Another promising trend catching up among the teenagers is the plethora of multipurpose products which provide quick fixes, thus reducing the number of products needed.

Cross-Border E-Commerce: Value Beyond Bargains

Today's teenagers are futuristic, savvy, and well-informed and a considerable amount of their interaction happens via blogging, tagging, and social networking, leading to the creation of new opportunities to be tapped by marketers. Cross-border e-commerce websites are gaining popularity among teen consumers in South Korea as they offer a variety of products at affordable prices. Many brands have already caught up with these teen consumer habits and have taken interactive steps to connect with them through internet advertising and online marketing. From a business perspective, cross-border cosmetics' selling is one of the safest and the most rapidly

growing segments in the country. But what makes it so lucrative? Cosmetic products are comparatively low-risk, less expensive to ship, and their prices vary across different regions. What appeals to the companies is that teenagers are the early adopters of new products, hence brand loyalty can be built at an early age.

They may shift to other brands due to personal recommendations and wow factors, but always tend to come back to the tried-and-trusted brands with which they have associated.

A Spot to Bother: Are You Compliant?

While cross-border e-commerce cosmetics' sales are rising exponentially, the responsibility for product safety lies solely with the cosmetics companies.

Some counterfeit products are being marketed and sold, taking advantage of the e-commerce boom, as there are no stringent Regulatory evaluations conducted for these products.

The usual victims of this illicit activity are teenagers who fall prey to the falsified advertisements. To restrain such malpractices, every country has unique Regulatory requirements. Moreover, the regulations are constantly being revised. Therefore, it is important for businesses to avoid non-compliance and penalties associated with it, which is a key factor to build a brand and gain customer loyalty.

When introducing a new product into a market, there are often unique requirements and Regulatory processes, with which the manufacturers must comply. For example, South Korea requires testing of the cosmetic products in the MFDS (Ministry of Food and Drug Safety) accredited laboratories every time a shipment enters the country.

Key Regulations to Consider when Selling in South Korea

In South Korea, as per the *Korean Cosmetic Products Act* (KPCA), 2000, cosmetic products are regulated by the MFDS and are categorized into three major groups:

- General cosmetics such as moisturising skin products
- Functional cosmetics such as anti-wrinkle, sunscreens and whitening products
- Quasi drugs such as oral rinse products

For cosmetics, the MFDS review process is limited to product shipment evaluations and other administrative processes, but products are still subject to post-market supervision. However, functional cosmetics and quasi drugs, both domestic and imported, must undergo evaluation for their quality, safety, and efficacy, and require an approval from the MFDS before being marketed. MFDS has also specified a list of ingredients which are permitted to be used in cosmetics in South Korea. If an ingredient is not listed in any of the Korean references, it is required to undergo an approval process wherein the MFDS evaluates the safety and other specifications related to that ingredient. In addition, labeling in Korean language on primary cosmetic packages is required for all domestic and imported products under the KPCA. Simply placing a translated label over the original one is accepted. Information such as the name of the product, manufacturer/importer, expiry date, lot number, net weight, usage, precautions, effects, storage, price, etc. is required to be presented on the artwork in Korean language. When a company imports products in South Korea, it is mandatory to appoint a local agent who is responsible for ensuring the safety of products once they are in the market. According to the KPCA, the products must be tested for quality by lot/batch, based on the product type such as general cosmetic, functional cosmetic or a quasi-drug.

Take Note and Nurture

Having identified teenagers as the most important target group, it is important to keep in mind that the moral and Regulatory responsibility to ensure the wellbeing of these young consumers lies with the cosmetics companies. Even though cosmetics' sales in the South Korean market are rising, to survive and stay relevant in the eyes of teenagers, the companies must avoid resorting to non-compliant measures. They should prioritize safety for easy market access and leverage abundant market opportunities. Be informed. Be compliant.

A list of ingredients specifies the ingredients permitted for cosmetic use in South Korea

A non-listed ingredient has to undergo **a stringent approval process**

Primary cosmetic packages have to be labeled in Korean language

This article was first published by

COSSMA
www.cossma.com

References are available at

http://media.cossma.com.s3.amazonaws.com/epaper_en/2018/10/159D9A4C67/CSDE1810_online_Teaser.pdf#page=9

FREYR
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POST BREXIT ARTWORK CHALLENGES FOR THE PHARMACEUTICAL INDUSTRY

The impact of Brexit is evident in almost every industry based in the European Union (EU) and the United Kingdom (UK). Pharmaceutical industry too is not to be spared. Although the UK is in negotiations with the EU to streamline the transitions, the European Medicines Agency (EMA) has requested the pharmaceutical marketing authorization holders (MAHs) to stay prepared in advance to ensure continued supply of medicines.

Impact on the Pharmaceutical Industry

The UK has been the base for market authorizations of many medicinal products which have been recognized in other EU countries via Mutually Recognized Procedure (MRP) to obtain market-entry approvals. Almost a third of approved products' MAHs in the EU are based in the UK and they must obtain an exclusive authorization from the Union to continue the supply. The companies marketing in the UK and based in any of the EU member states must also obtain a separate Medicines and Healthcare Products Regulatory Agency (MHRA) approval. Similar conditions will apply for market authorizations approved through Centralized Procedure (CP).

Artwork Regulatory Challenges

While getting approvals in the EU and UK is the endpoint, in order to be compliant, MAHs must also look into the artwork and packaging requirements that may rise due to the change in the country of origin. The packaging containers affected by artwork changes includes but is not limited to:

- Cartons
- Foils
- Containers
- Tubes
- Inserts
- Packets
- Shippers

All the packaging containers listed above might have representatives details as per existing MAHs. But with the need to obtain new approvals, the registered addresses of the legal entities and other mandatory details might also be changed. Aligning with all the requirements and obtaining a market approval in the midst of stringent timelines will be a challenging task.

With Brexit transition deadlines inching closer, pharmaceutical manufacturers must ensure they are adequately prepared to continue marketing without any compliance issues.

To expedite the process of submission for marketing authorization approvals (MAAs), consulting a Regulatory expert for artwork and submission is advised. Be compliant.

DATA INTEGRITY IN CLINICAL TRIALS - WHY IS IT IMPORTANT?

In 2017, 60% of the warning letters issued by the United States Food and Drugs Administration (USFDA) were result of lack of data integrity. Referring to which, it is clear, how important is data integrity in any clinical trial. To address the importance of data integrity for Good Clinical Practices (GCPs), FDA and Medicines and Healthcare Products Regulatory Agency (MHRA) having been taking considerable measures by conducting workshops and discussing concerns of all the stakeholders across the world.

Achieving data integrity is not rocket science. A set of pre-defined standards and best practices can help you acquire necessary and unbiased data. Using these best practices will also ensure the reliability, quality and purpose of the data. For example, if data is collected for oncology trials, it should help to examine its effects throughout the process and keep a track of them which can be better managed with the help of reliable data. But with the advancement of technology, the data collected by companies is also increasing exponentially. This is making it difficult for organizations to maintain the integrity of humongous amount of data as there are multiple factors which may influence the data. How can companies come over the gap? Let's have a look.

Errors in Blinding

Earlier, the trials were mostly paper-based which made it easier to keep the results blind. Blinding or blind is a method of keeping the specifics of a clinical trial secret from the participants of the trial for optimal results. But as the times have changed, many elements are now part of the clinical trial system, which may unblind the results of a trial and expose them to unknown biases.

Interactive response technology (IRT) has proved to be a boon for blinding in clinical trials. IRT is a software which introduces activities, such as randomization, into the system of clinical trials to ensure blinding. It helps organizations to maintain integrity throughout the process, right from the collection of data to final analysis, to identify any manipulation in the sequence of events. Interactive Voice Response Systems (IVRS) or internet based, Interactive Web Response Systems (IWRS) are some of the examples of IRT.

To keep the data unbiased, all the stakeholders who

are involved in the trial must make sure that the blind is enforced at each step. A well-planned approach is a key to maintaining the blind in clinical trials. The schedule of the clinical trial must be examined thoroughly to identify elements which may unblind the trial. Any system or document which may reveal the process must be efficiently managed by the organization. If any errors are found, they must be addressed immediately.

Data Management

As it is well known, ensuring and maintaining the quality of data is highly important for error-free clinical trials. The best way to manage the quality is by developing well-planned case report forms (CRFs). If the CRFs do not define the roles and responsibilities clearly for the trial, it may lead to inadequate data, thus, compromising the trial. To avoid this, the access and control of end-to-end data must only be with the clinical investigator. Also, while managing the CRF data, it is important to ensure that the collected data is accurate and has a reliable source of origin. The personnel handling the data should also abide by the rules of blinding.

Apart from this, what type of data (for example, safety data, ECGs, vital signs etc.) should be collected from the clinical trial must be clearly defined during the earlier stages of the trial. If the trial involves high-level of risk, the importance of data should also be assigned and documented. System specifications, data management SOPs, guidelines, and work instructions should be made aware to all the stakeholders in the research by providing training sessions on each function. Once the trial is over, the CRF should be directly sent to the clinical site via electronic means and should be kept away from the stakeholders to retain its authenticity.

Lack of Resources

Often, organizations have limited resources when it comes to conducting studies which can turn into an obstacle. In such cases, instead of building in-house expertise, organizations should focus on finding the right outsourcing vendor. The focus on finding the right vendor has increased after the release of GCPs under ICH E6(R2).

Selecting a vendor requires thorough assessment of their capabilities regarding handling the clinical trials. Apart from the infrastructure and resources, evaluation of their approach, documentation and training will help you understand how the vendor can protect the integrity of your data. Even if the vendor is well-known, it is a good practice to evaluate their approach and compare it with other vendors, just to be on the safer side.

Considering the request for proposals (RFPs) before selecting a vendor is always a good decision as it helps you understand the ecosystem of the vendor. It also helps to understand if the vendor can meet the requirements of the trial or not. The practice is highly recommended by regulators.

Audit Trails

Audit trails are necessary to improve compliance and the overall effectiveness and quality of the system. Without conducting audit trails, an organization might end up facing challenges during the trial.

The trails also help to review and verify the activities of the trial and store them for future references. Audit trails information helps clinical investigators to assess the products effectively but the inability to decode this information may lead to unknown challenges. Audit trails may also disclose the discrepancies of the system, if any.

There are many ways to maintain the integrity of data produced from a clinical trial. It is the obligation of the organizations to protect the data by taking the right measures. For this, the roles of those involved should be properly defined along with the process and the technology used. Also, the process should be well-planned and documented to meet the goal. All of this must be done prior to the start of study as once the study has commenced it may become difficult to backtrack. A Regulatory expert in clinical monitoring can help you manage your data and maintain its accuracy. Be compliant with your data to stay ahead of the competition.

Center of Excellence
Regulatory Medical Writing

REGULATORY MEDICAL WRITING - HOW CAN YOU BE METICULOUS?

While researching for an innovative drug/device/cosmetic/food supplement, a huge amount of clinical data is expected to be generated. The conclusions of such data must be clearly reported with an appropriate level of detail to the Health Authorities (HAs). The information to be reported or documented might be research data, trial descriptions, findings, warnings etc. in the form of safety reports, clinical and non-clinical summaries etc.

If collating the data is one side of the challenge, in such scenarios, the other side is to report it accurately and consistently to the HAs. Penning down all the details isn't that easy, as it requires a high level of scientific understanding for easy review of documentation. In such scenarios, Regulatory medical writing would be a savior to transform the clinical study data into submission-ready and reviewable information for quick market approvals.

Why Medical Writing?

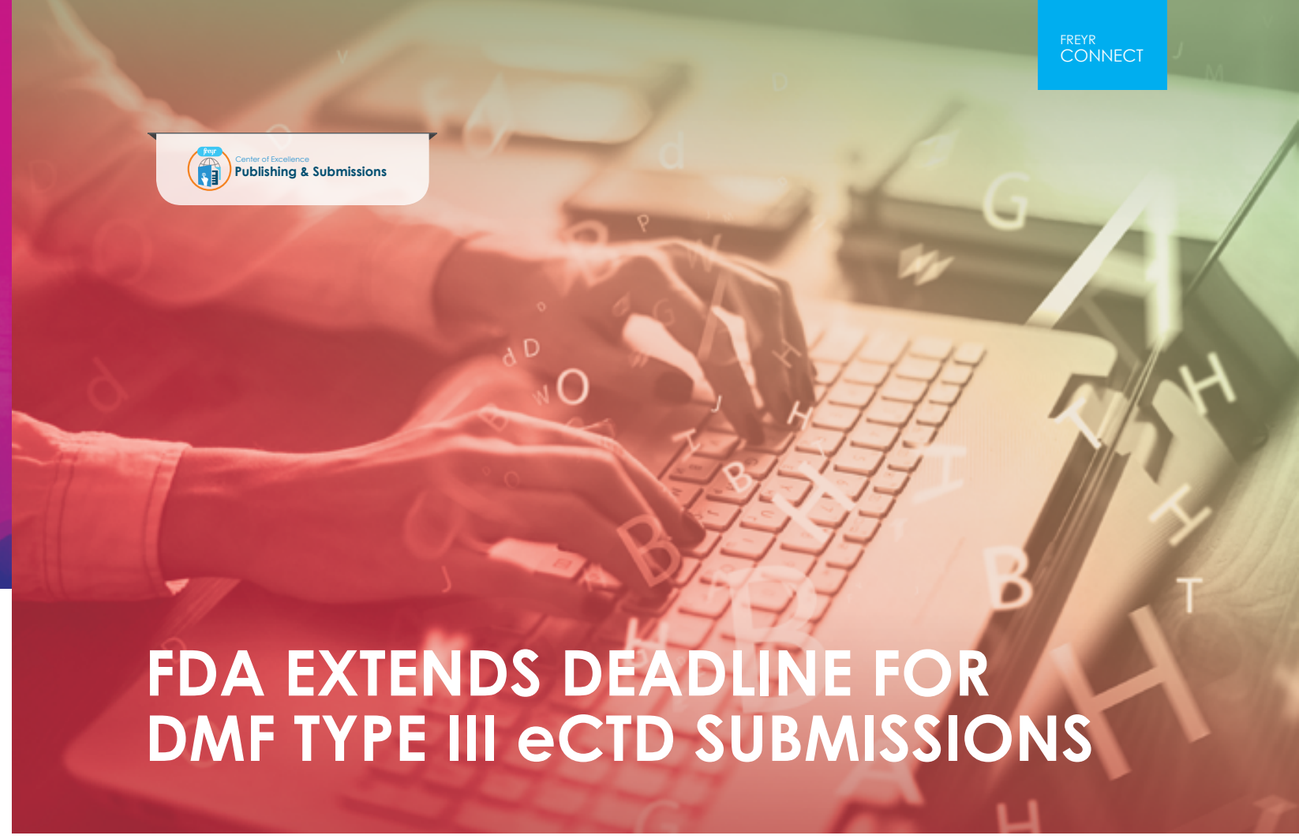
Medical device functioning, drug and cosmetic formulations, and novel foods with multiple ingredients are getting more complex with time. Considering this fact, there is a growing demand from all HAs to simplify the conveyance of such information. Especially when submitting the application and other related documents to HAs for Regulatory approvals, it is very important to ensure clarity and accuracy, as it might lead to misinterpretation of information and application rejection. With that said, how medical writers can meet the intended purposes and stand up to Agency expectations?

Meticulous Medical Writing

Medical writing is required not just to give out the science behind the product, it must ensure effective knowledge transfer concerning the efficacy of the product and medicinal product usage. Listed below are some of the common practices, a medical writer should adhere to optimize the quality of their writing.

- Adhere to the Health Authority guidelines
- Research and develop the domain knowledge including product development processes, clinical trial procedures, pharmacology, drug safety etc.
- Interpret and present the research data with logical discussions and conclusions
- Take into consideration the ethics and legal laws such as copyright issues
- Be simple and use correlation and analogies familiar to the end-users to simplify understanding
- Ensure the content developed addresses the common user queries
- For clinical purposes, state the problem and content of study to describe issues
- Explain the clinical outcomes in simple and abstract sentences avoiding jargon

Projecting clinical outcomes as accurate as they are to the HAs, and then to the end users is the first success for any product. Even a single typo or misrepresentation may challenge all your efforts of introducing an innovative medicinal product. Therefore, having a dedicated medical writing expert will help you understand the intricacies involved and push for consistency, simplicity, and accuracy in delivering safe information to end-users. Opt for one.



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Publishing & Submissions

FDA EXTENDS DEADLINE FOR DMF TYPE III eCTD SUBMISSIONS

For the third time in a row, the United States Food and Drug Administration (USFDA) has extended the compliance date for Type III Drug Master Files (DMFs) to be submitted in electronic Common Technical Document (eCTD) format. With the deadline extended till May 5, 2020, the first and foremost question every applicant should ponder upon is, what are the DMF Type III requirements and how is the data built, validated and published accurately for effective electronic submissions? Post the deadline, all DMFs which are not submitted in this format will be rejected.

If a DMF already exists in paper format with the FDA, it doesn't need to be resubmitted in the eCTD format. However, post the new target date all new submissions including any amendments, supplements, and reports pertaining to existing Type III DMFs will have to be submitted in the eCTD format. The DMF holders may continue to hold the same DMF numbers as before, with some minor changes. For instance, if the previous DMF number was 5678, the DMF holder would now have to pad left with two zeros. Thus, 5678 would be converted into 005678, when the DMF is converted into eCTD format; but would essentially remain the same number.

Type III DMF for Confidentiality

In case of confidential information, or if the manufacturer wants to withhold certain proprietary information from the applicant or sponsor, all such information may then be placed in a Type III DMF and incorporated into the application, accompanied by an authorizing letter from the manufacturer.

DMFs to be Updated Annually

According to the DMF Guidance, DMF holders are recommended to update their DMFs annually. FDA also sends "Overdue Notice Letters" (ONLs) to DMF holders for DMFs that have not been regularly updated in the last three years. If a DMF holder fails to respond to an ONL, his/her DMF may be closed by the FDA.

Even with complete knowledge of all the Regulatory updates regarding DMFs, sometimes, compiling, validating and publishing the data would be a difficult task unless you start preparing for submissions before time. In addition, if your current DMF is in paper format, converting it into eCTD format will be challenging especially while keeping pace against the extended deadline. Act now to be compliant.

Center of Excellence
Global Medical Device Regulatory Services

HEALTH CANADA'S MEDICAL DEVICES ACTION PLAN AND 3-PART STRATEGY

Health Canada (HC) has one of the most stringent regulations for medical devices. To further increase the safety and effectiveness of devices, and optimize the health outcomes for end-users, the Canadian health authority (HA) is aiming to strengthen the current Regulatory framework. The three-part strategy announced recently as an action plan is the part of the same. The aim of the action plan is to take the end-users' perspective into consideration while developing policies and regulations in future and thus to improve communication.

Each one of the three parts of the proposed medical device action plan has a sub-set of activities with approximate timelines. In order to successfully complete these activities, HC has also set milestones to ensure the objectives are achieved. All the three steps with necessary milestones are listed below.

Improve Devices Market-Entry

- Increase research by medical professionals and increased patient protection – starting early 2019

  Milestones:
  - Note of intent – June 2019
  - What we heard report – September 2019

- Review evidence requirements and expand scientific expertize – starting January 2019

  Milestones:
  - Call for members for the new Expert Advisory Committee on Women's Health – January 2019
  - Meeting of Scientific Advisory Committee – March and May 2019
  - Draft guidance document on evidence requirements – November 2019

Strengthen Monitoring and Follow-Up

- Implement mandatory reporting and expand the Canadian Medical Devices Sentinel Network – starting February 2019

  Milestones:
  - Publishing of regulations to report medical device

incidents in Canada Gazette, Part II – June 2019
- Expansion of CMDSNet to include additional healthcare settings outside hospitals, such as long-term care facilities and private clinics – June 2019 and ongoing
- The launch of education program for other healthcare settings – September 2019

- Establish ability to compel information on medical device safety and effectiveness and expand the use of real-world evidence – starting early 2019

  Milestones:

  - Publishing of Draft Regulations in Canada Gazette, Part I – June 2019
  - Establish how real-world evidence will be used for Regulatory decision-making – June 2019

- Enhance capacity for inspection and enforcement – starting 2019

  Milestones:

  - Hiring of additional 8 inspectors and 2 investigational analysts – March 2019
  - Increase in the number of foreign inspections from 80 to 95 – April 2019
  - Increase in compliance promotion activities – fiscal year 2019/2020

Provide More Information about the Devices to the Canadians

- Improve access to medical device clinical data – finalized by early 2019

  Milestones:

  - Publication of regulations in Canada Gazette, Part – II – June 2019
  - Launch of searchable public web portal - Following publishing in Canada Gazette, Part II

- Increase the information on device approvals and publish medical device incident data – starting January 2019

  Milestones:

  - Publishing and regularly updating a de-personalized data extract file of medical device incidents, complaints and recalls – January 2019
  - The launch of publishing of more review decision summaries – January 2019
  - Publishing searchable medical device incident database – December 2019

The year ahead might be dynamic with multiple activities proposed in the action plan. Aligning with the possible amendments, device manufacturers marketing their products in Canada must be prepared. Increase in Regulatory scrutiny being the foremost result of the strategy, stakeholders should be quick in adapting to the new changes on the go. But to know the full scope of amendments, consulting a Regulatory expert will prove beneficial. Stay informed. Be compliant.

12 MAJOR CHANGES IN FDA'S NEW NUTRITION FACTS LABEL

On May 27, 2016, the United States Food and Drug Administration (US FDA) published the final rule for nutrition and supplement facts label in the Federal Register. The final rule ensures that the label reflects new scientific information including the link between diet and chronic diseases like obesity and heart disease. The new rule intends to ensure that the product label is in line with current food habits and practices which are not clearly established in the old label rule. Another significant update of the rule is that the FDA has declared compliance deadlines basing on the annual food sales of the organization.

Compliance Deadlines

Nutraceutical manufacturers aiming the USA market entry must adhere to the new label rule by the specified deadline failing to do which, they may face product recalls. The deadlines are:

- January 1, 2020 for manufacturers with $10 million or more in annual sales
- January 1, 2021 for manufacturers with less than $10 million in annual sales

Major Changes in Nutrition Facts Label

To comply with the new rule, it is required that stakeholders decode the revised rule and abide by it accordingly. The revised rule includes but is not limited to the changes listed below.

- Eliminate the declarations of 'Calories from fat'
- Ensure declaration of grams (g) of 'added sugars' in a serving of the product
- Establish Daily Reference Value (DRV) for added sugars and declare the percent Daily Value (DV) for the same
- Change 'Sugars' to 'Total Sugars' and declare "Including 'X' grams Added Sugars" directly below 'Total Sugars'
- Update the list of vitamins and minerals of public health significance
- Update reference values used in the declaration of present DVs of nutrients on Nutrition Facts labels
- Revise format of Nutrition Facts labels to increase the prominence of the declaration of 'Calories'

- Remove requirement of footnote table listing the reference values for certain nutrients for 2000 and 2500 calorie diets
- Maintain records to support the declaration of certain nutrients under specified circumstances
- Amend the definition of single-serving container
- Require dual-column labeling for certain packages
- Amend reference amounts customarily consumed that are used by manufacturers to determine their label serving size

To gain more insights as to how the new label shall appear, the FDA has provided side by side comparison of new and old labels. Below provided is the adaptation of the same.

SIDE-BY-SIDE COMPARISION

Original Label

Nutrition Facts

Service Size 2/3 cup (55g)
Servings per container about 8

Amount per serving

Calories 230	Calories from Fat 72
	% Daily Value*
Total Fat 8g	**12%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**12%**
Dietary Fiber 4g	**16%**
Sugar 12g	
Protein 3g	
Vitamin A	10%
Vitamin C	8%
Calcium	20%
Iron	45%

* Percent Daily Values are based on a 2,000 calorie diet. Your daily value may be higher or lower depending on your calorie needs.

Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholestrol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

New Label

Nutrition Facts

8 servings per container
Serving size 2/3 cup (55g)

Amount per serving

Calories 230	Calories from Fat 72
	% Daily Value*
Total Fat 8g	**10%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**13%**
Dietary Fiber 4g	**14%**
Total Sugar 12g Includes 10g Added Sugars	**20%**
Protein 3g	
Vitamin D 2mcg	10%
Calcium 260mg	20%
Iron 8mg	45%
Potassium 235mg	45%

* The Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily det 2,000 calories a day is used for general nutrition advice.

As the deadline for final nutraceutical and supplement facts label rule is approaching closer, manufacturers and other stakeholders should plan for compliance with the assistance of dedicated labeling expert. Ensure your product label is reviewed within time. Be informed. Be compliant.

Center of Excellence
Regulatory Affairs

WHAT ARE CEP AND SISTER CEP SUBMISSIONS?

The Certification of Suitability (CEP) is a certificate that certifies compliance of the active pharmaceutical ingredients (API) or pharmaceutical ingredients with that of the rules laid down in the monograph of the European Pharmacopoeia (EP). CEP should consist of an explicit description of the chemical composition of the substances. The manufacturer should provide an evidence that the quality of the substance is controlled by the monographs of the EP and is granted by Certification Secretariat of the European Directorate for the Quality of Medicines (EDQM). The CEP also helps to bridge the gap between the Health Authorities and the industry, providing an added advantage for API manufacturers to enter the EU market.

The CEP is necessary for all the manufacturers and suppliers who are seeking market authorizations for:

- Checking the use of active substances to control the purity and quality of their product
- Reducing the risk of TSE risk products in accordance with the general monograph
- Checking the suitability of the monograph for herbal products based on control of herbal drugs and herbal drugs preparations.

Sister CEP Submissions

Any CEP holder who wishes to file for second CEP for the same API can file a new application known as 'Sister CEP submissions' or 'Sister File'. This application is valid for all the files except sterile, TSE or herbal applications. This can be due to various reasons such as differences in API specifications with an alternate process or to cover alternate grade of material. A sister CEP is, ideally, approved on a fast track basis compared to the timelines of the original CEP applications. A set of pre-defined conditions are set by EDQM that must be fulfilled in order to file a Sister CEP. Reaching out to an expert with information on sister CEP will help in quick approvals of the application.

Requirements for Sister CEP Submissions

- The manufacturer should be the same for both CEP and Sister CEP application
- The holder is same for both applications
- The substance should be same as in the original document
- The differences in the sister file and the original file should be classified properly

Freyr has an experienced team of Regulatory experts with hand on expertise in compilation, review, and submission of CEP to EDQM in line with EDQM guidelines. To know more about CEP and sister CEP submissions, contact our Regulatory Affairs experts at sales@freyrsolutions.com.

Center of Excellence
Global Medical Device
Regulatory Services

WHAT IS INMETRO CERTIFICATION?

Brazil imports most of its medical devices, making it a lucrative market for foreign device manufacturers. Medical devices in Brazil are regulated by National Health Surveillance Agency (ANVISA) which grants the registration certificate for marketing. Medical devices with electrical components and some non-electric devices such as surgical gloves and condoms require additional certification issued by The National Institute of Metrology, Standardization and Industrial Quality (INMETRO) prior to initiation of ANVISA registration process.

Brazil's Instituto Nacional de Metrologia, Normalização e Qualidade Industrial, also known as INMETRO, is the body responsible for recognizing certification organizations responsible for certification of products for compliance and authorization of approved certification marks. This certification scheme is known as the Brazilian Conformity Assessment System (SBAC).

To qualify for INMETRO certification, medical device manufacturers should get their products tested as per SBAC recognized standards by an INMETRO accredited testing laboratory.

INMETRO Certification: Necessary Steps to be Followed:

- Document Analysis
- Pre-License Inspection
- Certification and Product Marking

At the end of a certification process, an applicant is authorized to use certification marks to demonstrate a device's compliance. These marks are placed on both the approved medical device and on the product packaging.

After obtaining INMETRO certification, the medical device manufacturers are required to carry out certain periodic activities to retain the certification.

Once approved, the INMETRO certification is valid for five years. During this period the manufacturer's facility is subject to annual surveillance inspections. Appointing a local entity with sound knowledge on the requirements of INMETRO specifications & local certifiers is mandatory to simplify the process. In addition, INMETRO certification comes with many other significant unknowns.

Freyr has extensive experience with INMETRO certification in terms of requirements, communication, translation among other things. We can answer your queries and address any concerns you may have. Contact our experts at sales@freyrsolutions.com.

Center of Excellence
Compliance, Audit and Validation

freyr®

AUDIT AND THE WORKFLOW

Last-minute audit notifications are cumbersome.
To face them confidently, manufacturers are required to set their processes and audit them periodically. But, where should they start and what should they consider? Here is the workflow…

Pre-Audit Preparation

- Requirement gathering using self-appraisal checklist
- Audit scope definition
- Determination of audit type- Onsite / Web / Paper /Hybrid audit
- Tripartite CDA sign off, as applicable

Audit Planning

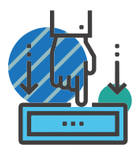
- Audit agenda
- Audit schedule
- Identify lead and co-auditors
- Identification of auditees
- Audit tour plan

Auditing

- Audit the site when it is functional, and operational
- Audit the facility and not just the documentation
- Review and monitor audit progress
- Collection of artefacts to support audit report

Audit Reporting

- Reconcile between on-site audit vs. Documentation audit
- Comprehensive report inclusive of facts and findings
- Findings classification based on risk and impact
- Audit metrics preparation- trends, patterns (CPP, CQA)



Follow-up Audit and Closure

- RCA, correction, corrective action and preventive action
- Monitoring efficiency and effectiveness of CAPA
- Follow-up and closure

With the audit workflows defined, the next challenge for manufacturers is to practice the audits based on them comprehensively right from the first step. Freyr can meticulously work with clients to easily overcome such challenges in multiple ways.

Know more about Freyr's Compliance & Validation Expertise

CLICK HERE

Comic

Center of Excellence
Regulatory Strategy

Sustain
The Winds of Brexit

Stay Rooted To
The Compliance Best Practices

CONSULT

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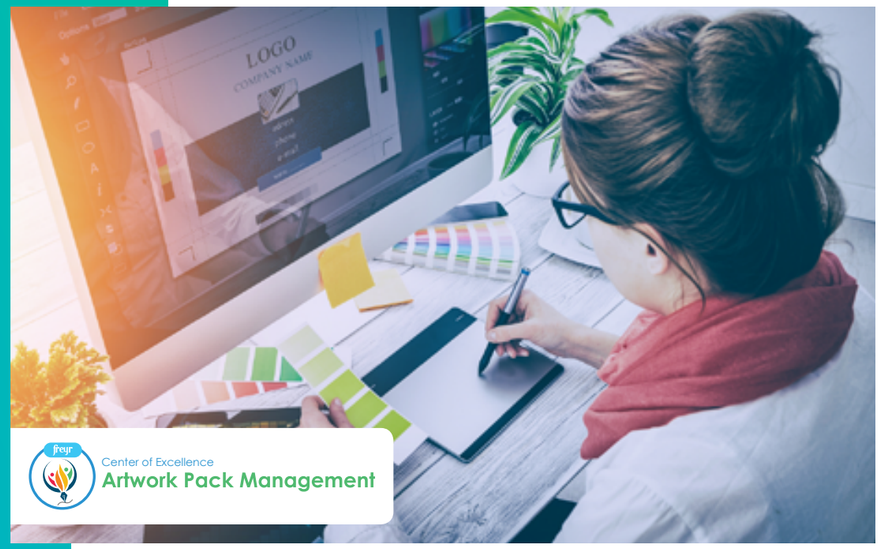
Case Study

COMPREHENSIVE REGULATORY ARTWORK SUPPORT WITH 99.99% QUALITY



Center of Excellence
Artwork Pack Management

Client

Canada-based Global Pharmaceutical Company

Geography

Canada

Solution

- Artwork Process Consultation
- Artwork Lifecycle Management
- Artwork Coordination
- Artwork Creation
- Artwork Proofreading
- Artwork Tech Transfer
- Artwork Print Proofing
- Artwork Technology Consultation & Implementation

Therapeutic Area / Indication

Biosimilars, Monoclonal Antibodies, Respiratory, Autoimmune Therapies, Cardiovascular, Anti-infectives, Gastrointestinal, Central Nervous System, Mental Health, Pain Management and Respiratory

Products

Medicinal products - Blister, Bottle, Ampoules, Sachet, Tube, Glass Vial, Pre-filled Injections and Medical Devices

FREYR CONNECT

Benefit Highlights

- 4+ Years Relationship
- 24% CAGR
- 24x7 Service
- 99.99% Quality Delivery
- Improved TAT
- Central Artwork Studio Services
- Proofreading/QA Services
- Technology Enablement

Business Imperatives

- To improve Artwork business processes.
- To save cost of operations.
- To create a tailored business culture and ways of working.
- Harmonize disparate systems and different processes for stakeholders across the sites and groups - Canada, 3rd Party, Private Label, Australia, India, Saudi, Mexico etc.
- Create technological capabilities.
- No proper tool to manage workflow and asset management issues.
- Remove operational efficiency problems:
  - Turn around time for artwork
  - Non availability of proper escalation matrix to ensure timely resolutions
  - Coordination with stakeholders

Challenges

- SLA tracking a big challenge
- Local and manual processes
- Decentralized operations
- No defined process documentation for one or more processes that may lead to high risk non-compliance findings
- Significant lack of Process adherence and deviations from documented SOP with potential for high risk non-compliance findings that require immediate CAPA
- Routing of work through inefficient and archaic channels
- Lack of transparency
- Longer workflow cycles (over 60 to 75 days or more for each request)
- Delayed timelines
- Non-compliance due to manual documentation
- Long audit preparation periods
- Assets management was not proper
- Artwork management landscape was heavily dependent on institutional knowledge and resource continuity.

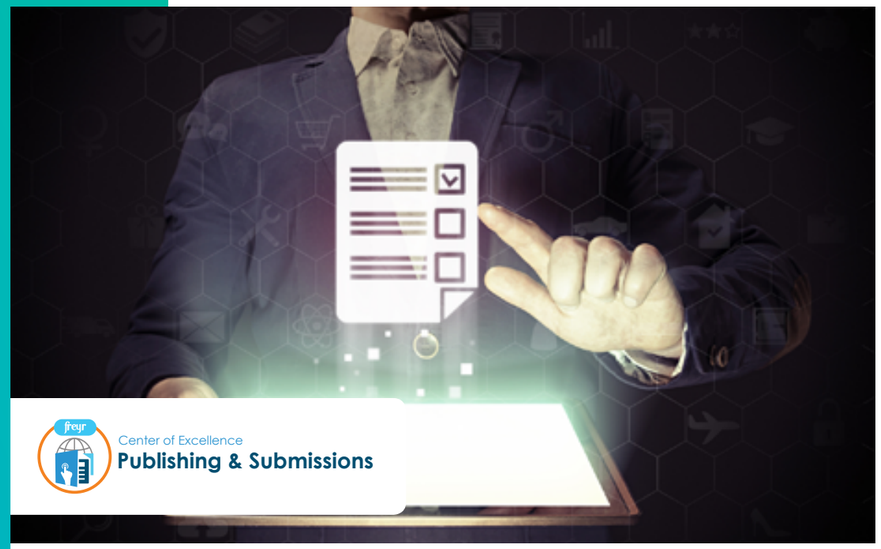
Freyr Solutions & Services

- Pharmaceutical packaging Artwork harmonization - Across the globe operations
- Streamline the entire change request processing, end-to-end
- Introduce right-first-time methodology to improve accuracy levels
- Full understanding of the complex current situation with comprehensive current state assessment report (People, process, systems integration & information flow).
- Future state operating model, including a centralized process management with plug and play framework built over time.
- IT architecture to support the new operations.
- Change program design to deliver the new capabilities.
- Operational efficiency of more than 50%.

Business Imperatives

- More than 1 million saving in each year as against the estimated 800K.
- Before outsourcing, resource cost at customer stood at 2.81 million which excluded adobe license, font, all the hardware and per seat cost etc.
- After outsourcing to Freyr, entire global operations including the technology implementation resources stands at 1.9 million only which includes software license, font cost, seat cost etc.
- All customer graphic resources released on-time as per the project implementation plan agreed. In some instances resources were released in advance as well.
- Cost and timeline estimates for the entire project was achieved. Overall all the project objectives were met.

SUCCESSFUL 50+ SPL SUBMISSIONS IN 20 DAYS



Client
USA based fast growing generic pharmaceutical company

Geography
USA

Solution
SPL Creation

Therapeutic Area / Indication
ORAL

Products
Human Prescription Products

FREYR CONNECT

Benefit Highlights

- Freyr as a competent partner is associated with client for content labeling SPL conversion services
- Fast, accurate, and cost-effective service
- Performing in-depth SPL Validation for US FDA compliant SPL submission
- Ensuring data values are according to format (DUNS Number, Labeler Code, etc.)
- Lifecycle management for SPL submission

Business Imperatives

Client is a fast growing generic pharmaceutical company in the areas of development, manufacturing, marketing and distribution of high quality and cost-effective generic pharmaceutical products.

Challenges

- Need 50+ SPL submissions within 3 weeks.
- As those are updated in 2015 year, validation errors appeared.
- As per new rules they require Freyr support.
- Label updates.

Freyr Solutions & Services

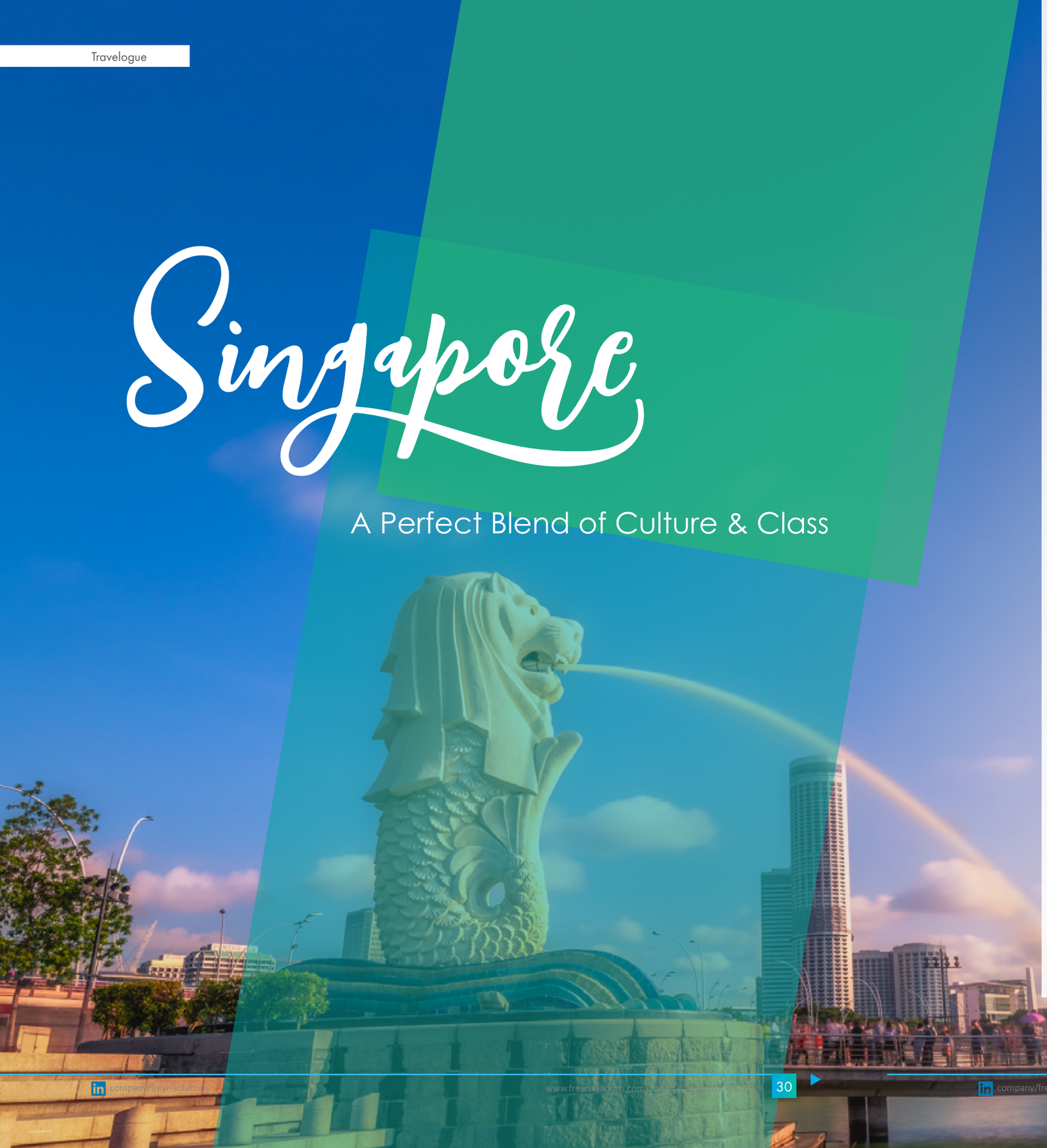
- Conversion of submission content into proper XMLs.
- Quality Control - XML Validation , Manual QA/ QC on individual sections, Metadata verification.
- Aware of evolving new guidelines for quick and effective SPL.
- Tier 1 & Tier 2 validation.
- Character eye-balling.
- Ongoing life cycle maintenance.

Client Benefits

- Fast, accurate, and cost-effective service.
- Performing in-depth SPL validation for US FDA compliant SPL submission
- Successful SPL submission within 20 days.
- 100% submissions acceptance.
- Ability to store and archive labeling info and supporting documents.
- Assured data security.

Singapore

A Perfect Blend of Culture & Class



What does a traveller look for, while planning an itinerary? Is it a nice touristy place? Or a place which pump up the adrenaline? Or an abode for tranquillity? Or a perfect mixture of cultural representations? The opinion is totally individual. But, what if I tell you that there is one destination that matches with all of those desires? It is none other than an Island city-state off Southern Malaysia - Singapore. Being a metropolitan country and a tropical island, Singapore is a perfect amalgamation of Malaysian, Indian, Chinese and English cultures, with shades of its own.

Not only that! Singapore, the Lion City, is fondly known for its clean roads and responsible citizens. Chewing gums and spitting are completely banned in the "Lion City," and it's followed with no excuses. That makes it the most beautiful and clean countries in the world. I spent 4 days in the country and there was never a boring moment and was all occupied walking around. It made me mesmerized and how!? Let me take you through the country place-by-place.

But first, let's decide upon the way of commuting. Though there are local taxis and commercial taxi service providers, like Grab, it is suggestible to use public transport majorly. The Mass Rapid Transit (MRT) is one of the most user-friendly and well-connected public transport systems I have come across. It's cheap and easy-to-use, and you can buy a Singapore tourist pass to enjoy unlimited travel for a certain number of days. Now that we are clear on our commuting pathways, should we decide upon must-visit places?

Chinatown & Little India

While Singapore is mostly picturized and portrayed with skyscrapers and tall gardens, places like Chinatown, Arab Street and Little India holds up the true cultural essence of Singapore. Let me start with Chinatown; the place that gives you true China feels. This historic district of Singapore is a home to many Chinese immigrants. The moment you enter this place; you would get to know that you are in Chinatown with the beautiful red Chinese lanterns and the aroma of Chinese speciality dishes that pats your hunger pangs. If you are in Chinatown, do not miss the street food. It is the only place where street hawkers have earned Michelin Stars. It is a paradise for foodies! Same is the case with Little India. I was actually quite surprised to find a part of India in the heart of Singapore. Little India is known for its famous dish called "Roti-prata," which they say is a must try! Apart from the delicious food, there are many monasteries and temples in Chinatown and Little India, which are worth visiting.

Amidst the classy and sophisticated areas of Singapore lies the Arab Street, showcasing Arab's colourful heritage. The area includes many small yet culturally rich streets surrounded by colourful artworks, garments, rugs and is filled with the aroma of Arab tea. The main attraction of Arab Street is the Masjid Sultan Mosque, which has a history that traces back to 200 years. One can easily spend hours roaming around in the Arab street and can feed themselves with delicious Mediterranean food while being indulged in shopping around unique indie boutiques.

Marina Bay

Marina Bay is the downtown of Singapore. It is not just an area, it's a district in itself, which represents all the modern and stylish aspects of Singapore. Marina Bay stands an epitome for the development in the country. When I was told that we were going to spend an entire day by the Bay, I was quite sceptical and in fact curious about the time to be spent. But the moment we reached there, I figured we may need more than just one day as it has the best tourist attraction spots, such as:

- Merlion

For tourists, Merlion maybe just a statue. But for Singapore, it is the symbol of their culture and heritage. The half-lion, half-fish statue is one of the most visited spots.

- Sands SkyPark

Sands SkyPark is one of the four lavish hotels of Marina Bay Sands. Located on the 56th floor, the hotel has an observation deck which provides the tourists a panoramic view of the city. It is one of the most enthralling experiences one can undergo in Singapore. It's amazing patisserie makes the hotel even more exotic.

- Singapore Flyer

Singapore Flyer is the best observation spot for the adventurous you. The Flyer is a giant wheel and stands tall with 165 meters in height, giving the riders a stunning view of Marina Bay.

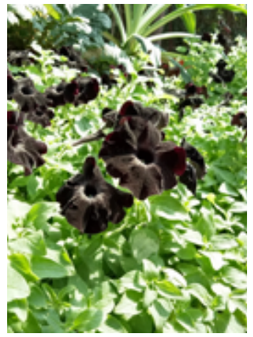
- Spectra Light Show

Each night, Marina Bay mesmerizes its visitors by showcasing a beautiful light show. The jaw-dropping light show illuminates the Marina Bay with florescent lights and water sprays. The visuals cannot be described in words! It's absolutely spectacular and free to experience.

Gardens by the Bay

It's quite normal to see gardens are filled up with trees, but have you ever seen Supertrees towering over towering over 128 meters, just like tree-cyborgs from

the movie Avatar. Gardens by the Bay is filled with such giant metal-interconnected trees, more than 12 in number. Though these trees are visible from distance, watching them from up-close is very fascinating. Spread in more than 101 hectares of area, Gardens by The Bay is home to more than 2,00,000 plants of over 800 species. Though the whole garden is aesthetically pleasing, there are two specific highlights of it.



- Flower Dome

The dome is quite unique in itself. I was amazed to see the variety of flowers and plants inside this huge man-made crystal structure. The place is a perfect mixture of nature and technology. They have a super-cool system where they collect rainwater from the surface of the dome to power their cooling system. Very impressive! Isn't it? Earlier, I took pride in saying that I know a lot of species of flowers, but after visiting the flower dome, I understood how minimal my knowledge was. There are flowers that you know and then there are flowers that you have never ever seen. I even came across a black flower, and that is one of the most beautiful things I have seen in the Flower dome.

- Cloud Forest Dome

The cloud forest is surreal. Entering it feels like entering some humid and tropical forest. The cloud-forest dome is a mystical man-made structure with big green lush trees, bushes and plants everywhere. It also has a continuously flowing waterfall right at the entrance which creates several rainbows to add-up to your experience. There is a cloud walk too, which takes you through the forest inside-out to finally give you a breath-taking view of the dome. And the most beautiful thing about cloud forest dome is that there is a secret garden and limestone cave too.

After roaming around in the garden and visiting both the domes, we have decided to stay back after sunset to enjoy the Garden Rhapsody Show. Once the sun has set, the garden lights up all the supertrees and these lights of supertrees groove to the music of the 70s and 80s. Honestly, it was one of the coolest shows I have been to. It was spell bounding right from the beginning till the end.

Sentosa Island

Derived from the Sanskrit word "Santosh" (meaning peace and tranquil), Sentosa is actually the peace and fun capital of Singapore. With attractions for every age group, Sentosa is a place which should be a must-visit on everyone's bucket list.

- S.E.A. Aquarium

South East Asia (S.E.A.) Aquarium is a magnificent world of underwater realms. Walking through the aquarium is one indescribable event. Imagine walking through a tunnel and watching dolphins and other sea animals gliding by you. It is a sight worth witnessing. The aquarium is a home to various species of sea animals, including more than 200 sharks and some endangered species. It also has a cinema-sized ocean to please your eyes.

- Museums

The island also has a range of museums for everyone to enjoy. There are Images of Singapore which showcases the heritage and culture of Singapore. The other is Trick Eye Museum, where you get to have a lot of fun with augmented reality apps. And the most captivating is the Madame Tussauds Singapore! It was extremely fun to click pictures with the wax statues of my favourite celebrities.

- Other Attractions

To boost your adrenaline, there are a tons of other activities on the island, such as high rope courses, rock climbing, zip wire etc. Since, it is an island there are a few beaches as well, where you can chill with your friends and family. Or you can just enjoy a nice meal by the beach watching the sunset.

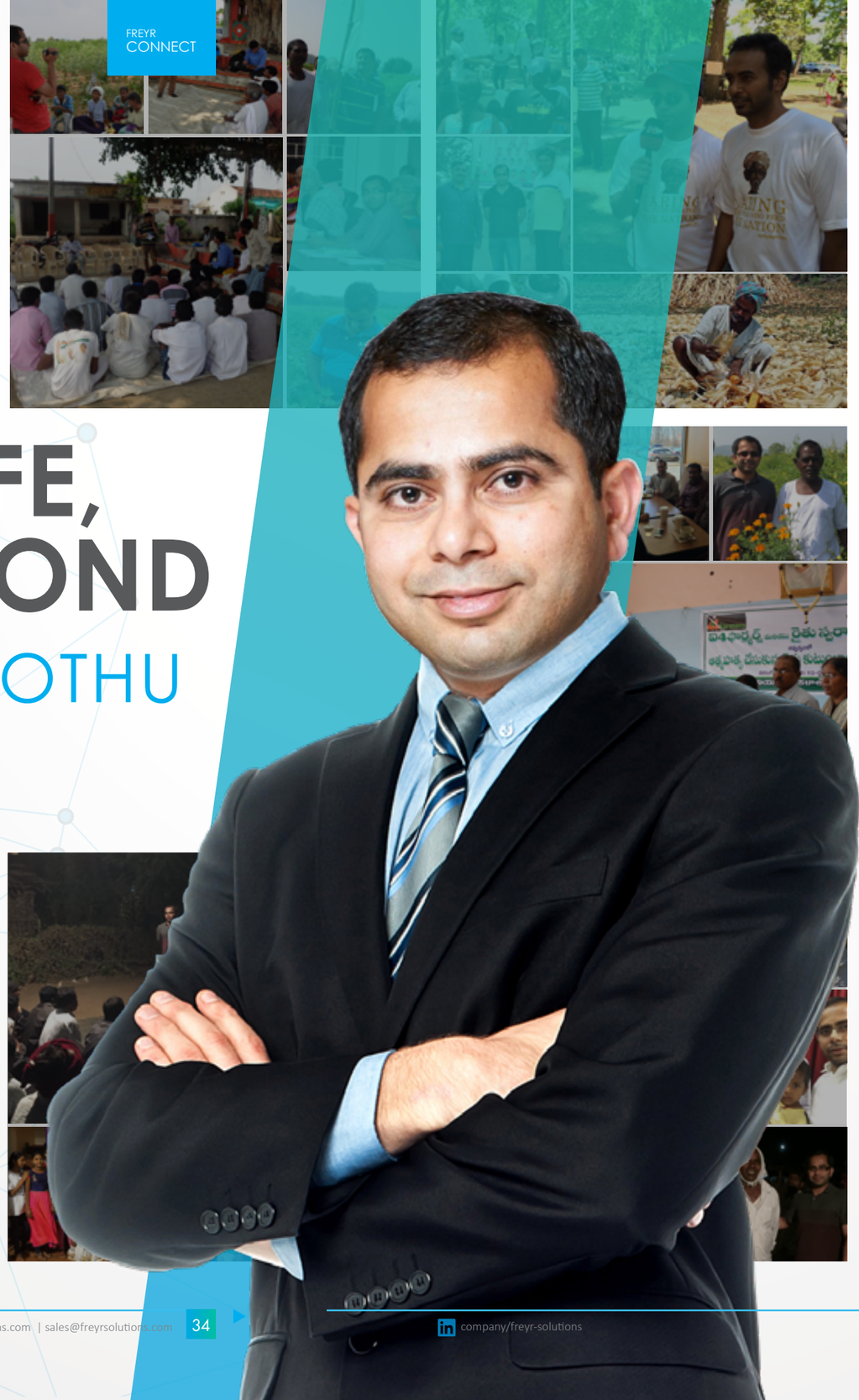
Your day at Sentosa cannot end without watching their extremely famous light and sound show called "Wings of Time". It was unlike any other light and sound show. With Pyro techniques, 3D-projectors, lasers and robotic fountains, Wings of Time unfolds a tale of the mystery and magic against the sumptuous backdrop; the sea.

Universal Studios

This place is my Disney land! Universal Studios is a paradise for all movie lovers. Entering this place is like entering a whole new world of fantasy, fiction, sci-fi and MINIONS! The place has seven movie-themed zones, right from Madagascar to Jurassic Park and with equally amazing rides and shows. There is a sci-fi city, too, which has theme-rides of Battlestar Galactica and Transformers, including the 3D battle rides. There are even various shows and live performances that run throughout the day to entertain everyone. Oh! If you are lucky enough, you may even sight Minions, Shrek and Optimus Prime roaming around you and eager to get clicked. Being a movie buff, that one day spent in Universal Studio will be etched on my heart forever.

They say that 'Singapore is the happiest place in Asia.' Finally, I am in terms to agree that. Right from the places to people to culture and to heritage, everything is so warm and welcoming that you can't help but cherish, enjoy and get lost in the free spirit of Singapore. While sitting at the Changi Airport to take a flight back to India, I couldn't help but fathom, if I could have ever witnessed the true beauty of Asia, had I not visited this small yet surreal country.

Xièxiè Singapore for introducing me to the beautiful culture that you behold.



BUSINESS & LIFE, BASICS & BEYOND

WITH VASU RANABOTHU

Great work is a result of disruptive thinking, innovation, value addition and the ability to handle multiple challenges We, at Fryer, are fortunate that Mr. Vasu Ranabothu from the Executive Management team endorses and personifies these traits.

A conversation with Vasu helps you unravel a persona that is cut throat and business savvy on one hand while highly compassionate on the other. As we spoke to him...

Hi Vasu. At the outset, we are very happy to see you back in India, and we really hope you could spend more time with us here. You have always come across as calm, composed and grounded. How do you manage it?

I can't really call myself composed (Laughs!). It's all about learning. That is one thing I learned while living in the U.S. Over there, everything around you is organized. Punctuality and discipline are a way of life and the work ethic is impeccable. The priority is always work; quality work, no matter what. I carry that learning and those values everywhere I go. I adjust wherever required but I don't get easily influenced by surroundings. I'm trying to enforce the same in my team as well and I sincerely hope that they will follow this approach.

Freyr is growing in harmony with the ever-evolving Life Sciences Regulatory landscape. Do you think that the organization has been successful in propelling the change that the industry needs? Is Freyr on the right path?

Yes, of course! We are coping really well with the industry's requirements. We are not lagging in any way. Since we are in the Regulatory industry, we have to be in tune with the latest and the greatest. We cannot do the same thing every day. What we deliver is extremely dynamic and since regulations change constantly, we need to evolve and cope with the demands of the industry. However, it is not possible to constantly change our working style. Our greatest challenge and strength lies in our capability to be stable while delivering the most dynamic services.

In terms of growth, the industry is moving towards outsourcing. Historically, Regulatory functions were always considered to be inside functions; therefore, people didn't envision that it could be outsourced. However, over the last five to six years, the industry has realized that outsourcing could be a viable business strategy. Freyr is lucky that we were able to capitalise on the opportunities that came our way.

What was your motivating factor in joining the top FIVE in establishing Freyr?

Honestly, the idea wasn't mine. We (Srini, Rajiv, Suren, Sunitha, and I) have been friends for more than 2 decades. In 2008, we started thinking of building an IT development company. Our goal was to be a niche player and fill the gaps in the Life sciences industry. One gap that we identified was the lack of a single platform that captured all the necessary regulatory information and updates. We decided to build a software system that would bridge this gap by creating a platform that would track all submissions, registrations, related

documents, Regulatory information, health authority communications, etc., in one tool.

While conceptualizing the idea, we were fortunate to meet some prospective customers who needed similar solutions and Regulatory specific services. That's how we entered the Regulatory services zone. We were successful in delivering cost-effective, global Regulatory services with high quality. We never had to look back. We have been constantly updating and upscaling ourselves to meet the industry needs. Our first customer led to the next and another, and our journey continued. We will always be thankful to our first few customers who referred us to their peers and colleagues in the industry. It is these customers who played a vital role in Freyr's growth and success story.

APAC and the Middle East (ME) are challenging for foreign market players in terms of the Regulatory scenarios. How do you perceive them? How can strategic companies expand their business in this region?

As far as Freyr is concerned, APAC and ME are part of our Rest of the World (ROW) strategy. Some of them are emerging markets while others are established markets. If you consider Europe (EU), multiple countries fall under the EU region. They do have different regulations, but they primarily follow the European Medicines Agency (EMA) guidelines. We might perceive Middle East as a region but there is no common Regulatory body that sets the guidelines. Every country in ME has its own guidelines. Same is the case with APAC; 10 ASEAN countries have different regulations.

Hence, market entrants should first find which markets have common regulations and guidelines. To gain a foothold, International companies need to identify the countries which are relatively similar to their country of origin in terms of regulations. Once this is done, they can attempt to enter other countries within these regions. Planning and prioritizing the primary and secondary markets will help them tackle the situation in a better way. However, while executing this strategy, the constantly changing hurdles could pose challenges which the in-house team might not be able to handle. It is highly advisable to engage a partner like Freyr to develop a strategy and execute the same.

What does Freyr offer for APAC market-entry enthusiasts?

Everything! Freyr provides end-to-end Regulatory services for almost all the product categories such as pharmaceuticals, medical devices, beauty wellness, food supplements, etc., For any product regulated by the authorities, we can help companies by developing a strategy for go-to-market, Regulatory approvals, and post-market changes. We can help them with everything required to enter a particular market.

Describe Freyr in 10 words or fewer. We didn't mean the caption, of course.

I don't think I can define Freyr in 10 words. Any company, when it enters into the market, comes with a USP. To be successful, you need to be disruptive. Freyr is that company which always thinks out of the box and comes up with disruptive thinking to benefit the customers. That is our USP. We always try to provide innovative solutions. While cost effectiveness is a major part of our solutioning, it is the value addition we bring to the table that we are really proud of. That's what we care about the most and that's what Freyr is all about.

"Thinking Innovative and Doing Innovative with Disruptive Ideas"

Starting-up, sustaining the success or scaling up; which phase can Freyr relate to in its current situation?

That's a tough question again. I would say we are at the stage of scaling up. Right now, we are in the growth stage. However, there is always something new happening at Freyr. People may feel that we are a start-up because what we do is always new. Initially, we did not cater to all the product categories but now we are geared up for all of them. So, while we are established in certain categories, we qualify as a start-up in a few.

Similar is the case with some new service areas we are offering. We are also relatively new in some remote geographies, and since we have to start establishing ourselves there, we are a start-up in those geographies. However, as an organization, we are 600 people strong, operating from 13 global locations with expertise in 120+ countries and with 330+ customers. We are continuously growing.

So, we are doing both; scaling up in one area, starting up in some new areas, that's essentially called "growth phase."

Apart from being a key part of a successful organisation, we see you participating in marathons, propagating organic food, working toward upliftment of farmers and supporting socially relevant causes. Could you give us an insight into this aspect of your personality? Did anything in specific trigger these interests?

Nothing in specific, actually. It didn't start due to any incident. These aspects of mine are a result of my upbringing and the environment I grew up in. I have seen disturbing situations very closely.

Anything can be manufactured, but not food. Food has to be grown in the fields. At the dinner table, if you pause to wonder where the food is coming from, you realise the enormous hard work that goes into producing it. I love interacting with people, and I also read a lot. The plight of farmers has always been in the news. Their suffering, the dismal conditions they face and work in, the crisis in Indian agriculture and the fact that farmers were committing suicide disturbed me. Despite the tremendous hard work they put in, there are factors beyond their control; it's always a dependency by design. When I read these things, I felt we owe them something. Especially if you think through, the food coming to our table is always subsidized, as food prices are always controlled. These restrictions aggravate their situation and worsen the crisis.

I discussed this with a few likeminded friends and five of us started i4Farmers. We felt that among us five, even if each one of us helps one farmer, together, we would have helped five families. That was our motivation to start a non-profit organization. Over the years, we have been able to help more than 600 farmers.

On that note, when is your next marathon? Does Freyr support the cause?

My next marathon is in November 2019. This time I am targeting a full marathon. I feel great when I see that Freyr is always involved in social initiatives; including this, as part of Corporate Social Responsibility (CSR).

If someone who is starting his career wants to learn something from you, what would it be?

I always tell people "don't do only one thing in life." If you do only one thing, you're doing a disservice. You should strive to do everything that comes your way.

"We have only one life. Don't do a disservice to it. Take up multiple challenges."

I am a chemical engineer by education, worked as a material scientist by profession, then I didn't want to do it because I did not like to sit in a lab for long hours and experiment. Since everyone was focussed on Information Technology (IT), I also wanted to explore it. Coming from a Chemical Engineering background, adapting to IT was a huge change but within a short span I completed a short-term course and started training the very next day as an IT developer. That got monotonous too. I was offered sales and business development and I took up the challenge. Post that, I moved into project management. After that, we started Freyr and I have become an entrepreneur juggling between the functions and processes here. The best part about Freyr is the multiple opportunities and the freedom to explore many areas. For people who believe that magic lies beyond comfort zones, Freyr is the place to be.

I firmly believe that since we have only one life, work on every opportunity that comes your way. Restricting ourselves to doing only one thing is a waste of our life. We have to take up challenges and learn new things; success or failure is a by-product of these challenges and is secondary.

Vasu — Off work. Describe in one word.

ONE WORD!!! (CHUCKLES)

Boring. I'm very boring outside work (Laughs!). However, I play a few sports when I get the opportunity. Apart from that, I like to travel and explore new cultures and meet new people. Also, I am a constant learner. I love to interact with people and learn new things in life.

Freyr CLIENT WINS

- **The Customer:** A Sweden based, leading medical devices company

  Project Details: Provide support for Mexican Registration Holder Services (MRH) in Mexico for 02 Medical Devices

- **The Customer:** An India based, fast growing pharmaceutical company

  Project Details: Provide variations submission to Europe markets

- **The Customer:** A USA based, leading multinational health care company

  Project Details: Provide eCTD publishing support to Bahrain

- **The Customer:** A UK based, leading multinational consumer healthcare products company

  Project Details: Regulatory compliance of home care products across 4 CEE countries

- **The Customer:** A USA based, organic ingredients cosmetic company

  Project Details: Label Assessment for a single product for 2 markets.

- **The Customer:** A USA based, personal care products company

Project Details: End-to-end product registration support in Thailand and Malaysia along with responsible person support

- **The Customer:** A China based, contract research organization

  Project Details:

  - ANDA Compilation, Publishing and Submission Services.
  - US Agent Services
  - Pre-Submission activities

- **The Customer:** A USA based, global largest pharmaceutical company

  Project Details: Label comparison for Switzerland and Russia

- **The Customer:** A USA based, leading skincare products company

  Project Details: Regulatory resource support

- **The Customer:** A Germany based, innovative medical devices company

  Project Details: Medical device registration and Legal representation support in Argentina

- **The Customer:** A France based, multinational pharmaceutical company

  Project Details: Veterinary Master File Publishing for US market

CLIENT TESTIMONIALS

PDE, Medical Writing

We really appreciate Freyr's team effort in submission of PDE reports of requested products at very short notice period. We hope to receive the same support from your end for all future endeavors.

An India-based Healthcare Organization

Cosmetics Regulatory Services

Thank you very much for working with us on the India Cosmetic project. We appreciate your resource's diligence and focus and attention to detail. Very lucky of you to have them in your team.

A Leader in Skin Health

Publishing & Submissions

We appreciate the great support received from Freyr for their successful communication with the FDA while offering extended support for transmitting submission and sharing the acknowledgments. Thank you for managing and completing the task in a very short period.

Awesome!!! Great Team work.

Head – Global Regulatory Affairs, An Integrated Pharmaceutical Topical Organization

Regulatory Affairs, Medical Devices

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

Regulatory Affairs Officer, A Global Industry Leader in Medical Device Design and Manufacturing

Regulatory Software & Services

Special thanks to Freyr team for their patience and co-operation while developing and customizing a leading workflow and content management solution for our requirements. Without your collaboration we could not have developed such a functional tool for documents' sharing, submission management and status tracking.

Kudos to entire Freyr team for excellence. Keep up the good work.

US-based, Global, Pharmaceutical Company

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

About Freyr

Freyr is a leading, niche, end-to-end global Regulatory solutions and services company supporting large, mid, and small global organizations across different life sciences verticals - Pharmaceuticals | Generics | Medical Devices | Biotechnology | Biosimilars | Consumer Healthcare | Cosmetics | Nutraceuticals. Freyr supports life sciences organizations in their entire Regulatory value chain - Intelligence Driven Submissions/Product Registrations | Labeling | Artwork | Post- Approval Change Management | Regulatory Software and other related services.

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