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GLOBAL REGULATORY
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AN ISO 9001 & 27001 COMPANY

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CONNECT

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LEAD STORY

Post-Brexit Impact
On the EU and the UK's
Life Sciences
Regulatory Framework

Responding to COVID-19,
In a Healthy and Committed Way

REGULATORY : CONSULTING | SUBMISSIONS | AFFAIRS | SUPPORT | INTELLIGENCE | LABELING | SOFTWARE

WHAT'S INSIDE?

FREYR 360°

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- Labeling Experts
- Eisha Dingre

FOREWORD

Dear Patrons,

We really hope and wish all your family members, friends, employees, colleagues, customers, and well-wishers are staying safe in these difficult times of International Health Crisis - COVID-19.

This extraordinary situation has pushed us to relook at the internal operations only to align with the rapidly changing business scenarios. At Freyr, we are in fact treating this as a best opportunity to reengineer our processes and build more sophisticated, and efficient systems that can streamline both clients' and our efforts of bringing novel medicinal products to market and advocate the patient safety on a larger perspective.

With that positive hope, let us bring you the first ever Issue of **Freyr CONNECT - Volume 8.**

All thanks to our functional support team at the back end, we could complete this Issue even in the remote working conditions. It stands a testimony to our commitment and assurance to our valued subscribers, clients, and partners.

If not COVID-19, the biggest update every one of the global life sciences industry had looked for in the last quarter was the Brexit and its implications. Now that it's been a reality, we feel it's our responsibility to give you the best possible information about it in the form of a lead story followed by a deep dive thought leadership article on the EU MDR.

This Issue also covers Regulatory recommendations from varied health authorities like, USFDA's nutrition facts label & checkpoints for a compliant transition, roles & responsibilities of an EU qualified person, TGA's assessed claim on medicinal labels and various thought leadership articles.

With the major Regulatory insights listed out, we would like to convey that some of the mandatory equations are expected to be changed in the existing scenario. We are truly optimistic that we can notify them to you on time and together we can comply with them all.

Until then, stay safe and let us know your feedback as always.

Happy Reading!

Suren Dheenadayalan

CEO

Responding to COVID-19

The unprecedented times of COVID-19 outbreak, has made the entire world standstill. It has challenged every aspect of life but not the spirit of humankind to fight back. Governments have quickly made significant measures to respond and businesses are rapidly changing their ways of functioning; so is Freyr.

We at Freyr are closely monitoring the worldwide outbreak of COVID-19 and complying with all the recommendations from World Health Organization (WHO) and regional government bodies. Our first priority is to protect our employees and ensure their wellbeing and safety. We have quickly adjusted to social distancing, and avoided client visits at the first go, cancelled all our global events, and encouraged all our employees to operate remotely.

For large-scale, remote-working scenario, we have significantly ramped up our VPN/Internet bandwidth, VOIP phone connectivity lines, simultaneous conference lines, mobile internet connectivity and have rigorously tested our infrastructure and processes. Come what may, clients' business continuity is paramount to us. Glad to share that we have no reported delivery outage or disruption to any of our Global client programs till now.

As usual, we are continuously tracking all the global Health Authority updates on upcoming regulations and expedited pathways to ensure our clients' novel products reach out to market right on time.

As we always believe, information from accurate sources shall help us address the situation in a right way. Here are a few resources we follow and suggest you access for information on COVID-19.

https://www.cdc.gov/coronavirus/2019-nCoV/index.html
https://www.who.int/emergencies/diseases/novel-coronavirus-2019

Stay Informed.
Stay Safe.
Stay Healthy.

Freyr.

Case Study

Expedited Product Classification and NIOSH Certification for N95 Respirator

The Need

The most pressing need in the times of COVID-19 is making the Personal Protective Equipment (PPE) like N95 respirator available for healthcare workers. But, as you may know, the rapid spread of the pandemic in the U.S., and the shortage of such equipment has triggered more challenging scenarios. Addressing to the demanding times, one of our clients – manufacturer of novel technology based medical devices, set out to take their filtering face masks to the U.S. market.

Given the unprecedented times of COVID-19 and FDAs numerous guidance documents and Emergency Use Authorizations (EUAs), the manufacturer required Regulatory support to enter the U.S. market without any compliance hurdles.

Come what may, clients' business continuity is paramount to Freyr. Glad to share that with all proactive measures quickly taken in this scenario, Freyr has made the client enter the U.S. market with successful NIOSH certification.

The Approach

As the client had minimal knowledge on the U.S. Regulatory process for the product category, the first aspect Freyr took upon is to decode multiple USFDA guidance documents and pathways for EUAs.

The client's product included Novel technology which has demanded us to interact with NIOSH and USFDA to understand the classification status of the product.

With proper gap analysis, Freyr has aligned clients' existing documentation as per the FDA/NIOSH requirements.

Apart assisting client on decoding product classification and necessary requirements, Freyr has provided end-to-end support with NIOSH process that includes the receipt of manufacturer code, compilation of the NIOSH application and submission.

The Outcome

End-to-End Gap Analysis | **Health Authority Interaction** | **Timely Submission**

Product Classification | **NIOSH Certification**

Quick U.S. Market Entry of N95 Respirator

The Crux

At Freyr, we always believe enabling life sciences companies to reach out to the market right on the required time. What made us delighted in this scenario is not just clients' successful market entry or NIOSH certification, but the positive impact the N95 Respirator – our clients' product - is going to create for many lives, especially in these extraordinary times.

On an end note, we would like to appreciate and thank our client for giving us this wonderful opportunity of serving the humankind in need on a larger perspective.

FDA's EXPEDITED REGULATORY PATHWAYS FOR MEDICAL EMERGENCIES

Center of Excellence
Regulatory Affairs

While the world is tussling with COVID-19 pandemic, there's an emergency need for its treatments and vaccines. Though, currently, there is no FDA approved therapy or vaccine for COVID-19, the agency has several tools to expedite the review and approval of a COVID-19 biologic treatment or vaccine, after it emerges.

FDAs Tools

The rising concerns of COVID-19 outbreak, triggered FDA to accelerate the process for quick clinical trials based on pre-IND discussions and highly expedited initial reviews. It is encouraging the sponsors of investigational COVID-19 treatments to submit information and questions through the Pre-IND Consultation Program. Addressing the unmet medical emergencies in treating serious and life threating conditions, FDA has multiple programs to facilitate and expedite development, review and approval of therapies, including biologics.

If the therapies justify their benefits over the risks, they will be available in the market at the earliest with supportive FDA programs like,

- Fast Track Designation
- Breakthrough Therapy Designation
- Priority Review Designation
- Accelerated Approval Pathway

The animal rule and Emergency Use Authorization (EUA) are other FDA expedited approval programs.

4 FDA Programs for Expedited Approvals

Therapies treating a "serious condition" are all qualified for the four expedited review programs. They include, the diagnostic products, vaccines and products that detect, prevent and treat the effects of serious conditions. Let us understand the programs in detail.

Fast Track Designation: It expedites the review of drugs with a potential to meet the medical emergencies. Demonstrating the drug potential, the sponsors may rely on non-clinical evidences, more frequent meetings and correspondence with FDA, and rolling review of completed sections of the marketing application.

Breakthrough Therapy Designation: Potential drugs showing improvement over existing therapies are provided faster approvals through this program. As there is no existing treatment or vaccine for COVID---19 currently, this program is irrelevant at this stage.

Priority Review Designation: It accelerates FDAs projected approval time from ten months to six, provided the drug exhibits effective prominence to treat a serious condition in terms of safety and effectiveness. Though the review is based on clinical trials comparing an investigational drug to a marketed drug, other scientifically valid information can also be used, where inadequate therapy currently exists.

Accelerated Approval Pathway: Diseases with long courses, such as, cancers, demanding excessive time periods to measure ultimate clinical efficacy with adequate and well-controlled clinical trials are reviewed here.

Other Expedited FDA Approval Programs

Animal Rule: Unethical human efficacy studies or unfeasible field trials demand adequate and well-controlled animal studies for drug approvals. Though animal trials are highly probative for human efficacy, developing and validating a predictive animal model has its own unique challenges. For COVID-19 disease, where the human course is still being determined, some researchers are directly proceeding to human clinical trials of investigational vaccines and treatments.

Emergency Use Authorization (EUA): The FDA commissioner is permitted to approve the emergency use of a vaccine or treatment for a particular purpose, irrespective of not having a license. Relevantly, as COVID-19 is declared an emergency by the HHS (Health and Human Services) Secretary, the FDA commissioner may issue an EUA for a COVID-19 vaccine or treatment, after consulting with the directors of NIH (National Institutes of Health) and CDC (Centers for Diseases Control and Prevention) .

With the ongoing pandemic, there is a possibility that an EUA may be issued, if a highly promising COVID-19 vaccine or treatment is developed. Alongside, FDA is already granting EUAs for diagnostics and personal protective equipment for treating COVID-19.

Conclusion

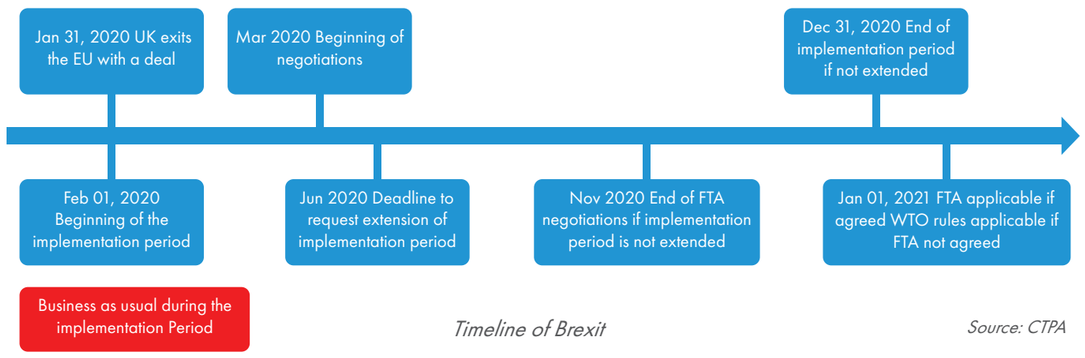
Though, all the above programs are not appropriate for expediate approval of COVID-19 treatments and vaccines, the fast track and priority review designations may be the most germane pathways. As these programs don't demand the comparison of investigational drug to available therapies, they stand promising for expedited approval of a treatment or vaccine for an emerging disease like COVID-19. Meeting the criteria, the sponsor may receive both priority review and fast track designations. The Emergency Use Authorization is a potential interim measure, though FDA reviews applications for investigational therapies and vaccines using its expedited programs.

POST-BREXIT IMPACT ON THE EU AND THE UK'S LIFE SCIENCES REGULATORY FRAMEWORK

Center of Excellence
Regulatory Affairs

It's OFFICIAL! On Jan 31, 2020, the United Kingdom (UK) left the European Union (EU) leading to the Brexit come alive. Though global life science manufacturers have already started comprehending the implications of this huge update, the present scenario seems to be uncertain for both the UK and the EU market entrants. Because, they are still negotiating the terms of agreement of Brexit. Though a short transition period set till Dec 31, 2020, market entrants must also be aware of current situation of COVID-19 pandemic for any further amendments to regulations.

At present, the timeline for life sciences manufacturers during the Brexit transition period looks like:



Timeline of Brexit

Source: CTPA

To ensure pharmaceutical/medical device/cosmetic product manufacturers are better prepared for the transition period, the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) have released certain Regulatory guidelines. These guidelines, however, are said to be considered only during the transition period. Going further, both the governments are expected to be set free to define their regulations to ensure harmony in their Regulatory framework. What are the current guidelines? Will there be any key changes industry-wise? Here we explain...

Pharmaceuticals and Clinical Trials

According to the EMA, the existing EU law for Pharmaceuticals will still be applicable in the UK throughout the transition period until Dec 31, 2020. During the transition, Marketing Authorization Holders (MAHs), applicants and Qualified Person for Pharmacovigilance (QPPVs), and quality control testing sites for the EU registered medicinal and medical products can remain in the UK. The MAHs, however, will have until the end of the transition period to make necessary changes to their authorized products in order to align with the EU standards.

To help pharmaceutical manufacturers better prepare for the transition, the UK legislation has already published the Medicines and Medical Devices Bill. With a purpose of providing base for the UK regulations, the Bill does not deviate much from the EU laws, but it is expected to evolve more in the coming future. The Bill proposes regulations for medicines and clinical trials which complement the EU regulations.

For clinical trials, the EU's current Regulatory framework will still work in the UK during the transition period, under the EU Withdrawal Act. Once the transition period ends, the EU Clinical Trial Regulations (CTR) 536/2014 will not be effective in the EU, therefore, they will not be incorporated in the UK laws.

Medical Devices

For medical devices, the MHRA has notified manufacturers about its commitment to continue to align with the EU regulations (including the upcoming EU MDR regulations that will come into effect from May 26, 2021. However, the Agency will no longer require EU-based representatives for devices placed in the UK market and will continue to perform third-party conformity assessments in the UK. The result of these assessments will still be accepted in both the UK and the EU. Additionally, any information to be reported with respect to medical devices to the MHRA will remain the same during the transition, including reporting of serious adverse events.

In case of CE Marking and other certificates, the UK will continue to recognize the validity of certificates issued by the EU notified bodies, post-Brexit. The CE Markings will also remain the same in the UK during the transition period. By the end of transition period, the UK is expected to come up with a UK Conformity Assessed (UKCA) marking of its own. Devices placed in the UK market before Dec 31, 2020, will be continued for distribution in the market with their CE marking. However, post the transition period, products that do not have markings, will be assessed again as per the UKCA marking.

Cosmetic Products

Post-Brexit, the EU Cosmetic Products Regulations will be applicable in the EU27 member states. Although, the UK based cosmetic manufacturers who wish to continue to distribute their products in the EU region will be required to comply with the EU regulations. The UK based companies will also be required to adhere to the guidelines of Responsible Person (RP) in the EU to ensure compliance. However, the UK cosmetic regulations post the transition period are not yet clear. The regulations depend heavily on the terms of the negotiations. Therefore, it is advised that the manufacturers should keep abreast of global Regulatory updates.

As mentioned earlier, the EU Withdrawal Act allows the UK to retain the EU law in the country, post-Brexit. The agreement allows the UK to transpose the EU law into their regulations while changing a few aspects. This means that post the transition period, the UK will have regulations similar to that of the EU. However, the UK is allowed to make further changes in the regulations. Given the political scenario, it is safe to assume that there will not be any mutual recognition of entities such as Responsible Person or databases like Cosmetic Product Notification Portal (CPNP). But, the outcome of Brexit terms is expected to create harmony between both the region's Regulatory frameworks.

In addition to this, the UK legislation is also likely to mandate a few Regulatory requirements such as UK responsible person, name of the UK on the packaging, a notification portal similar to CPNP, etc. to ensure smooth distribution of cosmetic products in the market. Furthermore, distributors belonging to the EU27 Member States selling their products in the UK will be considered as importers and, thus, they will have to comply with the UK import regulations.

To conclude, post the Brexit, the UK and the EU have agreed to work upon a deal for the future arrangements until the end of the transition period. While both the governments are working towards a harmonized agreement, life sciences manufacturers must gear themselves up to adhere to the upcoming Regulatory changes.

For medical device manufacturers who are eying an EU market entry, the immediate action point would be to comply with the EU MDR which is, as expected, postponed by one year, i.e. May 26, 2021. It is all due to the industry halt created by COVID-19 pandemic. Let's discuss about EU MDR in detail in the very next thought leadership.

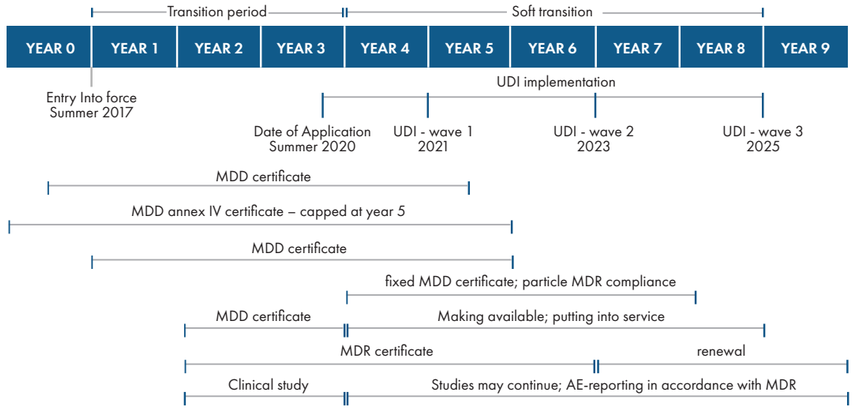
EU MDR - THE NEW EUROPEAN REGULATORY GATEWAY FOR DEVICES

Center of Excellence
Global Medical Device Regulatory Services

In Europe, there have been most significant compliance reforms, which replaced the decades' old legislations of the medical device industry. The Medical Device Directive (MDD) and the In-vitro Diagnostics Directive (IVDD) are set to replace with Medical Devices Regulation (MDR) and In-vitro Diagnostics Regulation (IVDR) respectively.

As mentioned in the previous write up, due to COVID-19 international health crisis, the EU MDR is postponed by one year. The new deadline is May 26, 2021.

The MDR and IVDR were introduced in Apr 2017, to strengthen the Regulatory platform in terms of development and surveillance processes, to adapt to the technological advancements, and to achieve harmonization across the European Union (EU). Being in force since May 2017, the regulations lay down rules for medical devices ('placing in the market', 'making available in the market' or 'putting into service' as mentioned in the Regulation (EU) 2017/745) for human use in the EU. With the new deadline for EU MDR, i.e. May 26, 2021, organizations are expected to understand EU MDR comprehensively and be compliant throughout the transition period.



In comparison with the MDD, the MDR is more comprehensive and detailed. The latter is intended for a comprehensive scrutinization of the entire product lifecycle with special emphasis on clinical evaluations and clinical data. The new regulation contains a series of critical and important developments to modernize the current system.

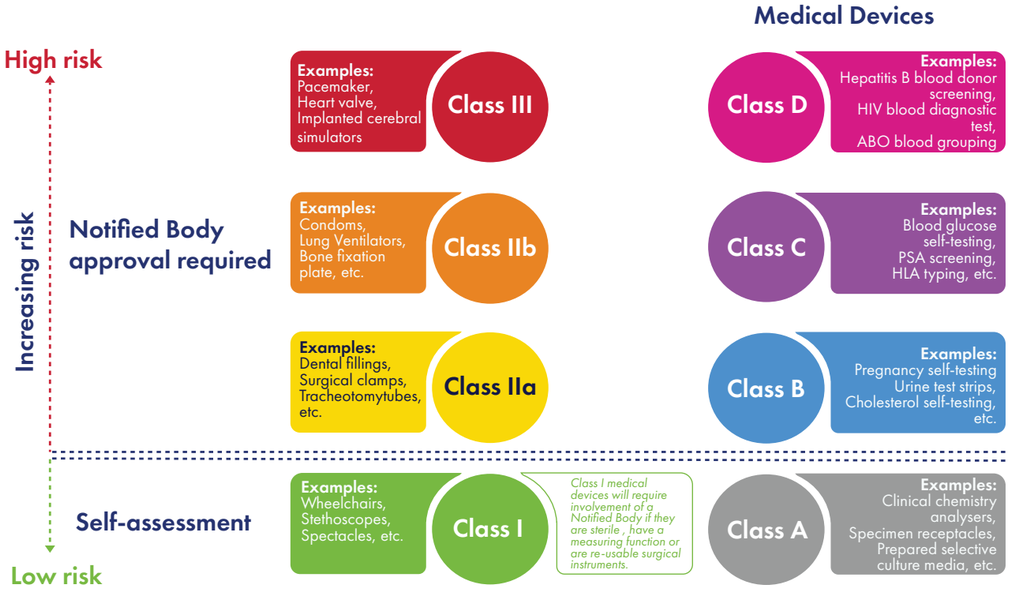
The following are the notable changes from the MDD to the MDR:

- The definition of medical devices and active implantable medical devices have been changed, i.e. significantly expanded and devices that do not have medical intended purpose were also included
- With MDR rolled out, manufacturers would need to review the classification rules and update their technical documentation by considering the Regulatory scrutiny process
- In case manufacturers do not have sufficient clinical data to support the claims of safety and performance of the device, they need to conduct clinical investigations to provide rigorous clinical evidence
- Stringent Regulatory documentation
- Identification of person responsible for Regulatory compliance
- Implementation of Unique Device Identification (UDI) for better traceability
- More surveillance from Notified Bodies to reduce safety risks from unsafe devices
- No 'grandfathering' provisions - all currently certified medical devices must be recertified in accordance with the MDR

Classification of Devices under the MDR: Conformity Assessment and the Role of Notified Bodies

Under the MDR, all medical devices, in vitro diagnostic medical devices, and their accessories are reclassified. With reclassification, certain combination products will also be covered as medical devices. The medical devices and in vitro diagnostic medical devices are divided into four risk classes.

Depending on the risk class of the device, a different conformity assessment procedure is implemented before the device is placed in the EU market. In case of medium or high-risk class devices, Notified Bodies might be involved in the assessment process.



Conformity Assessment:

The conformity assessment in the MDR is unchanged from the MDD. It includes 'Product Quality Assurance' and 'Product Verification', which are majorly adopted from the MDD. Though the procedure remains the same, it does not make the transition easy, as the MDR added additional requirements about the Notified Bodies.

The objective of conformity assessment is to ensure devices meet the provisions of the MDR. Other than custom-made or investigational devices, the remaining devices, which are

considered to conform with the MDR, shall bear the "Conformité Européene" [literally, "European Conformity"] (CE) marking.

Role of Notified Bodies:
In the MDD, medical devices were not subject to pre-market authorization by a Regulatory authority. Medium and high-risk medical devices required conformity assessment, involving an independent third party known as a 'Notified Body', which are designated and monitored by the Member States. Hence, under the MDR, before the final decision on the certification of certain high-risk products, independent experts are required to provide an opinion to the Notified Body. This helps the Notified Bodies to make more-informed decisions thereby preserving the safety and performance of the devices.

Impact of The MDR on Medical Device Manufacturers:

The MDR will impact the medical device manufacturers in multiple ways. The transformative changes brought by the MDR will affect processes concerning product development, manufacturing, and post-approval product monitoring impacting the economic operators such as distributors, suppliers, and Notified Bodies. As MDR has broadened the

Main implications of MDR and IVDR for manufacturers and Notified Bodies

definitions of medical devices including devices that were not previously classified, manufacturers have to reclassify their products accordingly.

The Notified Bodies and Competent authorities will implement rigorous control to enforce Regulatory compliance. Hence, more inspections, sample checks, and audits encompassing the entire device lifecycle can be expected. On the other side, manufacturers of currently certified devices are advised to consult their respective Notified Body to evaluate compliance requirements and accordingly devise a plan to address them.

Impact of Brexit:
Device manufacturers must also take the recent overhaul of Brexit into consideration. Existing derogations in the MDD and IVD, allowed the Member States to authorize the UK certificate holders to continue placing their products on the market of the Member State for a limited period, but only in duly justified cases. Post the Brexit, manufacturers must evaluate their stance on compliance with the EU legislation. They should plan for their replacement by those located in the remaining 27 Member States of the EU.

The Product Lifecycle:
The MDR is expected to amplify nearly every aspect of the medical device production lifecycle in the EU. It imposed greater clinical evaluation before approval, tracking through UDIs, and post-market surveillance, and product performance reporting for recertification as depicted below.

As there is no more 'grandfathering' under the MDR, all the devices already in the market have to be reassessed and recertified.

Clinical Evaluation and Data:
MDR requires that the devices submitted for certification or recertification demonstrate the 'conformity with the relevant general safety and performance requirements', which includes clinical evaluation. In addition, data reporting requirements extend beyond the development phase to include post-market follow up and surveillance. As comprehensive clinical data is shared among the Notified Bodies and manufacturers, there is scope for increased device visibility.

Under the MDD, referring to an equivalent medical device and its scientific data for clinical effectiveness documentation was a common practice. However, with the MDR, manufacturers have to document each individual devices' effectiveness, safety, and usability irrespective of the availability of equivalent medical device. Hence, manufacturers have to put more time into planning their clinical investigations and post-market activities to be in line with the product lifecycle.

Manufacturers need to register their devices, upload relevant documentation, apply for clinical investigations and performance studies and upload post-market surveillance documentation through the European Union's Database for ▶

Medical Devices (EUDAMED) to make them publicly available.

EUDAMED, which earlier stored all medical devices and Notified Bodies related Regulatory information, will now store information regarding post-market surveillance activities, safety and clinical performance studies, periodic safety update reports, and is set to provide more detailed information on clinical investigation data, manufacturers and device registrations.

Vigilance and Post-market Surveillance:
Under the MDR, manufacturers need to amend their post-market surveillance and vigilance procedures. When manufacturers are aware of a potentially reportable incident, they must submit a report within the specific timeframe to the EU.

UDI/Traceability:
Under the MDR, the Unique Device Identification (UDI) system for all devices placed in the EU market has gained significance. The UDI enhances the identification and traceability of devices and the effectiveness of the post-market safety-related activities, giving labeling a prominent position. Under the MDR, medical device labels are required to have additional information on potential risks or concerns along with the UDI numbers and website location for more information about the device.

Medical devices in the EU can be tracked online with a Unique Device Identification (UDI) number, making it easier to extract information on individual products. The UDI numbers will be available in the EUDAMED.

Challenges in Transitioning to the EU MDR:

- Reclassifications and recertification of devices are certain
- Manufacturers must focus on greater clinical evaluation before getting approvals
- As the Notified Bodies are significant in the new regulation, a decrease in the availability of Notified Bodies leads to delay in the product approvals and device's market entry
- Increased emphasis on post-market surveillance makes it necessary for manufacturers to monitor device performance for recertification, safety updates, and reporting of safety incidents, which requires additional resources
- The new regulation requires a reassessment of clinical data for devices which are already on the market. If the data does not meet the new requirements, devices will be required to undergo additional testing for recertification, increasing the expense of maintaining legacy devices

If manufacturers can overcome the above-mentioned challenges and come up with a consolidated action plan, transitioning to MDR presents many opportunities for manufacturers in terms of gaining a competitive edge in the market.

EU MDR and Compliance Roadmap:
Given the complete scope of changes required, it is likely that manufacturers would require a considerable time and cost to align with the EU MDR. To do so, they need to adopt a comprehensive step-by-step plan that will help them overcome the challenges in transition and lead them to compliance by May 26, 2021. For this, manufacturers will have to:

1. Conduct a product portfolio assessment
2. Review existing products and go for recertification as there is no grandfathering of devices allowed
3. Improve the quality, safety, and reliability of medical devices
4. Strengthen transparency of information for consumers
5. Enhance the vigilance and post-market surveillance

Apart from the above-mentioned, manufacturers have to appoint a Qualified Person (QP), who is responsible for Regulatory compliance, and an Authorized Representative, who acts on behalf of the manufacturers, based outside the Europe.

Role of a Qualified Person:
Under the MDR, an agreement must be in place between the manufacturers and the Qualified Person (QP) quoting that the QP is the critical supplier of the manufacturer's quality system. The QP have to ensure:

- The device conforms to the manufacturer's quality system before it is released
- Accurate maintenance of technical documentation and the EU declaration of conformity
- Compliance with the post-market surveillance obligations
- Fulfillment of obligations in reporting the serious incidents and field safety corrective actions

Role of an Authorized Representative:
Under the MDR, the Authorized Representative is legally liable for defective devices, in case if a manufacturer established outside the EU has not complied with the MDR obligations. The Authorized representative will have to:

- Verify the declaration of conformity, conformity assessment, technical documentation, and registration requirements
- Keep a copy of the declaration of conformity, technical documentation, and certificates
- Establish systems for the provision of information to Competent Authorities and manufacturers, Corrective and Prevention Action (CAPA) plans, registration, ▶

complaint handling, establishment, maintenance, termination of the mandate, person responsible for Regulatory compliance

With limited time to comply with the new legislation, manufacturers have a significant number of requirements to meet before May 26, 2021. The only way out for manufacturers is to take a structured and well-managed approach depending on their product portfolio.

In this scenario, all it takes for manufacturers for compliance is to deploy expert Regulatory resources with a clear-cut and focused operational structure to navigate the new regulations within considerable time and with low cost of implementation.

Get ready for the EU MDR compliance.

Reference Links:

- https://www.thefdagroup.com/blog/the-first-step-in-transitioning-to-eu-mdr-compliance
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/640404/MDR_IVDR_guidance_Print_13.pdf
- https://www2.deloitte.com/content/dam/Deloitte/ie/Documents/LifeSciences_Healthcare/New-EU-Medical-Device-Legisalation.pdf

FREYR CONNECT

UNDERSTANDING THE NEED FOR LABEL TRACKING

Center of Excellence
Regulatory Labeling

Tracking and implementing label changes are crucial to the lifecycle of a marketed drug product.

Safety and efficacy data of a drug hold a key position in the entire drug lifecycle. Handling labels for vast product portfolios, regularly tracking label data and changes, and meticulously implementing changes at both artwork and supply-chain levels can be challenging. But, despite the risks involved, many companies are tracking their label data through local trackers and legacy tools rather than using modern technology. This article discusses some of the problems that can occur and some best practices for labeling workflows.

For a marketed product, the change triggers received from disparate sources tend to increase over time owing to the product's momentum in the specific market. These triggers, despite their source, are crucial because their impact could extend to local labels and corresponding artwork. It is important for Marketing Authorization Holders (MAHs) to track all of these triggers, regardless of their execution/implementation. Going further, the significant task for MAHs can be:

- Scrutinizing and categorizing the triggers as per the safety and non-safety related parameters
- Assessing the safety and non-safety related changes
- Identifying the potential labeling processes that could be impacted, and
- Implementing the changes within the timelines

Change assessment

A critical safety-related change could potentially impact all the downstream labeling processes (i.e., core, local product documents [LPD], and artwork). Hence, it's important to track these triggers and to assess how critically they may impact the other areas of labeling. Inefficiency in doing so can lead to compliance issues as submission timelines may exceed, leading to further repercussions. In the current industry practices, companies track their data manually in local trackers, which could be helpful to an extent. However, this practice is risky if the frequency of triggers is high and if the product portfolio is large. In such a scenario, it's advisable for companies to use a centralized system to track all the variations/triggers, assess their criticality in real-time, and identify the processes they may impact, if implemented.

It is also important to assess the documents that could be impacted at each functional level (i.e., core and local/regional labels). At the core label level, changes can be applied to company core data sheet (CCDS), and company core safety information (CCSI) documents, and at the local/regional label level, changes can be applied to product information, promotional material, the inserts, and so on. Some changes may also be extended to the artwork.

Functional-level linking

At each functional level, a link must be established between the trigger and safety- or non-safety related change and the impacted areas of the label. If the change extends to all the ▶

downstream processes, then there must be a consistent link between the core labels, local labels, artwork components, printing, and the non-printing components (i.e., supply-chain items). Depending on the linkage and its robust incorporation, there is a possibility of tracking the supply-chain items even after they've been dispatched from the warehouse. This process might, in fact, enable the possibility of reverse tracking of finer items back to the upstream processes. Figure 1 shows an ideal workflow for labeling processes, to ensure end-to-end tracking at all levels.

Notifications

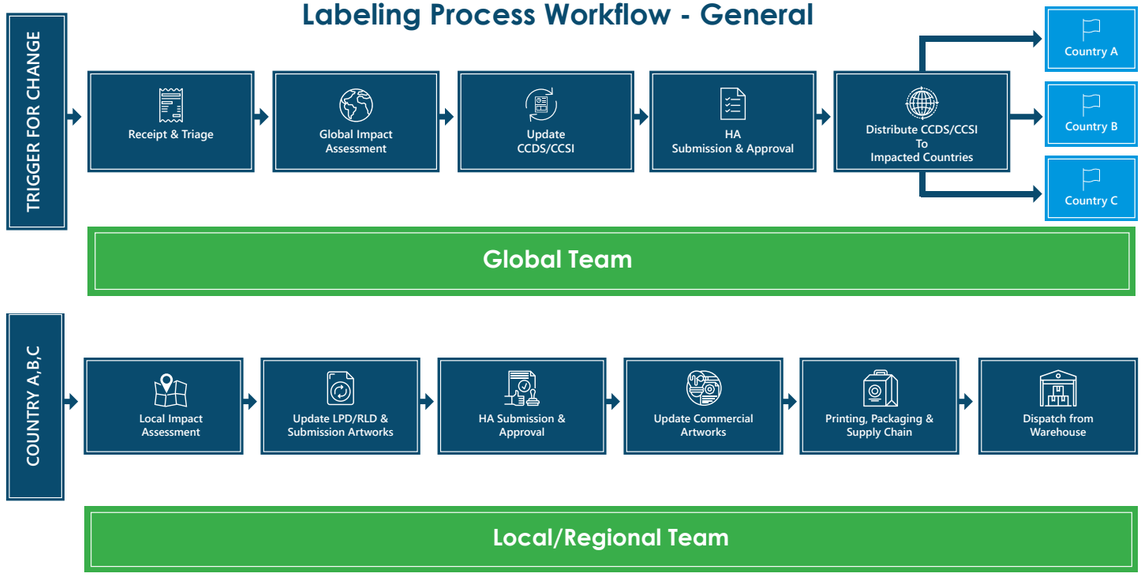
Current industry practices, however, are too conventional to achieve this level of granularity in tracking for several reasons. One reason is outsourcing of downstream activities (e.g., artwork and supply chain). In such cases, even if the inflow of data is managed efficiently, there is a possibility that the link between the changes and their subsequent processes could be lost. Moreover, if the notifications sent out to the stakeholders are manual, there could be a delay in aligning with timelines, leading to compliance issues. Right from the time a trigger is received to the time it is implemented in the core documents and distributed, all the stakeholders (global, local, artwork, and supply-chain teams) must always be notified on the procedural progress. Without a robust system in place, notifying all the stakeholders in real-time could be hard to achieve.

Deviations

Another dimension to efficient tracking is to be able to manage deviations. Both content deviations and timeline deviations have their own significance and must be tracked, regardless of their approval/disapproval status. It is important to maintain a record of health authority correspondence linked to these deviations. This aspect is critical for tracking and it has timeframes fixed to it for on-time submission of local documents to the health authorities.

Solution

Companies should integrate sophisticated technology solutions in their labeling operations, using a system that can accommodate and track the data from the time a variation is received to the time it is incorporated into the labels and onto the artwork. This level of tracking can be achieved if the product registrations are linked to pack sets and pack sets to printable/non-printable components, which in turn are linked to the finished products. This linking would ensure comprehensive label traceability.



Ideal workflow. Images courtesy of the author.

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BIOSIMILARS AND GENERICS
MARKET TRENDS, ROUTE, AND THE REGULATORY OVERVIEW

Center of Excellence
Global Biologics Regulatory Services

Necessity is the mother of invention! On that note, pharmaceuticals and biologics revolutionized the treatment of many diseases and rare disorders. Interestingly and perhaps not surprisingly, a great number of factors like, the increased geriatric population, rocketing prevalence of chronic diseases, costly branded pharma and biologic products, rigorous R&D procedures, stringent Regulatory laws, looming patent expiries, and limited accessibility triggered the invention of biosimilars and generics, globally. Feeding all the necessities, biosimilars and generics emerged as promising alternative treatment options to original pharmaceutical and biologic products at lower costs and for easy access. With thin differentiating line, biosimilars are highly similar to already approved biologics known as the 'reference or innovator product', having no clinical differences in terms of quality, safety and efficacy; and generics are exact identical copies of a reference drug product with structural and therapeutic equivalence.

The Route of Generics and Biosimilars

On its voyage to global acceptance, the biologics rose, and witnessed several challenges and opportunities. The biologics are challengingly exorbitant, with limited accessibility and patent expiries, they spell inventing opportunities for "Biosimilars". Stated by the US FDA, biosimilars have no clinically meaningful differences and are highly similar to their licensed originator biologics in terms of biochemical, immunological, safety, and biological properties. With rigorous analytical, non-clinical, immunogenicity, and clinical comparative evaluations, biosimilars are manufactured through defined and stringent Regulatory processes. As the natural variability and more complex manufacturing of biological medicines don't allow the exact replication of the molecular microheterogeneity, a biosimilar is not regarded as a generic of a biological medicine. To ensure minor differences don't affect the safety or efficacy, more studies are needed for the Regulatory approvals of biosimilars than for generics.

Biased, generics are chemically synthesized medicines/drugs containing the same active ingredients, dosage, intended use, risks, side effects, and route of administration in accordance to the branded equivalents. The approved generic products should meet the stringent US FDA standards with respect to safety profile, quality criteria, strength, purity and potency as the original drugs. Some of the generic drugs tend to vary from the original medications, in aspects of color, flavor, appearance or in combination of inactive ingredients. This is because, the USA trademark laws doesn't allow the exact ▶

resemblance of brand name, expect for the active ingredients and medicinal efficacy being same in both the preparations. Comparatively, generics' manufacturing and development process is cheaper and cost-effective, offering patients the same high-quality medicine as the brand-name drug, at an average price that is 39% lower, as stated by the US FDA. Patient benefits and availability of these drugs in the market triggers further retrenchments.

Significance and Market Growth

Biosimilars:

Market: The global statistics for the biosimilars market is expected to expand substantially in the coming years. Recently, the Global Market Insights, Inc., estimated a revenue graph for the global biosimilars industry, which is poised to exceed a valuation of $69 billion by 2025. The biosimilars market is expected to reach US$ 20.2 billion by 2024, growing at a CAGR (Compound Annual Growth Rate) of nearly 33% during the next five years according to the IMARC Group.

Significant Market Drivers

- Rising prevalence of chronic diseases
- Lower prices
- Cost-saving initiatives from government bodies and third-party payers
- Increasing demand
- Patent expiries of blockbuster biological drugs
- The ability and affordability to perform same as the reference product

Significantly, biosimilars are 10% to 30% lesser in cost when compared to the original parent product, which is one of the primary factors fueling the market growth. For example, the first biosimilar product received marketing authorization in the European market at a cost of 20%-25% less than the original growth hormone drug, which is used to treat growth disorders.

Significant Market Constraints

- Need for complex infrastructure for the production
- Patent extensions
- Lack of consumer's brand preferences and Regulatory guidelines
- Reluctance of physicians to prescribe biosimilars
- Lengthy clinical trial procedures for Regulatory approvals

Generics:

Market: With forecasts, the global generics market is estimated to read a value of US$ 475 billion by 2024, growing at a CAGR of 5.3% during 2019-2024. The generics industry draws more significance from patent expiries - companies developing the innovator drugs are given patents and an exclusive right to sell the drug till the patent expires. Upon a patent expiry, drug manufacturers take the FDA permission to sell the generic version of the drug without startup costs of the clinical studies and R&D activities. Thereby, the companies can market the generics reasonably with ease and approachability, and lower costs.

Significant Market Drivers

- Increasing prevalence of chronic and lifestyle diseases
- Patent expiration of the key blockbuster drugs
- Cost-effectiveness and easy availability

Significant Market Constraints

- Stringent government regulations
- Adverse effects of the drugs
- Shortage of generics in some parts of the globe

Regulatory Pathways in the EU and the USA

Biosimilars EU Regulations & Approvals: Acknowledged as the most highly regarded Regulatory system, the EU constitutes, the European Parliament, Council of Ministers and the European Commission. The EMA (European Medicines Agency) is a decentralized agency of the European Union (EU) responsible for the scientific evaluation of biosimilars developed in the region. The EU has established a solid framework for the biosimilars development and for their approvals, and the region has the highest number of approved biosimilars. Almost all the approved biosimilars in the EU have been approved centrally, as they use biotechnology for their production; except for some low-molecular weight biosimilars like heparins may be approved at a national level.

The biosimilars approval criteria are aligned with all the standards of pharmaceutical quality, safety and efficacy of the biological medicines approved by the EU. Biosimilar developers should demonstrate comprehensive comparability studies with the reference biological product in terms of similarity, notwithstanding the natural variability inherent to all biological medicines along with no clinically meaningful differences between the biosimilar and the reference medicine in terms of safety, quality and efficacy. Every application should be inclusive of:

- Comparative quality studies with the reference biological product
- Comparative non-clinical studies with the reference biological product
- Comparative clinical studies (safety and efficacy, PK/PD, immunogenicity)
- Risk management plan

Biosimilars USA Regulations & Approvals: As described in one of the US FDA's Regulatory guidance documents for biosimilars development and approval, the Biological Product/Reference Product is mentioned as the single biological product, licensed under section 351(a) of the PHS Act, against which a biological product is evaluated in an application submitted under section 351(k) of the PHS Act. The biological product in a 351(k) application should not be evaluated against more than one reference product and should be similar to the reference product in terms of: utilizing the same mechanism(s) of action, conditions of use, same route of administration, dosage form, strength, and also the manufacturing and packaging processes must adhere to standards of safety, purity and potency.

Alongside, the biosimilar application for approval should hold in the analytical, clinical, and animal (toxicity) studies. Manufacturers showcasing the proposed biosimilar product to be highly similar with no clinically meaningful differences from the FDA-approved reference product may rely on the FDA's previous determination of safety and effectiveness for the reference product for approval. This enables the manufacturers to skip lengthy clinical trials, leading to faster access of these products in the market with additional therapeutic options and cost reduction for patients. The applications should enclose:

- Scientific considerations in demonstrating bio-similarity to a reference product
- Quality considerations in demonstrating bio-similarity to a reference protein product
- Clinical pharmacology data to support a demonstration of bio-similarity to a reference product
- Biosimilars questions and answers, formal meetings between FDA and biosimilar sponsors
- Labeling for biosimilar products, rules etc.

Generics EU Regulations: The EMA is responsible for the scientific evaluation of generic medicines developed by the pharmaceutical companies for their usage in the EU. Regarding a generic drug submission, the decentralized procedure is followed which involves the submission of application to all the member states, where the drug is intended to be marketed, and choose one of them as the Reference Member State (RMS). An assessment report is prepared by the RMS and other concerned member states and based on both their comments the Marketing Authorization (MA) is granted.

Generics EU Validation and Approvals: After the MA is granted, EMA will evaluate and validate the application relating to GMP inspections, GCP inspections, and data completeness. If validated positively, the EMA gives a written consent of successful validation, and if there is lack of information, failure to adhere to the EU format, the validation will be negative. Supposedly, the applicant will receive a written consent to either collect the application or have it destroyed by the Regulatory authority. The healthcare professionals and consumers can report any side effects of the product into the EudraVigilance, the EU web-based information system operated by the EMA, which collects, manages and analyzes reports of suspected side effects of medicines. The data is continuously monitored by the EMA and the Member States.

Generics EU Guidelines: The EMA provides guidance on the latest developments and product-specific scientific advices to companies for the compliant development of Generic medicines.

- A generic drug manufacturer should ensure their drug meets all the necessary criteria (efficacy, safety, quality and performance characteristics) to be therapeutically equivalent to the innovator drug product
- The manufacturers, distributors, and importers of generic medicines must be licensed before selling their drug in the market. And, each member state is responsible for granting the license
- Before any medication is released into the EU market, it must be certified as being manufactured and tested in accordance with the GMP standards and in conformance with the marketing authorization
- In cases where the product is manufactured outside and is imported to the EU, there is a need to undergo the analytical testing in the EU, unless a Mutual Recognition Agreement (MRA) is in place between the EU and the exporting country

Generics USA Regulations & Approvals: The drug registrations in the USA is majorly segregated by two type of applications, namely: New Drug Application (NDA) and Abbreviated New Drug Application (ANDA). The ANDA is filed for generic drug products which are a close or exact copy of already approved drugs. FDA's review process ensures that the generic medications perform the same way in the human body as the branded medications and assure the healthcare consumers that they meet the highest standards as similar as the innovator drugs on the aspects of quality, strength, purity, and stability.

Generics USA - The Review, Receipt & RTR: For a generic drug application to be approved, it typically takes multiple review cycles, with each cycle lasting several months to almost a year. The Office of Generic Drugs works closely with the Center for Drug Evaluation and Research's Office of Pharmaceutical Quality, and ensures that the generics are reviewed, inspected and researched. Post the review, depending upon the deficiencies, the applicant will receive an acknowledged approval receipt for a complete application and a Refuse to Receive (RTR) for the incomplete one from the US FDA. After approvals and market-entry, generic drugs

undergo post-marketing surveillance to monitor and detect any quality and therapeutic inequivalence issues. The FDA also encourages the healthcare professionals and consumers to report any adverse drug effects through the FDA's MedWatch program.

Generic USA Guidelines: As guided by the US FDA, the generic applicants should ensure the documents are inclusive of the following data for seamless review and approval.

Pharmaceutical and Bioequivalence - The pharmaceutical equivalence of a generic drug should be in line with the innovator drug in terms of active ingredient, strength, dosage, route of administration and conditions of use. For bioequivalence, the generic product should not have any significant difference between the rate and extent of absorption, when compared to the branded counterpart.

Chemistry - It considers the CMC (Chemistry, Manufacturing and Controls) section of ANDAs, Drug Master Files (DMF), Supplemental ANDAs, Annual Reports and Controlled Correspondence and assures that all manufacturing processes comply with the Good Manufacturing Practices (GMP).

Labeling - FDA guides generic manufacturers to maintain their drug's labeling as same as the branded (pioneer) drug labeling.

Overall, giving a second life to innovator drugs and biological molecules that reach the end period of intellectual property protection, the global biopharmaceutical industry welcomes a future of biosimilars and generics. Besides, the global Regulatory framework are surfacing new developments and challenges and encouraging the generic and biosimilar manufacturers to concisely tailor the information in accordance to the Regulatory guidelines and robust manufacturing and quality control procedures. With stringent Health Authority (HA) protocols, aiming for successful Regulatory approvals is no cakewalk. To avoid pitfalls in the nick of the time, a clear-cut and region focused approach will cater suitable solutions for a streamlined and compliant Regulatory submission to expedite review processes and approvals. How compliant is your generic and biosimilar market-entry approach? Plan for end-to-end Regulatory evaluation.

USFDA FINALIZES eSUBMISSIONS RULE FOR MEDICAL DEVICES

Center of Excellence
Global Medical Device
Regulatory Services

The United States Food and Drug Administration (USFDA), to enhance the submission process for medical devices, has introduced a final rule to replace the paper submissions with electronic submissions. The rule which was proposed in Sep 2018 is expected to come into effect in 2020. The final rule is aimed at improving the device's premarket submission program and targeted towards making the medical device submission process more efficient.

Submissions Required in Electronic Format

The criteria for electronic format extend to all forms of device submissions falling within the requirements of section 745A(b)(3) of the FD&C Act. Some of them include:

- 510(k) submissions – Premarket notification submission
- Evaluation of De Novo under 513(f)(2) for automatic class III designation request
- Premarket approval applications (PMAs) including transitional PMAs as per 515(c) and 515(d)
- Modular PMAs as per 515(d)(4)
- Product development protocols (PDPs) under section 515(f)
- Investigational device exemption (IDE) including the original IDEs, IDE Reports, IDE Supplements and Amendments
- Humanitarian device exemption (HDE) as per section 520(m)
- Emergency Use Authorizations (EUAs)

FDA may also identify and recommend electronic submission formats for the following:

- Master Access Files (MAFs)
- 513(g) Requests for Information (513(g)s)
- Clinical Laboratory Improvement Amendments of 1988

Submissions Exempted from the Electronic Format

FDA has also established certain criteria for exceptions from the electronic format submission. The following forms of IDE submissions will be exempted from section 745A(b)(3) requirements:

- Adverse event reports
- Compassionate use requests

The final rule of electronic submissions for devices intend to increase cost savings without putting new Regulatory burdens on submissions along with reducing timelines for submission evaluation and review for the authorities.

To conclude, the FDA intends to finalize single electronic submission for medical devices only to overcome the multiple submissions and paper copies. The rule is expected to come into force from Jan 15, 2020. Thus, device manufacturers entering the U.S. market are required to comply with the new rules and binding and non-binding provisions. Stay updated. Stay compliant.

TGA ASSESSED CLAIM ON MEDICINE LABELS - WHAT YOU NEED TO KNOW?

FREYR REGULATORY ARTWORK SERVICES

DYK? Australian Regulatory framework for therapeutic goods has been evolving with regards to labeling requirements. It is clearly evident with the Therapeutic Good Administration's (TGA's) recent announcements and proposed labeling requirements. Recently, it has announced certain guidelines for using the 'TGA assessed claim' on medicine labels. Aimed at the sponsors, these guidelines are targeted towards both assessed listed and registered complementary medicines. These guidelines clearly detail the usage of the TGA symbol and the TGA-compliant statement on a medicinal label. What exactly these guidelines mean to the sponsors? Let us deep dive.

What Does the "TGA Assessed Claim" Mean?

The TGA assessed claim is a symbol and/or statement, which describes that medicine has efficacy for the indications claimed and is assessed by the TGA. The TGA assessed claim must be displayed as the TGA assessed statement with or without the 'TGA assessed' symbol. But, if the symbol is used, it should be displayed with the statement. The wordings in which the statement is presented is also important for compliance. The TGA requires these to appear in the below-mentioned way.

The TGA Assessed Symbol	
TGA assessed	

The TGA Assessed Statement	
The TGA Assessed Statement	**Example label with statement**
Evidence for the approved indications has been assessed by the TGA	

Compliant and Non-compliant Wording of the Statement

Compliant and Non-compliant Wordings of the Statement
Compliant: Evidence for the approved indications has been assessed by the TGA. **Non-compliant:** The TGA has assessed our evidence and has approved all of our indications.

As these assessed claims are required to be presented on 'listed assessed medicines and registered complementary medicines,' the Sponsors should clearly evaluate what do they require prior to using their symbol and statements. The Sponsors must apply for using the TGA Assessed Claim for their medicines.

If in the claim, the presentation of the medicine is not acceptable as per legislative requirements, the authorization won't be provided. At times, to understand the complete perspective of the TGA assessed claims, consulting a regional Regulatory expert is all that is required. Stay informed. Stay compliant.

4 KEY FACTORS TO SELECT A SUBMISSION SOFTWARE

Center of Excellence
Technology
Regulatory Services

Drug development is an extensive and multifaceted process. In each phase of the development, manufacturers are obliged to demonstrate the safety and efficacy of their drugs in the form of Regulatory submissions. These submissions are intended to report how drug companies manufacture their drugs, design clinical trials, report safety findings, and create promotional material. The entire process involves near-constant correspondence between Regulatory affairs departments and the global Health Authorities (HAs).

Given the increasing demand for globally acceptable products, life sciences companies are continuously trying to expand their footprint to the global markets. But with myriad and diverse regulations and submission formats to be followed, and numerous data points to keep track of, the submission process for global market entry and product registration may become complex for manufacturers. Thus, even health authorities are working towards harmonizing the global Regulatory requirements to ensure streamlined and easy-to-review submissions. Keeping that aside, it is a priority for manufacturers to choose a reliable solution that suits their global submission requirements. In such cases, what exactly a manufacturer must consider while choosing an appropriate solution? What kind of factors they should ponder upon? Let's take a look.

1. **Flexibility:** Companies must understand and see how flexible a solution is, not only in terms of easy and smooth submission process but in terms of the deployment methods. Given the utmost data security requirements in the conservative field of life sciences, they must think twice in choosing an external software. They should clearly validate the flexible deployment methods like cloud-based and on-premise models that suit their eCTD publishing and submission requirements.

2. **In-depth knowledge and expertise**: Sometimes, software alone won't fit the submission requirement, the personnel that assist the software integration is also important. If the company is opting for external software, they must also validate the vendor's expertise and knowledge on the required submission process. Because that knowledge might have actually been put to use while designing the base platform of software. It is the software vendor's in-depth knowledge and expertise that drives the submission process successfully even in the times of complexities. In addition, it is wise to validate the software in terms of its cutting-edge technology like machine learning, which makes for compliant eCTD publishing and submissions.

3. **Global reach:** As with evolving regulations, each region has its defined set of submission processes and requirements – most of them are already accepting the electronic Common Technical Document (eCTD) format. In such cases, the software that companies are adopting must be equipped to be suitable for all regional formats, which can enable a hassle-free transition while aiming for time-bound global reach. The software should be compliant supporting 21 CFR Part 11 standards for various health authorities. In addition, it should be equipped with features like cloning, cross-reference, and the capability to integrate with the leading rDMS and PDF manager.

4. **Interoperability:** The submission tool or software must easily be integrated with other tools such as content management solutions and other authoring tools that help in smooth submissions. It should facilitate seamless integration with leading Regulatory Document Management Systems (rDMS), the client is already using, in a secured manner. So that the applicants can assuredly call their confidential data into the new platform without any need to create any extra folders.

To conclude, as several HAs making eCTD submissions mandatory, there persist global differences in Regulatory submission requirements. We do agree that there is a dire need that health authorities should quickly harmonize the global Regulatory requirements to ensure the streamlined and easy-to-review submissions. Meanwhile, companies must have explicit knowledge about the software they are about to integrate and its intended impact on their submission processes. Companies must act wise and deploy all the possible ways to validate a software solution. Evaluate Freyr SUBMIT PRO with that of your submission requirements. Request a demo.

ROLES AND RESPONSIBILITIES OF AN EU QUALIFIED PERSON

Center of Excellence
Regulatory Affairs

Thanks to the evolving global Regulatory landscape! Each country now has its own, defined regulations and requirements in governing the quality, safety, and efficacy of the medicinal products entering or being manufactured in their market. In this scenario, it is necessary for organizations to know about specific Regulatory requirements of their targeted markets. If their targeted market is the EU, the first thing they should know about is the requirement and importance of a certified Qualified Person (QP).

As defined in the European Union's (EU) legislation, Directive 2001/83/EC, Article 51 for Medicinal Products and Article 13 of Directive 2001/20/EC for Investigational Medicinal Products (IMPs), a QP is any licensed pharmacist, biologist, or chemist who has several years of experience working in pharmaceutical manufacturing operations and is based within the EU. Every sponsor company wishing to undertake trials in the EU or market a product in the EU must undergo the process of certification from the QP. Without the certification, no single batch of a finished pharmaceutical product or an IMP can be released for both sale and supply in the EU.

The QP will not only fulfill basic principles of certification but will also ensure that an appropriate Quality System is in place for the market-entry process. To operate as a QP in the EU, there are certain prerequisites that needs to be considered:

- QP has to be named by the Marketing Authorization Holder in the EU and must be registered/accepted by the EU member state where the company resides
- QP has to be linked to an existing European Manufacturing Authorization and license [EU/European Consumer Centre (ECC)]
- QP must be registered by the authority of the respective the EU member state (the requirements might differ from member state to member state)

As a key person in the quality system of the EU, key responsibilities of a QP include to check:

- Compliance of batch manufacturing as per market authorization requirements
- Product has been manufactured according to the GMP standards
- The principal manufacturing and testing processes of the products have been validated
- Account has been taken about the actual production conditions and manufacturing records
- Any deviations or planned changes in the production and quality control of the products have been authorized by the persons responsible as per the defined system
- Any changes requiring variation to the marketing or manufacturing authorization have been notified and authorized by the relevant authority
- All the necessary tests have been performed on the products, including additional sampling, and inspection initiated because of deviations or planned changes
- All necessary production and quality control documentation has been completed and endorsed by the authorized staff
- All audits are carried out as required by the quality assurance system

In addition to the above-mentioned key responsibilities, for medicinal products manufactured outside the EU, the QP ensures:

- Each imported batch has undergone a full qualitative analysis and a quantitative analysis of at least all the active substances
- All the other tests necessary in ensuring the quality of medicinal products as per the requirements of the Marketing Authorization (MA)

Though the role of QP changes with each EU member state, product quality remains to be common across the EU. In such cases, thorough understanding of the roles and responsibilities of the QP can de-risk the Regulatory hurdles and expedite the product's time to market for organizations willing to enter the EU. Stay informed. Stay compliant.

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WHAT IS AN SmPC?

Center of Excellence
Regulatory Intelligence

SmPC or Summary of Product Characteristics is a legal document which is a part of the marketing authorization of every medicine. The document acts as a basis of information on the use of medicines for healthcare professionals. The information included in the SmPC is updated regularly as per the emergence of the latest information. SmPC contains more information than a Package Leaflet.

The SmPC information can be found through the following sources:

1. Websites of Health Authorities; such as the European Medicines Agency (EMA)
2. Medicine dictionaries

What consists of an SmPC?

- Information related to the medicine usage
- Qualitative and quantitative information on medicines' benefits and risks
- Dosage information
- Administration method
- Pharmacological information
- Individual care information

Structure of an SmPC

The structure of the SmPC is defined by the European pharmaceutical legislation. The information included in the SmPC should be product specific and can be cross-referenced to avoid any redundancy. It should be documented in a clear language and should not lead to any ambiguity. The SmPC is divided into 6 major sections:

1. Name of the product
2. Composition
3. Pharmaceutical Form
4. Clinical particulars – Includes therapeutic indications, recommendation for dosages and safety information
5. Pharmacological properties – Takes into account the therapeutic indications of the clinical elements and their potential adverse drug reactions
6. Pharmaceutical particulars – Includes Regulatory information related to the drug

As per the EMA, structure of an SmPC can be depicted as:

- 1. Name of the medicinal product
- 2. Qualitative and quantitative composition
- 3. Pharmaceutical form
- 4. Clinical particulars
  - 4.1 Therapeutic indications
  - 4.2 Posology and method of administration
  - 4.3 Contraindication
  - 4.4 Special warning and precautions for use
  - 4.5 Interactions with other medicinal products and other forms of interaction
  - 4.6 Fertility, pregnancy and lactation
  - 4.7 Effect on ability to drive and use machines
  - 4.8 Undesirable effects
  - 4.9 Overdose
- 5. Pharmacological properties
  - 5.1 Pharmacodynamic properties
  - 5.2 Pharmacokinetic properties
  - 5.3 Preclinical safety data
- 6. Pharmaceutical Particulars
  - 6.1 List of excipients
  - 6.2 Incompatibilities
  - 6.3 Shelf life
  - 6.4 Special precautions for storage
  - 6.5 Nature and contents of container
  - 6.6 Special precautions for disposal and other handling of the product

Reference: EMA

What Information is Excluded from an SmPC?

- Information available in the public assessment reports (scientific development details)
- Unapproved indication information
- Issues which lack data
- General advice on pharmacological conditions

Maintaining an SmPC is important for the life cycle of any medicine, as it is a part of its marketing authorization. Therefore, authoring a compliant SmPC is highly recommended. Are you looking for expert Regulatory assistance to develop an SmPC? Reach out to Freyr @ sales@freyrsolutions.com.

ISO 22716 - A GMP GUIDE FOR COSMETIC PRODUCTS IN THE EU

Center of Excellence
Compliance, Audit and Validation

Cosmetic products are one of the most widely used category of personal care products across the globe. Hence, they should be manufactured in a safe and effective manner. To ensure the same, Health Authorities across the world have established certain Good Manufacturing Practices (GMP). In Europe, the Cosmetic Regulation (EC) 1223/2009 directs manufacturers to adhere to the ISO 22716 standard while producing the cosmetic products.

Good Manufacturing Practices as per the ISO 22716 standard

ISO 22716 defines certain quality and safety standards for cosmetic products to be placed in the European market. It standardizes below-mentioned aspects to be taken care of:

1. Premises

The premises should be located and designed in such a way that it should ensure the product's safety and efficacy and must be regularly sanitized and maintained properly to avoid contamination of raw materials/products/operational flows.

2. Equipment

The equipment used must be suitable for the purpose of the product and manufacturing process. They must be kept in a condition that avoids any cross-contamination.

3. Raw Material and Packaging Items

The raw material and packaging items used in the manufacturing process are required to meet a defined and relevant set of criteria to ensure the quality of the finished product. The manufacturers must establish a dynamic supplier chain process for the raw materials to easily trace any issues that might arise during procurement. In addition, the purchase and reception of raw materials are also subject to strict rules and must only be carried out by qualified personnel.

4. Manufacturing Process

To ensure that the finished cosmetic product meets the quality standards, various precautionary steps must be taken, such as:

- The process of manufacturing must be summarized and documented properly along with the relevant information about raw materials, formula, and the equipment required
- Quality control points must be clearly identified
- Batches should be numbered and labeled properly for easy identification
- To minimize the contamination risk, manufacturing facility must be checked thoroughly for uncompromised safety

5. Finished Product

Organizations must set certain quality standards for the finished products prior to the initiation of the manufacturing process. These quality standards must also be maintained throughout the storage, supply, and distribution of the product. When the product is placed in the market, it must comply with the defined quality standards.

Complying with the GMP requirements of a region is necessary in order to deliver safe and effective cosmetic products to any market. Failing to do so may result in possible product recalls and a significant financial burden. To avoid them, start aligning with region-specific GMP requirements; in case of the EU, align with the GMP guidelines as per the ISO Standard 22716 and be prepared for sudden audits.

Freyr performs around 700 checks at a preliminary level spread across 18-19 GMP functional areas

USFDA's NUTRITION FACTS LABEL & CHECKPOINTS FOR A COMPLIANT TRANSITION

Center of Excellence
Global Food and Food Supplements Regulatory Services

In 2016, the United States Food and Drug Administration (FDA) released final rules for the revised Nutrition Fact Labels, a part of which will be effective from the year 2020. It was initiated by the USFDA to help consumers make informed food choices and promote a healthy diet and lifestyle. As per the new nutrition guidelines, manufacturers with annual sales of more than USD 10 million or more will be required to comply with the new rules from Jan 1, 2020.

Let's take a look at the major changes that have been made to the Nutrition Labels and how they are going to impact the manufacturers:

- **Prominent Serving Sizes** - The new rules suggest bolder and bigger typeface for serving sizes to make it easier for consumers to assess the nutrition label's context.
- **Modified 'Servings per Container'** - There will also be a larger and bolder typeface for container servings to make it easier for consumers. Packaging size regulations are also proposed to be applicable to food products that are generally consumed in a single serving.
- **Clear 'Calories'** - Calories, one of the most important nutrients to be recognized by the U.S. customers, are proposed to be represented in a larger and bolder type.
- **Elimination of 'Calories from Fat' -** Nutrition labels may no longer require the declaration of 'Calories from Fat.'
- **Mandatory Use of 'Added Sugars'** - Whether 'Sugar-Free' claim is mentioned on the label or not, 'Added Sugar' must be included on nutrition label in grams and as percent Daily Value. This includes added sugars used during processing and packaging, along with the sugar percent present in any other form.
- **Changes in Vitamins and Minerals** - Vitamin A and Vitamin C may no longer be required on the nutrition labels. However, Vitamin D, Potassium, Calcium, and Iron are proposed to replace Vitamin A and Vitamin C.
- **Updated '% DAILY VALUE'** - The amount of Daily Value (DV) should show how much a nutrient adds to the daily diet of a meal portion.

The proposed new labeling rules are expected to come into effect from the first day of 2020 for large-scale manufacturers. These adjustments to the nutrition label not only reflect preferences of new scientific research, but also align with contemporary consumer's preferences, expectations, and behaviors. Start aligning with the new Nutrition Fact Labels before the deadline. Stay current. Stay informed.

EMBRACE COMPLIANCE, THE eCTD WAY

Center of Excellence
Publishing & Submissions

The changing landscape of the life sciences industry makes it necessary for the companies to adapt to the global Regulatory requirements, immediately. Companies need to evolve themselves for the necessary transition with each mandatory requirement from the health authorities. One such mandatory requirement in recent times is the Electronic Common Technical Document (eCTD) format, an electronic equivalent to the Common Technical Document (CTD) format.

The purpose of introducing the eCTD was to reduce the burden on the reviewers of the health authorities and to simplify the process of submission as some of the key Regulatory authorities have already consigned to use it as a standard format for submissions. To ensure all the applicants practice the same, there are certain mandatory deadlines imposed by global health authorities. Though many of the deadlines for eCTD adoption have already passed, there are many in the pipeline to be adhered to. As an end-to-end Regulatory partner, aiming for successful compliance at every step, here we bring you a list of mandatory eCTD requirements that are still active and need to be complied with by Jan 1, 2020.

Health Canada

In 2014, Health Canada had published a guidance document on the preparation of drug Regulatory activities in eCTD format. It also started accepting individual requests for exemptions for those unable to use the eCTD format for Regulatory activities, with appropriate justification. However, as of Sep 13, 2019, Health Canada summarized the mandatory eCTD format requirements for Regulatory activities already implemented or effective at a future date.

In its recent notice, Health Canada has made eCTD format mandatory for Master File Submissions effective from Jan 1, 2020. Once a Master File is submitted in eCTD format, all additional filings must also be submitted in the eCTD format.

EDQM

The European Directorate for the Quality of Medicines (EDQM) has been updating the guidance for preparing and submitting eSubmissions.

As per the recent EDQM roadmap, all CEP applications have to be submitted in eCTD from Jan 1, 2020, failing to which, the EDQM will stop accepting Non-eCTD electronic Submissions

(NeeS) for notifications, revisions and renewal applications.

HALMED
Agency for Medicinal Products and Medical Devices of Croatia (HALMED), has committed to implement a common European strategy for the introduction of electronic filing requirements in Regulatory procedures for medicines.

To ensure this, from Jan 1, 2020, HALMED has made it mandatory for all the Regulatory submissions to be filed in the eCTD format.

With region-specific submission formats and compliance timelines becoming crucial for global market-entry, companies need to opt for a smart eCTD publishing software to smoothen their eCTD submissions. All we can say is that the mandatory phase for eCTD has already begun. It is time that the companies need to adapt to make submissions easier for the health authority reviews. Submit the eCTD way.

Global Health Authority Mandates

Health Canada mandates eCTD format for all new Type I, II, III, IV Master File Submissions.

Convert existing applications into eCTD

Effective Since: Jan 1, 2020.

EDQM has announced that eCTD is mandatory for all CEP applications including notifications, revision, renewal and new applications.

Switch to the eCTD format, RIGHT NOW!

Effective Since: Jan 1, 2020.

Croatia's Health Authority, HALMED, has announced the adaptation of eCTD documentation.

Would you like to consider converting to eCTD?

Effective Since: Jan 1, 2020.

CONSULT

COSMETICS SAFETY STANDARDS: SOUTH KOREA TO ALIGN WITH THE EU REGULATIONS

Center of Excellence
Global Cosmetics Regulatory Services

The Ministry of Food and Drug Safety (MFDS) of South Korea is modifying its Cosmetics Safety Standards to align with the European Union (EU) legislation for cosmetic ingredients. The purpose of these modifications is to increase the safety of the cosmetic products and streamline the Regulatory framework for cosmetic ingredients. The updated regulations will be applicable to all the cosmetics manufactured, imported, and distributed in South Korea.

According to a report, once the regulations are updated, the allowable concentration limit for more controversial chemicals will be reduced, which includes the following five preservatives:

- Methylisothiazolinone (MIT)
- Dimethyloxazolidine
- P-chloro-m-cresol
- Chlorophene
- Propionic acid and its salts

The decision of changing the concentration of MIT is only to reduce the number of allergenic incidents. It is aligned with the EU Regulation (EC) 2017/1224, which came into force in the year 2018.

Additionally, the agency is also planning to upgrade the regulations of ingredients associated with the following category of products.

1. Hair Dye and Soaps

The proposed updates will also provide a list of additions to the allowed hair dye ingredients and their set concentration limits. The changes are aligned with the EU Regulation (EC) 1223/2009 in order to ensure that percentage of ingredients used in the products is safe. The list of restricted ingredients and their limited concentration is as follows:

- 2-amino-3-hydroxypyridine (1.0%)
- 4-amino-m-cresol (1.5%)
- Hydroxypropyl bis (N-hydroxyethyl-phenylenediamine) HCl (0.4%)
- 5-amino-6-chloro-o-cresol (0.5%)
- 6-hydroxyindole (0.5%)
- Hydroxyethyl-4, 5-diamino pyrazole sulfate (3.0%)
- Hydroxybenzomorpholine(1.0%)

The proposed regulations are also set to define standard tests and methods to calculate the free alkali content in solid soaps that are intended for face wash. Although, soaps are not regulated under the cosmetic law as of now, they are said to be classified separately in the upcoming regulations.

2. Customized Cosmetics

Customized cosmetics are defined as "Cosmetics Custom-made for Individual Use" in the revised regulations. The upcoming regulations are expected to provide rules specifying the ingredients allowed for use in this category of cosmetics too. Generally, all ingredients are allowed for this category except for those ingredients that are listed as prohibited, restricted or functional in the Cosmetics Safety Standards.

Additionally, the use of two substances (salicylic acid and its salts, and iodopropynyl butylcarbamate [IPBC]) are said to be banned for use in cosmetics intended for children under the age of 13. Earlier, these ingredients were banned for cosmetics for children under the age of 3.

Although these amendments were published through an MFDS administrative notice on Jul 23, 2019, the implementation date for the same is yet to be announced. Until then, cosmetic manufacturers planning to enter the South Korean market are advised to keep a track of the advancements of the Cosmetic Safety Standards to ensure successful market-entry and compliance. Stay up-to-date. Stay informed.

Global Health Authority Mandates

Indonesia's BPJPH Mandated HALAL Labeling for Cosmetic Products

Mandatory Deadline:

Effective From - Oct 17, 2026.

Align Your Product Labels Accordingly

CONSULT

FREYR CONNECT

FSSAI RE-CATEGORIZES HEALTH SUPPLEMENTS AS THE FSDU

Center of Excellence
Global Food and Food Supplements Regulatory Services

The Food Safety and Standards Authority of India (FSSAI) has published a guidance document announcing the re-categorization of all the health supplements for sports use as Food for Special Dietary Uses (FSDU). The guidance states that going forward health supplement manufacturers in India will have to comply with the Food Safety and Standards Act, established in the year 2016. It also mentions that the health supplements for sports use cannot contain any unauthorized hormones, steroids or psychotropic ingredients. In addition to this, the health supplements will be evaluated based on the composition of vitamins, minerals, amino acids, probiotics, etc.

In order to align and comply with the Food Safety and Standards Act, health supplement manufacturers must adopt the following five steps:

1. **Registering with the FSSAI and obtaining license**
   All health supplement manufacturers are required to register themselves with the FSSAI and obtain licenses. The manufacturers (domestic as well as international) must have a registered office in India along with local contact details to address the queries raised by the FSSAI. Additionally, regular audit of the manufacturing facilities must be conducted as per the FSSAI guidelines.

2. **Labeling and Claims**
   Manufacturers must ensure that the following claims are mentioned on the label of the product, as per the FSSAI:
   - "For Sportsperson Only"
   - Logo of the Food Safety Standards

FSDU FOR SPORTSPERSONS

- "Recommended to be used under medical advice or dietetic supervision only"
- "the product is not to be used by pregnant, nursing and lactating women or by infants, or children under 5 years, or elderly except when medically advised"
- "the food is not a sole source of nutrition and should be consumed in conjunction with a nutritious diet' for the article of food specially prepared for sportsperson"
- "the food should be used in conjunction with an appropriate physical training or exercise regime"
- "for oral consumption only"

3. Authenticity

Manufacturers must ensure that all the FSDU products have tamper-proof packaging in order to maintain the authenticity of the product. The sellers and distributors of these products must also be verified by the manufacturers.

4. Traceability

Manufacturers must maintain complete transparency of the supply chain of the product.

5. Expiry Date

In case the products are sold online, the date of expiry/ best before date must be clearly mentioned on the product.

Apart from the above-mentioned steps, manufacturers must also conduct periodical tests on the products, at least twice a year, to ensure that the health supplement is free from any unwanted substances. Additionally, manufacturers must also maintain a repository of Certificate of Analysis (COA) to showcase as a ready reference and maintain the control samples as per the safety standards of the FSSAI.

With the re-categorization of health supplements coming into force, manufacturers are advised to stay up-to-date and adhere to the FSSAI regulations. Failing to meet the regulations pertaining to the product may result in noncompliance. Be informed. Be adherent.

Global Health Authority Mandates

Indonesia's BPJPH Mandated HALAL Labeling for Food Products

Mandatory Deadline:

Effective From - Oct 17, 2024.

Align Your Product Labels Accordingly

CONSULT

Center of Excellence
Global Cosmetics Regulatory Services

Infographic

COSMETICS COMPLIANCE IN CANADA

5 Key Acts To Be Followed

Cosmetics, as they deal with the end-user's beauty, must be carefully manufactured and marketed in accordance with the regional regulations. Their formulation, ingredients, label information, claims, and notification must be compliant with the regional acts and standards.

Same is the case with Cosmetics in Canada, as they should be manufactured and marketed as per the below mentioned key Acts.

Food and Drugs Act (R.S.C., 1985, c. F-27)

Provides detailed description of the regulations and requirements

Cosmetic Notification Form (CNF)

Notify the product to the Health Canada by submitting a CNF within 10 days of the product launch

Consumer Packaging and Labeling Act

Defines how a cosmetic product should be labeled and packed along with the warnings and precautions

New Substance Notification (NSN)

Any ingredient that is not a part of the Domestic Substance List is required to be registered on the NSN as a new substance

Cosmetic Ingredient List

Provides the list of restricted ingredients and warnings related to them

For Compliant Cosmetics Canadian Market-entry, Decode the Acts in Detail.

CONSULT

Case Study

Center of Excellence
Global Medical Device Regulatory Services

Successful Identification of Medical Device Category in the EU Region

Client
A contract research organization and genome-scale diagnostics services company specializing in genome guided medicine

Solution
Product Classification

Products
Next Generation Genomic Sequencing (NGS) based medical device

Geography
USA

Therapeutic Area / Indication
Oncology

Functions
Determination of EU classification

BENEFIT HIGHLIGHTS

- Client is benefitted with the classification of the product in the EU region and Regulatory path-forward for the product
- Being a novel technology with no identified rule for classification in 98/79/EEC, formal classification with agency has helped the client in easy launch of the device under General IVD category
- Timely submission and interaction with agency

Business Imperatives

- The client supports researchers engaging in case-control, family-based, or proband-only genomic studies of disease, pharmacogenomics, and cancer. Since, the product in scope was based on latest NGS (Next Generation Sequencing) based technology, the classification was complicated

Challenges

- There were no regulations in use pertaining to the NGS technology-based devices

Freyr Solutions and Services

- Freyr collated all product specific information from the client
- Freyr classified the product as per the EU specific Regulatory guidelines
- Freyr also interacted with the competent authority and confirmed on the classification of the product with the respective Health Authorities
- Based on the classification, Freyr provided a high-level Regulatory approach for product registration as per the classification, for development of the overall global product registration strategy

Client Benefits

- The EU classification of the NGS based product

Case Study

Center of Excellence
Technology
Regulatory Services

Successful Management of Product Registrations with Freyr SPAR

Client
India based Healthcare Organization

Solution
Regulatory Information Management System (RIMS)

Products
SPAR - Product Registration Information and Submissions Management

Geography
India (Operations in EU, Asia)

Application Types Supported
RIMS

BENEFIT HIGHLIGHTS

- Tracking of all Regulatory submissions and approvals
- Tracking and management of product registrations
- Effective management of health authority queries, correspondence and interactions
- Document storage and DMS link with advanced search and storage capabilities
- Customizable and effective dashboards
- Event notifications and reminders

Business Imperatives

- The scope of the project includes creation of data repository of products and submissions, and HA interactions

Challenges

- Difficulty in handling and tracking products and submissions due to numerous products
- Need for normalizing data that is stored in multiple repositories, in varied formats
- Inaccessible data reports owing to multiple geo-specific teams functioning in silos, with zero to minimal communication
- Missing dashboard or application that displays all data and corresponding reports at one place
- Missing deadlines for submissions, renewals, and more due to lack of notifications through any mediums like email, application, etc.

Freyr Solutions and Services

- Freyr's SPAR software is designed as an integrated yet independent repository for products, devices, documents, and post approval product lifecycle
- SPAR handles the huge data available in company's repositories with ease and convenience, inculcating built-in relationship between specified data elements
- SPAR includes manageable metadata, making it available with few easy clicks
- SPAR showcases customizable reports specific for countries or regions
- SPAR application is easily accessible using a browser over the web. Audit trails are maintained and available on demand for the administrator
- SPAR user interface is very intuitive, easy-to-understand, navigating, and flexible to integrate with any other legacy software or import from conventional spreadsheets
- SPAR has powerful search filters that helps user to search and navigate to a specific record faster and easier

Client Benefits

- Increased operational efficiency with high quality data and reliable reports
- Streamlined teams within regions and throughout the organization with the help of a single platform
- Automated email and in-app notification of submissions, renewals, and HA updates
- Future ready platform based on the standards of the ISO
- Fast paced submission delivery by adopting RIMS platform
- Effective responses to critical HA queries with highly improved and standardized data

Industry Events

We were glad to be a part of the **BioNJ's 2020 Annual Dinner Meeting & Innovation Celebration**, and **Arena PHPL 2020 East Coast** in the previous quarter. It was great to be networking and conversing with industry thought leaders all through the sessions.

Here are some of our key collaborations at the event. Glance through them...

Testimonials

Thank you very much for the support. This was totally a new process for us and we were having plenty of doubts especially when having strong comments from other internal departments.

I'm sure Freyr's team has learned a lot about how to get an accession number. That's what is really important and gratifying. Thank you again and keep up the excellent work!

Manager, Regulatory Affairs
A Spanish Medical Devices Manufacturer

Please let us take this opportunity to thank the entire Freyr team for their kind support. We are using Freyr SUBMIT PRO with an increasing confidence and getting used to the advantages of the technology. We would appreciate Freyr's continuous support for this year and other years to come. Thank you.

CEO and Principal Consultant
A Japan-based Leading Pharmaceutical Consulting Company

SPAR has streamlined our processes, brought together our scattered data pieces and improved our data quality., ultimately helping us to better manage RI. SPAR intervention made lifecycle management easy by sending out automated notifications. Notifications drastically improved our operational efficiency. Appreciate Freyr team's devotion. Kudos to their technology and the teams that worked behind this.

VP, Regulatory Affairs
A leading India-based healthcare organization

I would like to thank Freyr for their fantastic performance. Their knowledge and attitude towards work is of top class, and their commitment towards work and technical expertise is outstanding. This has helped us deliver the POC and I am sure we will soon deliver the production environment as well. I would like to appreciate Freyr's sense of ownership and willingness to resolve issues that were sometimes beyond the expected line of duty.

Management Consultant
An Indian Multinational Corporation Specialized in Business Consulting

FREYR CONNECT

Freyr CLIENT WINS

The Customer: A Japan based, maternity and baby care products company

Project Details: Regulatory compliance check for products across APAC and Middle East

The Customer: A US based, leading food supplements manufacturer

Project Details: Provided product and label compliance for 10 products in India

The Customer: A Singapore based, beauty and personal care products company

Project Details: Regulatory compliance check for 25 products in Australia

The Customer: An India based, global healthcare products company

Project Details: Provided Regulatory support for formulation review and product registration in Sri Lanka

The Customer: A Germany based, multinational pharmaceutical and life sciences company

Project Details: Provided support across various Regulatory functions

THE VIBRANT JEWEL OF WESTERN INDIA

GUJARAT

FOR NATURE AND HISTORY LOVERS

Spend a Few Days in Gujarat – this is the famous tagline that Gujarat Tourism boasts upon. I must admit that the line is strategically coined. Because all you need is just a few days to fall in love with the vibrant culture of Gujarat. Vast natural beauty, stunning terrains and oceanic and picturesque landscapes - situated on the western most corner of India, Gujarat stands up to be a perfect blend of all. It was my second visit to the state. But, I was as excited as it was my first to explore the land of lions and treat myself with its intricacies and delicacies.

FREYR
CONNECT

Somnath

Being avid travelers, my family decided to take this trip up a notch by turning it into a road trip. So to begin with, we all took flights to Ahmedabad, from where we hired a car to travel around. Our first destination was the holy shrine of Lord Shiva, Somnath. Would you like some trivia? The Somnath temple has been looted, destroyed and resurrected 17 times. Interesting, isn't it? The current temple was built in 1951 and the deity was installed by the first President of India, Dr. Rajendra Prasad. Situated on the side of Arabian Sea, Somnath temple is an epitome of beauty and architectural intricacies and provides you the tranquillity that you look for in a pilgrim. Post praying, we spent some quality time by the sea and then headed to our next destination, Gir.

Gir Jungle

From Somnath, it's a 70kms ride to Gir/Sasan Gir. If you are a nature enthusiast, you might know that Gir is one of the largest habitat of Asiatic Lions. We reached our resort, which was right amidst nature, around evening and decided to end our day with good food, a small bon-fire and some live music as we had to start for our jungle safari pretty early the next day.

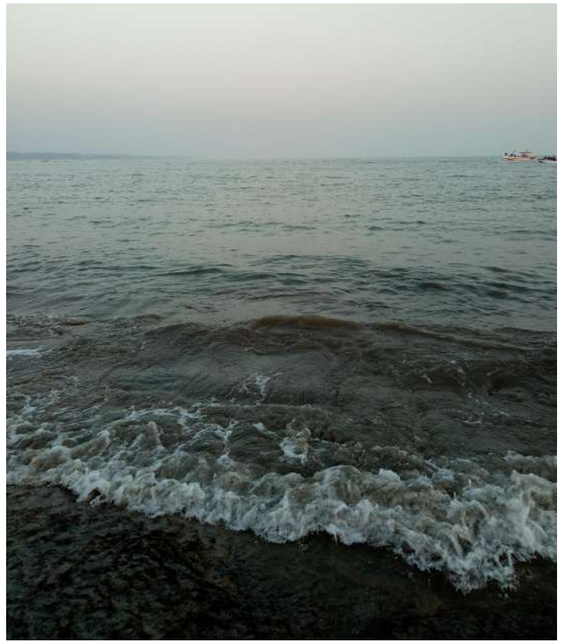
Being a wildlife sanctuary, one needs a permit from the Gujarat Forest Department office to take a jungle safari in the Gir Jungle Forest. The permits are available pretty easily online, given you book it at least 3 months prior to your visit. We started our safari at exactly 5:45 AM, and thus began 3 hours of natural bliss. While a lot of people are keen on just looking around for the lions (which, obviously, are the main attraction), they miss out on the other amazements of the forest. And amidst light fog and chilled weather, the experience of ▶

safari becomes unforgettable. Although we didn't come across any lions, we were lucky enough to encounter a lot of spotted deers, a couple of blue bulls, jackals and many exotic birds. Apart from the traditional safari, there is one more kind of safari in Gir called Devalia safari. If you need almost 100% surety to spot Asiatic lions and panther, well, this is the place for you. Although, let me warn you, it is more like a treatment and care centre for animals of the Gir forest. After wrapping up our safari, we decided to freshen up and enjoy some local cuisine and head for Junagarh.

Junagadh

Having traveled so much across India, I almost always forget the true essence of India which lies in its forgotten small cities. Once an important city of the Maurya Dynasty, Junagadh (translation: the old fort) now stands amidst the beautiful ruins of mosques, forts and huge gates. Since we had just half a day to explore the city, we decided to visit only the important sites. Thus, we navigated through the small streets and markets of Junagadh to find our way to the Uparkot fort. Guarded by two old and rustic temples of Lord Ganesha and Lord Hanuman, the fort is an embodiment of the class and rich taste of people back in the days. From the temples, tourists have to explore the entire place on foot, which is the correct way, if you ask me. The history of the fort is quite interesting in itself. It starts from the Mauryan Dynasty and end with the Nawabs of the Babi Dynasty taking over it and ruling over it until the independence of India. When you're walking towards the fort, you get to see a panoramic view of the entire Junagadh city. And it is surreal!

The fort is filled with breath-taking and intricate architecture, including two huge cannons names Neelam and Manek. Wait, travel trivia time! Did you know? These two canons were bought from Cairo (Egypt) to defend Diu from Portuguese invasion in 1537. The fort exemplifies the beauty of Indo-Islamic architecture and showcases the brilliance of planning and execution of such a huge structural marvel. And if you think this is the end of the fort's appreciation, then wait. The fort also has a communal well or step well, which is a great view in itself. After tiring yourself out by walking so much, how could you not crave for some local street food? Absolutely, it was time for some mouth-watering Gujarati snacks!

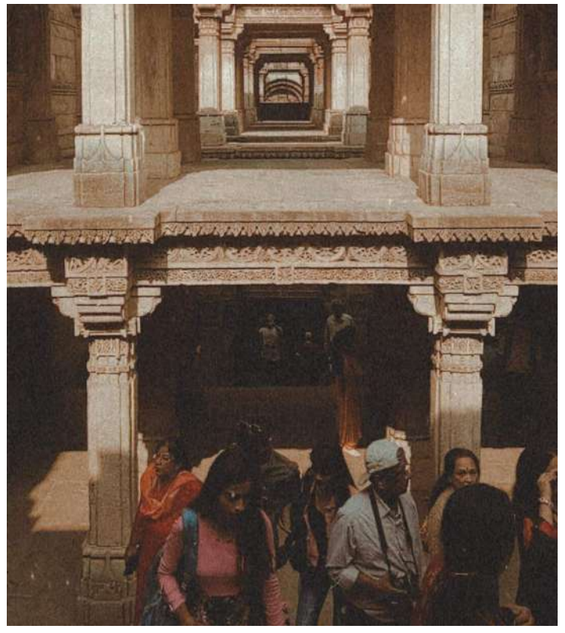


Diu

The next day, we headed to our next destination, which was Diu. Away from all the commercialization and buzz of crowd, Diu offers you an island of serenity and scenic beauty. The island takes your breath away from the moment you enter with stunning white salt beaches on both sides of the road. By the time we reached, it was already 4 pm. So we decided to chill for the rest of the evening and spend the evening watching sunset on the Nagao beach.

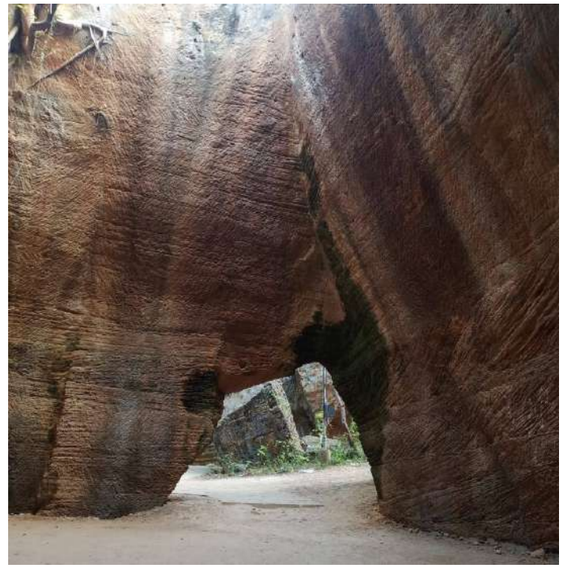
The next day we set out to explore rest of the Diu. We started our day by exploring the Diu Fort. The fort is a perfect example of the influence of the Portuguese era on India. Situated on the coast, the fort is a striking structure which stretches over a large area. And this is not it, the fort is also connected to three beautiful churches, a temple and a lighthouse. The lighthouse gives a stunning view of the complete fort and the sea – making it the most beautiful attraction of the fort.

Our next stop was Naida Caves. Structures like Naida Caves makes your realise the true power of nature. The caves are a network of more than 100 cavern and weather worn walls intertwined beautifully. While walking through the caves, you will come across random openings within the walls through which small rays of sunshine filter through. Trust me, it is more beautiful than it sounds. But here is the most interesting part, no one knows about the history of these caves. Nobody knows how these caves came into existence. However, it is certain that these caves have been preserved in the same manner since the Portuguese era. This wasn't the end of our exploration, we also visited a few small churches and temples, which were equally beautiful. We also planned to visit the INS Khukri Museum, but to our dismay, it was closed for restoration.



Ahmedabad

Our flight back to home was from Ahmedabad. So we went to Ahmedabad from Diu and decided to explore the city a bit before heading home. Our first spot was the Swaminarayan Temple. With a grandeur structure with stunning buildings and beautiful architecture, the temple is one of the top tourist spots of Ahmedabad. The simplicity of the temple brings you a wave of calmness. Our next stop was the Gandhi Ashram. Being born in India, everyone knows the role of Mahatma Gandhi in the struggle of independence. This is why the Ashram is of vital importance to Ahmedabad. If you want to take a closer look at the life and work of Mahatma Gandhi, this is the place to be.



After the Ashram, we went to a place that I had never heard of – Rani ki Vav (the Queen's stepwell). Time for another travel trivia! Did you know? It is the only stepwell across India to be declared as a UNESCO world heritage site. And it deserves that privilege due to its gigantic size and surreal architecture. I was stunned to see the detailing of work on the pillars. It was something I had never seen before. And you know why? Because the stepwell is made into 7 levels with more than 500 principle structures and 1000 minor ones.

To end our trip, we decided to spend some time in Kakariya Lake, which is the most famous picnic spot of Ahmedabad. While leaving Gujarat, a thought lingered in my mind – How much do we take our country for granted? We are blessed with so many beautiful places that glorify our culture and heritage. Yet, we fail to witness even half of them. On that note, I have decided that I'm going to explore our Incredible India and come back to Gujarat to enjoy its simplicity one more time. Abhara, Gujarat!

GOLLAPALLI NANDA KUMAR

Hi Nanda. Thank you for your time. We know, when we called you for this interaction, you were analysing some health authority guidance to chalk out a strategic plan for a clients' request. We should admit, because of these analyses, we have added some big names to the list of our customers. Thank you again!

Yes, currently looking into Regulatory submission road map for one of our prominent client's product registration with the US FDA.

Many say, Regulatory Affairs is a rewarding, intellectually stimulating and highly regarded profession within pharmaceutical companies. Instead, you have chosen to be in the RA department of a CRO like Freyr? Why did you choose to be with a CRO? What do you see as a main difference?

In the Indian Pharmaceutical companies, the role of a Regulatory Affairs resource is limited to specific region, product category, and specific to either pre-submission or post-submission activities. I think that limits the resource to have exposure/experience to specific activity of registration cycle of a drug product.

In contrast, with a CRO one will get an opportunity to handle end-to-end (Regulatory strategies to LCM of Applications) Regulatory activities. One can grow as a complete Regulatory Affairs professional, as proven in my case – from handling registration of Generic products Majorly for Drug Substance (API) & limited Drug Product registration activities for various clients at the first step to handle registration activities for Innovator products as well as Generic medicinal products for all kinds of dosage forms for different therapeutic category products.

Freyr has been on a trajectory of growth for a while now. With the recent Regulatory overhauls across the globe, what according to you stands as the biggest challenge for Freyr to sustain the growth?

Freyr is a leading Regulatory solutions and services company. With an already established brand image, the biggest challenge for Freyr at this point is to maintain it and sustain the business growth and requirements with more focused emphasis on aspects such as 'quality deliveries', 'easy to approach', 'aligning with client's time zone', and 'end-to-end support for all kinds of Regulatory activities' while maintaining the same trust factor.

Since the Brexit has finally taken place, do you see any major implications that RA experts should be aware of?

In fact, they should be aware of all the information updated by the authorities. As the Brexit has already taken place and been effective from Jan 31, 2020 with a mandate for implementation by Dec 31, 2020. That means from Jan 01, 2021, all new registrations to the UK shall be submitted through national procedure only and should have MAH Holder, Batch release site, Local point of contact, QP and QPPV (and PSMF location) within the UK.

Further, region specific (EU or UK) MAH Holder, Batch release site, Local point of contact, QP and QPPV information (and PSMF location) should be updated in the existing registrations submitted through DCP/MRP procedures. If the product is being imported from the UK,

the import license should be obtained from the respective the EU country as applicable and vice versa.

Regulatory Affairs and Regulatory Operations; often we see so much of confusion between these two segments. Why is it so? Is it for real or because of lack of clarity? Can you enlighten us?

Yes, different organizations follow different structure to manage their Regulatory activities based on their internal practices and practicality.

However, in global sense Regulatory Affairs team (CMC, Clinical, Non-clinical, Labelling/Artwork teams) handles the core Regulatory activities including, Regulatory strategies for drug development/clinical programs/ product registrations, authoring and review of product registration dossiers (CTD Modules 1 to 5) and subsequent LCM submissions such as variations, supplements, annual reports etc. Whereas, Regulatory operations team (Publishing, Project management, Regulatory heads) take up the responsibility for coordination, submission planning/submission strategy, publishing & submission, interaction/liaising with Health Authorities.

All across your stint with Freyr, as a key resource for RA CoE growth, did you find any project that was really challenging? Has there been any situation like that and if yes, what kind of strategy did you opt to overcome it?

Every project I have worked on has its own challenge, which might not be in Regulatory aspect, but majorly in documents availability, collation, delivery timelines & Regulatory knowledge of the few clients.

The recent challenge which we came across as a RA COE was updating the legacy dossier in line with the current regional Regulatory requirements and register the product with the Health Canada. In the process we had to ensure the availability of source documents, check data adequacy, and acquire timely support from different stake holders from clients' side.

Freyr had frequent meetings/interactions with client, provided detailed explanation about the requirement, provided justifications/commitments for the missing/ inadequate data for the administrative acceptance of the registration by the Health Canada.

If not Regulatory Affairs, which career pathway Nanda would have opted?

From the time I heard about Regulatory Affairs function during my Masters, I always aspired to be in the Regulatory space. Never thought of career other than Regulatory Affairs.

Still, if I had to think about career path other than Regulatory Affairs, I may have chosen either Project Management or Quality Assurance.

Quick to Answer ---

Your Inspiration
Manager and Management Team

Your Motivation
Challenges motivate me to deliver

Ideal Vacation
Few days with family/relatives/friends to any location

NEW EMPLOYEES

Abdul Raheem Danish
Junior Associate

Ashish Dubey
Deputy Manager

Ajith R
Trainee

B Praveen
Senior Associate

Akshata Shettar
Senior Associate

Bhaskar Potta
Associate

Ameenuddin Osur
Team Lead

Bittu Rambabu
Junior Associate

Asfia S
Trainee

Diksha Yeole
Management Trainee

Asha Gundapu
Senior Associate

Dr. Neeharika Satya Jyothi Allam
Assistant Manager

Dr. Para Sujana
Manager

Madhuri Gautam
Associate

G. Krishna Narendra babu
Senior Associate

Madhusudhan Juvvagani
Junior Subject Matter Expert

Gnana Prakash Bellamkonda
Architect

Mamidipally Soundarya
Senior Associate

Gnanesh Sakala
Senior Associate

Manasa Magapu
Team Lead

Jaikishen Narayanababu
Trainee

Manoj Mahadev Mathpati
Senior Associate

Jinal Naik
Senior Associate

Meenakshi Verma
Team Lead

Jogeswararao Loya
Senior Associate

Meghana Gumpini
Trainee

Mohammed Azharuddin Shetsandi
Team Lead

Narender Tirumani
Architect

Mohan Govindaraj
Manager

Naveen Kumar Doppalapudi
Assistant Manager

Mohankumar Palanisamy
Associate

Nikhil Gadekar
Senior Associate

Mounica Chityala
Senior Associate

Nikhil Khobragade
Associate

Naga deepthi Venigalla
Senior Associate

Nishita Gadekar
Associate

Nagesh Kumar Garapati
Architect

Parul Srivastava
Senior Associate

Nancy Gupta
Specialist I

Pradeep Thatipatti
Trainee

Pragnya Paramita Sahoo
Trainee

Ravali Patlolla
Assistant Manager

Praneeth Kumar Reddy Pallerla
Team Lead

Rethina Ebinesan
Associate

Prasad Reddy Gogireddy
Team Lead

Sanjeev Reddy
Senior Associate

Prashant Rakhecha
Associate

Santosh Gampa
Associate

Praveen Kumar Boga
Team Lead

Saravanan S
Senior Manager

Rajarshi Mukherjee
Senior Associate

Sarella Sreeja
Specialist I

Ramaiah K
Team Lead

Saroj Roy
Senior Manager

Sattar Sk
Trainee

Suman Nandi
Senior Associate

Shamiksha Shetty
Management Trainee

Sumanth Prabhakar
Assistant General Manager

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Sushma Yedunuri
Manager

Srikanth Vuppala
Vice President

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Kindly note that the Regulatory scenarios and mandatory deadlines discussed in this Issue may be altered in near future. This might be due to the current Pandemic outbreak or the periodic health authority updates. Hence, it is probable to find different perspectives/opinions in comparison. Kindly be aware.

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