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

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2021

CONNECT

LEARN | INSPIRE | INNOVATE

LEAD STORY

Throwback 2021
2022 and Further
Freyr - The Journey
Behind Success

freyr®

celebrating a decade of success!

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

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What's INSIDE?

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FREYR CONNECT

FOREWORD

Dear Readers,

Greetings!

We hope you had a great holiday season and a pleasant start to the new year 2022.

With great pleasure, we present you another Issue of Freyr CONNECT Volume 9. As we step into 2022, the first big thing we would like to announce is Freyr's completion of ten (10) successful years in the Life Sciences Regulatory landscape. From a start-up to a leading global Regulatory solutions and services provider, the journey has been incredible, and we must say that all the credit goes to our customers, stakeholders, and employees for their unparallel and continued support.

Also, we are glad to be a part of the Life Sciences industry in the continuous fight against COVID-19. Our recent collaboration with an American pharmaceutical company to get an FDA Emergency Use Authorization (EUA) for a COVID-19 oral pill stands testimony to the same.

Overall, the last quarter of the year 2021 has been an exciting one at Freyr, for:

- Successfully completing a decade in the industry
- Surpassing the 200+ medical devices' customers milestone
- Launching 'Freyr Digital,' an end-to-end Regulatory software suite
- Completing 40 PDE/ADE Reports for Ophthalmic and Otic products
- Winning Three (03) "Gamechangers 2021 Global Awards"
- Collaborating with Darnista to Implement Freyr's AMS
- Being featured by ELEMED as the "Best Supplier to the Industry"
- Supporting FDA EUA for a COVID-19 Oral Pill

The excitement shall never downplay the innate intentions. With that belief, we made this Issue with a comprehensive lineup pertaining to Regulatory thought leadership. Apart from a brief throwback on 2021 regulations, it gives a peek at what kind of mandatory deadlines to look for in 2022 and further. In addition, this Issue has insightful coverage from infographics to case studies to advertisements w.r.to compliance best practices, Regulatory tools, market-entry requirements, and customer appreciations.

We hope that you find this best suitable for your strategies and approaches. Stay safe and healthy, always!

Happy Reading!

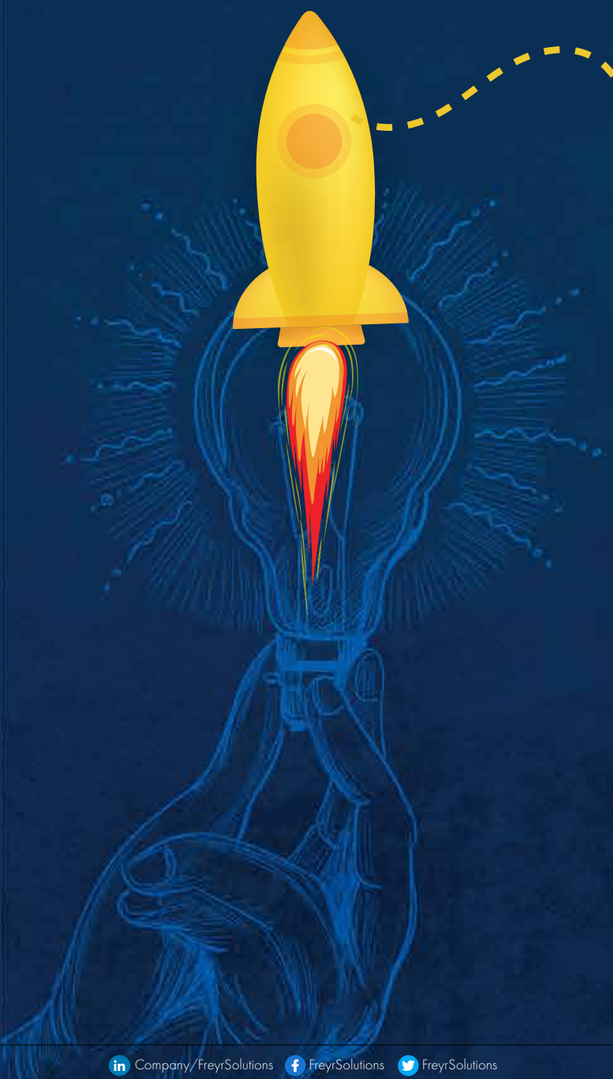
Suren Dheenadayalan

CEO

Freyr Celebrates a Decade of Success

Lead Story

freyr®



Do you know that Freyr, a leading global Regulatory solutions and services company started over a cup of coffee? Do you know that the Regulatory service provider forayed into the market with an aim to solve the Regulatory challenges and to fill the technology gaps in various processes in the life sciences industry? We guess, you must be thinking why these questions even matter at this point in time. Here we go!

On the completion of ten (10) successful years, Freyr, as an organization, wanted to take a moment and reflect on the humble beginnings a decade back, and how it has grown to be a leading, global player in Regulatory solutions and services across Life Sciences industry.

Yes! Freyr has successfully completed a decade in the Regulatory field of life sciences. The journey has been a roller coaster ride all through. Right from a month-long effort to design a logo, to winning the first-ever client with whose cheque we initiated website development, to surviving the Life Sciences industry shift in 2012 and ultimately creating a brand identity in the market, Freyr's journey was exciting, thrilling, challenging, and most importantly, fulfilling. Of course, this would not have been possible without the customers' support and their trust in us!

On this occasion, we are very excited and for once, thoughts would love to look back at the pathway that we have travelled, so far. Here is a simple narrative on Freyr's humble beginnings as a start-up to an industry leader.

Freyr – The Story Behind

Ideas

Strategies

CruX

A lot can happen over a coffee. Isn't it? Yes, of course!

Ideas, Strategies, Disagreements, Roadmaps, Conclusions, and a lot of political, movie, sports and spiritual banter. etc.

The idea of Freyr, too, popped up when a few likeminded people got together for a discussion over a cup of coffee on a bench outside a Starbucks coffee shop in Princeton, New Jersey...

Perhaps, they might have not imagined that the same will hook th em to a bigger responsibility of advocating the safety of the humankind on a larger perspective...

Disagreements

Roadmaps

Conclusions

2011
IDEATION

was all the technology boom in the late 2000s that was driving the entire business landscape.

and Bengaluru were also set out to be prominent technology hubs in India.

der, even we first thought to build a technology platform in the first go...

...but to serve a different business segment altogether.

ild a Regulatory Information Management (RIM) platform to address some of the pain points of the life sciences companies at that time.

Over so many cups of coffee, for six (06) long months...
ne product prototype and industry perspectives were discussed and chalked out.

Thanks to all the efforts, all the ideas were scrapped.

nths into the discussions, there was finally a seem-to-be-strong RIM product

ally, Freyr had its first product released and perfectly pitched with all the marketing methodologies applied.

The result was 26 leads, and we really experienced 'holy...,'
...we didn't realize that the leads were routed to a different tracking system.'

All said and done, life happens... and it continued for Freyr too.

Prepping up to the then mandate, in 2011 Freyr made its product EVMPD live, and roped in the first customer - a Germany-based multinational research-based pharmaceutical company.

In the same year, Freyr was titled and commenced the first web portfolio to showcase and first eMail campaign to let go.

2012
LEARNING

Like we need a good coffee every morning to freshen up, every strategy needs to be relooked into sometimes. Isn't it?

In 2012, Freyr started reinventing its service portfolio.

Apart from aiming at Regulatory Information Management, ventured into Regulatory affairs outsourcing.

Freyr's first big win in that segment was an American multinational corporation that develops medical devices, pharmaceuticals, and consumer packaged goods

However, Freyr did face the challenge to walk the unknown waters of Cosmetic Safety Assessment.

With the belief to try different scenarios, we took upon the challenge.

By partnering with global consultants and by recruiting in-house toxicologists, the project was delivered.

LEARNIN

2013 - 2016

IMPLEMENTATION

Post a brief set back, nothing refreshes us better than an aromatic sip of a coffee.
We hope you'll agree with this.

Freyr had consciously redefined itself to be adaptable to any kind of requirements.

The client list kept growing
Regulatory experts flocked Freyr
ISO certifications were done
Freyr's offerings were being acknowledged...

Thanks to all the business channels – Regulatory, technology, consultation, client relation, sales, and the promotional channels...

Freyr had begun to set the tone of its expertise,
in the minds of global market players.

...During 2015 and 2016, Freyr had set up an operational center in the UK.

With the help of FreyrX, Freyr brought in more consultants across the globe.
Eventually Partnered with 900+ Consultants across 120+ Countries.

Signed up by top 10 Forbes companies.

FREYR CONNECT

2017 & 2018

SUSTAINING GROWTH

If a single cup of coffee can make you go over the boundaries,
Won't you be ready for more?

Why not, we said!!!

With FreyrX setup, we had grown potentially.

We were experienced,
We were expanded,
and We exploded...

Crossed the first 100+ customers' milestone in 2017.
Established operational center in Mexico and Dubai, UAE...

Freyr became a leading global Regulatory Solutions and Services company
With end-to-end Regulatory service offerings right from strategy to submissions to lifecycle management

Flourished into the new phase of growth with 250+ new customers just in 1 year in 2018
Launched New Version of Freyr SUBMIT PRO, an in-house eCTD tool.

Pushed the boundaries to Sri Lanka,
Won back-to-back awards from GHP, IAE, GameChangers, and CPhI Pharma.

In 2019, too, Freyr continued doing the best...
Unveiled Freyr LABEL 360
Expanded Office space in the USA
Set up an exclusive operational center in Austria
Launched dedicated platform for Structured Product Labeling
Reached 450+ customers' milestone
Rose to a team of 650+ Global Regulatory Experts

2019

GHP Awards 2019 recognized Freyr as
'Best Full-Service Life Science Regulatory Services Company'

Freyr was Proven the Best at the AI's 'Global Excellence Awards 2019'

As they say, 'if you continue doing your best, the best will ultimately be at your side...'

2020

Apart from Australia Establishment, and reaching 100+ Medical Devices Approvals in 2020,
Freyr had a new reason for celebration.

Freyr entered a new spectrum of business.
Launched its own cosmetics brand - Slova.
Developed an exclusive ingredient database for Cosmetics - Freyr iREADY

But little we know that the unprecedented times of COVID-19
Would make the entire world standstill.

It might have challenged every aspect of life,
but not the spirit of humankind to fight back.

Freyr significantly ramped up the technical and non-technical aspects of the business.
Prioritized the employees' and customers' well-being, at the outset.
Quickly implemented remote operations.
Adopted to new ways of business.

Been with the customers and ensured the business continuity.

Freyr contributed to fight against COVD-19pandemic by supporting 2 of the 3 major COVID Vaccine players, as its global Regulatory strategy and submissions partner.

2021

In 2021, Freyr has progressively evolved its technology offerings ('Freyr Digital')
to provide industry-leading Digital Transformation solutions.

Launched Freyr Digital,
A full suite of next-generation Regulatory software and solutions.

Later in 2021, Freyr significantly won,
'Innovative Global Regulatory Services and Solutions for Life Sciences'- GHP Awards 2021
'ACQ5's Gamechangers 2021' awards in three segments
Elemed's 'Best Supplier to the Industry'

Partnered with Darnista
To Implement Freyr's AMS with Integrated GlobalVision Verify Tool

FREYR CONNECT

In December 2021, Freyr completed 10 successful years in business.

Been with the customers and ensured the business continuity.

Freyr contributed to fight against COVD-19pandemic by supporting 2 of the 3 major COVID Vaccine players, as its global Regulatory strategy and submissions partner.

THROWBACK 2021
Life Sciences Industry Outlook

It is apparent that COVID-19 has permanently changed the ways of business operations for many of the industries across the globe. In fact, it has subtly given a renewed purpose to industries to evolve and advance in terms of tech-enabled and automated workflows.

In the Life Sciences sector too, this has been true in all the ways, right from manufacturing to the products' market entry. Stakeholders have adopted the technological work-flows like never before, and have made successful attempts to bring out safe and effective medicinal products and medical devices. To ensure these attempts are compliant enough and safe for the end public, the global Health Authorities (HAs) have also initiated various programs to oversee the technological improvements in the industry.

In this article, we try reminiscing the major steps taken by the global HAs that transformed the Regulatory landscape of the life sciences industry in 2021.

Center of Excellence
Global Pharmaceutical Regulatory Services

EMA Guidance on Remote Pharmacovigilance (PV) Inspections

EMA revised the guidance on the steps to be followed during remote pharmacovigilance (PV) inspections for Marketing Authorization Holders (MAH). The purpose of this document was to help MAHs outline the specificities of remote pharmacovigilance inspections by identifying the inspection requirements for Centrally Authorized Products (CAPs) and Nationally Authorized Products (NAPs).

The revised contents include the following:

- The word 'distant/virtual' pharmacovigilance (PV) inspections have been changed to 'remote' pharmacovigilance inspections.
- Clarifications on the technical requirements for remote access to electronic systems and to maintain communication.
- Further inputs on the documentation and preparation conduct.

ANVISA Became a Member of PIC/s Committee

ANVISA of Brazil received the approval to become a member of the Pharmaceutical Inspection Co-operation Scheme (PIC/s) in November 2020. Considering the pandemic situation, for the first time in PIC/s history, the assessment was completed in a written procedure as opposed to at a meeting. On January 01, 2021, the PIC/s committee welcomed ANVISA as their valuable 54th member.

NAFDAC Announced Sensitization Campaign

The Director General of NAFDAC announced the commencement of a sensitization campaign in Nigeria. Through this campaign, NAFDAC intended to inform, sensitize, and educate the Nigerian citizens about the dangers of intake and use of bogus medicinal products surfacing in the market. With clear, concise, informative, and educative directives, the campaign spurred awareness about various infractions affecting the Nigerian healthcare system.

The Long-Awaited China eCTD Specification Published

Post the National Medical Products Association's (NMPA) membership in the ICH (International Council for Harmonization of Pharmaceuticals for Human Use) in 2017, China has to conform to the international guidelines with regards to the technical documents.

Consequently, the NMPA launched eCTD submissions for the initial New Drug Application (NDA) and Biologics License Applications (BLAs) on September 29, 2021. This document was released by the State Drug Administration, and came into effect on December 29, 2021. Per the new eCTD mandate, any applicant who chooses to make an eCTD submission must also submit a physical copy within five (05) working days of submitting the electronic version. Secondly, the content of the dossier should be the same for both the paper and the eCTD submissions, which are currently being allowed on a CD/DVD. Finally, any other submission types are out of the scope of the eCTD, and there are no plans to include them in the future.

ICH and SNOMED Collaborated to Evolve Clinical Decision Making

Understanding the scope of their collaboration, ICH and SNOMED, as a joint effort, have announced the release of new maps in the Regulatory and clinical spaces. Collaborative efforts under the project WEB-RADR 2 led to the release of two (02) important roadmaps (MedDRA to SNOMED CT and SNOMED CT to MedDRA) which have been structured around the repeatability of term usage and additional key pharmacovigilance MedDRA terms identified by the European Medical Agency (EMA). To promote drug safety, interoperability among the pharmacovigilance database (MedDRA) and electronic health records (SNOMED CT) helped identify possible side-effects and activated adverse events reporting simultaneously. The data collected through such reports was useful for conducting epidemiological research in patient demography. Key elements associated with MedDRA adverse event reporting was used to associate adverse drug events while providing "aid in clinical decision making."

EMA Released New Guidance for Nitrosamine Detected Response Template

The European Medicines Agency (EMA) evaluated the risk

of nitrosamine creation or presence during the manufacture of human medicines and advised Marketing Authorization Holders (MAHs) on how to avoid the presence of nitrosamine impurities. The following is the procedure to follow to remain compliant with the adjustments.

Risk Evaluation - Manufacturers had to conduct a risk evaluation process to identify the active substances and the finished product to check the nitrosamine levels. If there were any instances of cross-contamination, the same had to be included in the outcome report. The deadlines for submissions at this stage were set for March 31, 2021, for chemical medicines and July 01, 2021, for biological drugs. Since the deadline has passed, MAHs must adhere to the new guidance without fail.

US FDA & MAPP Proposed New Rules for Generic Drug Labeling

Per the revised Manual of Policies and Procedures (MAPP) of the United States Food and Drug Administration (USFDA) dated July 27, 2021, new labeling rules were proposed under Section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act (FD & C Act). This Section covers the FDA's approval of an Abbreviated New Drug Application (ANDA) even after a few changes in the labeling for the Reference Listed Drug (RLD). When the FDA's approvals of labeling changes for the RLD and the ANDA are scheduled simultaneously, the revised process needs to be followed.

The revised MAPP is sixteen (16) pages and has been effective from July 27, 2021. It administered Section 10609 of the Patient Protection and Affordable Care Act (PPACA), which was passed in 2010 and added to 505(j)(10) of the FD and C Act. The MAPP contained a detailed description of what needs to be done by the ANDA applicant when the changes in RLD's labeling are not included in the proposed ANDA labeling.

US FDA Issued a New Draft Product-Specific-Guidance (PSG) for Generics Manufacturers

Product-Specific-Guidance (PSG) documents lay down the United States Food and Drug Administration's (USFDA) current thought process on the evidence and markers needed to prove and qualify a generic drug being therapeutically equivalent to a Reference Listed Drug (RLD). On November 11, 2021, forty-eight (48) new drafts were added to the existing PSGs. Of these, twenty-one (21) are revised, and twenty-seven (27) are new PSGs. About nineteen hundred and forty-eight (1948) PSGs have been documented and released on this date, and they can be found here. Knowledge of these is mandatory for generics manufacturers to ensure compliant ANDA submissions.

Center of Excellence
Global Medical Device Regulatory Services

Medical Face Masks and Respirators – TGA's Standards and Key Performance Aspects

In January 2021, the TGA had undertaken a post-market review of face masks included in the Australian Register of Therapeutic Goods (ARTG) and identified common areas of non-compliance against claimed standards in this review process. Based on the same, the TGA has devised guidance intending to assist manufacturers in choosing the appropriate standards and to set out expectations for performance testing of respirators, surgical respirators, and medical/surgical facemasks before inclusion in the ARTG. To assess the performance of medical devices, the manufacturers must take note of several elements when considering the application of testing methods and must adhere to the guidelines to avoid market-entry pitfalls.

FDA's Action Plan for AI/ML-based Software as a Medical Device (SaMD)

In recent times, the use of Artificial Intelligence/Machine Learning (AI/ML) has made a huge technological sweep in the medical devices and healthcare industries because of their ability to diagnose, manage, and treat a variety of medical conditions and to enhance patient care. But there seem to be obstacles in implementing AI/ML in daily practices with respect to the transparency issues surrounding their software programs. Hence, it is crucial to regulate these technologies, and to do so, the Regulatory bodies are trying hard to govern the AI/ML implementation. Based on the same, in March 2021, the FDA had released a five-part action plan for its oversight of safe and patient-centric AI/ML-based SaMD. The Agency anticipates that this action plan will continue to evolve and provide additional clarity.

MDCG Published a Guidance for Medical Device Software

The integration of software with medical devices has rapidly increased and is driving incredible advancements in delivering healthcare solutions across various domains like diagnosis, disease prevention, and treatment of an injury

or illness. However, the effect of software on the safety and performance of medical devices has been dubious, particularly when the device itself is a software alone product. Hence, the medical device software regulations are constantly revised to determine the consideration of Software as a Medical Device (SaMD). In April 2021, the advisory board of the European Commission, the Medical Device Coordination Group (MDCG), had focused on improving the regulations of medical device software and published guidance describing the approach to be applied while determining whether a software is a medical device or not.

Swissmedic Released New Medical Device Regulations

You might be aware, in the context of pending agreements between Switzerland and the EU, there are certain modifications/amendments made to the Medical Devices Ordinance (MedDO) and the Federal Council-approved supplementary provisions for implementing medical device regulations which have been in force since May 26, 2021. These provisions are designed to offset the negative consequences in the absence of an MRA (Mutual Recognition Agreement) update and to ensure a sufficient supply of medical devices in Switzerland. As the MedDO changes have come into force on May 26, 2021, medical device manufacturers willing to enter the Swiss market must understand the amendments and ensure to align with them in their processes for successful compliance.

Australia Updated Regulation of Software as Medical Devices (SaMDs)

The application of software technologies in varied healthcare management, including diagnosis or treatment of a disease, is accelerating at an unprecedented rate. Global medical device authorities are revamping their regulations and guidelines to address these booming device technologies. In January 2021, the TGA released the original draft on medical device software regulations, which was further revised in February 2021. On July 27, 2021, the TGA released a detailed flow chart addressing the common ambiguities that device manufacturers and Regulatory professionals may have about the medical device software classification.

MDCG Initiated IVDR Implementation and Preparedness Plan

In July 2021, the Medical Device Coordination Group (MDCG) published a joint implementation and preparedness plan for the In Vitro Diagnostic medical devices Regulation 2017/745 (IVDR). The IVDR is expected to come into force later in May 2022. As the IVDR implementation sets specific challenges for the stakeholders, the European Commission (EC), and the Member States, the MDCG reviewed relevant inputs from all the stakeholders and established a joint implementation plan. The MDCG document highlighted the most critical aspects of the IVDR implementation process, to assist the parties involved in focusing on their resources and acting in the most efficient way. As per the document, the actual implementation of the IVDR will require the active involvement of all the stakeholders and will include some milestones.

FDA Published a Guidance on 510(k) Submission for a Software Change to an Existing Medical Device

The US FDA published a guidance document to help the industry and the Health Agency (HA) staff determine when software changes to a medical device require a manufacturer to submit and obtain FDA clearance of a new premarket notification (510(k)). This guidance intends to enhance the predictability, consistency, and transparency of the "when to submit" decision-making process by providing a least burdensome approach and describing the Regulatory framework, policies, and practices underlying such a decision specifically related to software changes.

Health Canada's Inspection Process for Licensed Medical Device Establishments

In July 2021, Health Canada released guidance describing how the Agency inspected the licensed medical device establishments, the inspection process, and explained how inspectors should assess the compliance with the Food and Drugs Act and Medical Device Regulations. One section of the guidance describes that the entities involved in manufacturing, promoting, or marketing the medical devices should achieve and sustain compliance with the appropriate requirements set forth under the Food and Drugs Act. The other section describes the factors to be considered by inspectors when assessing the compliance of a medical device establishment with the Regulatory requirements set forth by the Medical Devices Regulations.

MHRA Modified Regulations of Software and AI as a Medical Device

Software and Artificial Intelligence (AI) play an important role in the medical device sector with a fast-developing and wide set of applications in the health care system. However, alongside the rapid developments, Regulatory agencies are updating measures to further protect patient safety and ensure device efficiency. In September 2021, the MHRA developed an extensive work program that provides Regulatory changes across the software as a medical device lifecycle from qualification to classification to pre and post-market requirements. The changes provided in this program are expected to deliver a high degree of protection for patients and intend to ensure that the UK is the home of responsible innovation for medical device software.

Global Health Authorities' Guiding Principles on GMLP for Medical Devices

Over the past few years, evolving technologies have led to the exponential growth of Artificial Intelligence (AI) and Machine Learning (ML). While AI and ML create new opportunities for medical device organizations, the rapid adoption of AI and ML has several risks and complexities, and hence requires stringent regulations. Accordingly, global Health Authorities (HAs) and policymakers keep track of the growing number of AI/ML developments to ensure the laws and regulations are relevant to the new challenges and inventions. To avoid Regulatory challenges and ensure smooth functioning of AI/ML while implementation, the HAs have devised several guidance documents. In October 2021, the USA, Canada, and the UK Health Authorities have jointly identified ten (10) guiding principles for the development of Good Machine Learning Practice (GMLP) for medical devices. These guiding principles assist in promoting safe, effective, and high-quality medical devices that use AI/ML.

Center of Excellence
Global Food and Food Supplements Regulatory Services

The UK Implemented Natasha's Law for Prepacked Food Labels

On October 01, 2021, the UK passed a new labeling law, 'Natasha's Law', requiring all food retailers to display an entire list of ingredients and allergen labeling on each food item made on the premises and prepacked for direct sale. This law is named after Natasha Ednan-Laperouse, a teenager who died after eating a prepacked baguette containing sesame, which did not require allergen labeling at the time. After this event, the Government decided to implement severe laws that would protect the consumer from ingesting food with allergic ingredients.

This Law came into force in October 2021, giving businesses a transition period to prepare for the new rules. This law is expected to bring more consistency in the labeling regulations of prepacked food products, besides preventing end-users from consuming food that has allergic ingredients.

FSSAI Revised Nutraceutical Regulations

The Food Safety and Standards (Health Supplements, Nutraceuticals, Foods for Special Dietary Use, Food for Special Medical Purpose, Functional Food, and Novel Food) Regulations 2016 was implemented on January 01, 2018. Recently, the FSSAI, with the previous approval of the Central Government, made the first amendment in the above regulations. These regulations cover eight (08) categories of functional foods - Health Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purposes, Specialty Food Containing Plant or Botanicals, Foods Containing Probiotics, Foods Containing Prebiotics, and Novel Foods. All the Food Business Operators (FBOs) need to comply with these regulations' provisions from April 01, 2022.

FSSAI Announced New Category for Sweets & Savories

India has a rich tradition of sweets, snacks, and savories with a difference in taste, texture, and ingredients. Traditional milk-based sweets are mostly prepared from khoya, chhena, sugar, and other ingredients such as maida, flavors, and colors. In Additionally, there are sweets containing cereal, starch, or grain as the main ingredient. There are also sweet snacks coated with jaggery, sugar, honey, and other ingredients.

With no specific regulations in place, there are many challenges in the manufacturing and selling of sweets, snacks, and savory food. The packaging and labeling requirements are often neglected. As a result, small and medium food business operators are required to obtain a central license under the proprietary food products, which is costly and entails numerous compliance requirements. Hence, the FSSAI has come up with a new food category

to imply standard procedures for the aforementioned food categories.

Nutritional Label Updates for Food and Food Supplements by the US FDA

One of the amendments applied in the year 2020 for the labeling compliance of food and drinks is the update of the Nutritional Facts Panel by the United States Food and Drug Administration (US FDA). This amendment has been made by considering certain factors, most important of which was the ease for a consumer to choose better food and make informed food choices leading to a long and healthy life.

While existing manufacturers had time until July 2021 to comply with the updated regulations, the new manufacturers and distributors are already taking care of the label compliance in this regard. As per the US FDA, manufacturers with $10 million or more in annual sales were required to update their labels by January 01, 2020, and manufacturers with less than $10 million in annual food sales were required to update their labels by January 01, 2021.

Post-Brexit Labeling Updates for Food Products in the UK

January 01, 2021, was marked as the deadline for the United Kingdom (UK)-based food and beverages manufacturers to implement their product labeling changes. On November 05, 2020, the UK Department for Environment, Food & Rural Affairs (DEFRA) had published an update related to the information to be mentioned on the label of food products that are intended for sale in the UK and the European Union (EU), particularly in Northern Ireland. According to the update, from January 01, 2021, manufacturers distributing pre-packaged food or caseins in Northern Ireland must include the address of a Northern Ireland or EU Food Business Operator (FBO) on the product label. Manufacturers can also mention the address of a Northern Ireland or EU27-based importer.

Center of Excellence
Chemicals Safety and Regulatory Affairs

EPA Revised LCR and Mandatory Timelines - Here is Everything You Need to Know

The U.S. Environmental Protection Agency (EPA) revised the Lead and Copper Rule (LCR) to protect children and communities from the risks of lead exposure. EPA aims to get lead out of the drinking water and empower communities through correct information.

Mandatory Timelines

Effective date: The final rule was going to be effective from December 16, 2021.

Postponed Effective Date: Previously, the effective date of the final rule was published on January 15, 2021, and then delayed in a rule published on March 12, 2021, in which it was postponed until December 16, 2021.

Compliance Date: The compliance date for the final rule is delayed until October 16, 2024.

Registration of Chemical Substances in South Korea

Chemical regulations in South Korea are managed by various Ministries such as the Ministry of Environment, Ministry of Employment and Labor, Ministry of Health and Welfare, Ministry of Agriculture, etc., under numerous laws based on the uses and hazard properties of chemical substances. All the Authorities aim to protect human health and the environment from the toxicity of chemicals. The K-REACH amended Act was published in March 2018 and came into force on January 01, 2019. Any company with an intent to import or manufacture a new chemical substance or an existing chemical substance must register under K-REACH.

Based on the amended K-REACH, the deadline for the registration of new substances to manufacture or import the existing chemical substances greater than or equal to 1000 tonnes per year and CMR substances greater than or equal to 1 ton per year ends on December 31, 2021.

GB BPR Transition Period and Deadlines

Following the Brexit on December 31, 2020, Great Britain is no longer a part of the EU scheme for regulating biocidal products. The existing EU Biocidal Products Regulation (EU BPR) has been transformed to the Great Britain Biocidal Product Regulation (GB BPR). However, most aspects of the EU BPR will continue in the same way under the GB BPR.

Here are a few deadlines that ended in the year 2021 for GB BPR:

Authorization	Authorization Holder must be Established in	Deadlines
Northern Ireland	NI/EU/EEA/Switzerland	January 01, 2021
EU/EEA	NI/EU/EEA/Switzerland	January 01, 2021

Poison Centre Notification and Relevant Deadlines

Poison Centres take the responsibility to collect relevant information about hazardous mixtures and provide medical advice during health emergencies. With various notification systems and information requirements across different countries in the EU, ANNEX VIII of the CLP Regulation was implemented. It aims to harmonize the hazardous information and the format that must be submitted to Poison Centres to improve emergency responses.

Article 45 of the CLP Regulation describes the notification obligations for importers and downstream users who want to place hazardous chemical mixtures in the EU market. The first deadline ended on January 01, 2021, for mixtures classified as hazardous for consumer-use and professional-use products. Therefore, companies manufacturing these products must comply with the new harmonized Poison Centre Notification (PCN) format.

Center of Excellence
Global Cosmetics Regulatory Services

DTAB Advised Voluntary Specification of Veg/Non-Veg Symbols on Cosmetic Products

The CDCSO is responsible for regulating imported beauty and personal care products in India. Over the years, the DTAB had received several proposals and VIP references for an indication to classify products as per their vegetarian or non-vegetarian origin. After detailed deliberation, the Board had given an official notice concerning the indication. The notice specified that manufacturers may indicate red/brown or green dots on beauty care products to indicate their non-vegetarian or vegetarian nature, respectively. This labeling method is applicable for packaging tubes of toothpaste, shampoos, soaps, other cosmetics, and toiletries. The indication, however, would be voluntary for cosmetic manufacturers. This new indication will allow consumers to gain more information about product ingredients and make an informed decision as per their individual preferences.

Brexit and Cosmetics Regulations: What are the Changes?

Brexit had brought about significant changes in the EU and the UK in terms of regulations affiliated with cosmetics, pharmaceuticals, personal care products, and medical devices. The UK decided to leave the EU in 2016 and officially left the trading bloc on January 31, 2020. Both the countries decided to keep a few things unaltered until December 31, 2020.

In 2021, some of the significant changes that took place in the UK cosmetic industry include the role of a Responsible Person (RP), Product Labeling - Responsible Person (RP), Product Labeling - Country of Origin, and Notification.

ANVISA Published Three (03) New Resolutions for Cosmetics

In Brazil, the Agencia Nacional de Vigilancia Sanitaria (ANVISA), i.e., the National Health Surveillance Agency, regulates the production, import, and trade of cosmetics products. To ensure consumer safety and well-being, the ANVISA introduced three (03) resolutions of the collegiate Board (RDCs). These resolutions, published in the official gazette on August 11, 2021, are applicable to cosmetics, perfumes, and personal care products. They are as follows:

RDC 528/2021:

This resolution includes elements of preservative action that are allowed in cosmetics, perfumes, and personal care products. It contains a list with a description of sixty (60) substances.

RDC 529/2021:

In this resolution, the identification of one thousand four hundred and four (1,404) banned substances that cannot be used in personal care products, cosmetics, and perfumes, are listed.

RDC 530/2021:

The third regulation, RDC 530/2021, contains a list of more than a hundred (100) elements that are not permitted in cosmetic products except under the conditions and restrictions established by the Agency. The same Act also contains a separate list of twenty-six (26) components of fragrances and aromas.

These components must be indicated on the labeling of cosmetics, perfumes, and personal care items when their concentration exceeds 0.001% in non-rinse products and 0.01% in rinse-off products.

EC's New Regulation and Mandatory Deadlines For Plastic in Wet Wipes

In December 2020, the European Commission published the Regulation (EU) 2020/2151, which set out harmonized marking requirements for single-use plastic products. Plastic and plastic products have been a constant threat to the marine environment and have far-reaching consequences on marine life. One such example is the Pacific Trash Vortex - a garbage patch of a gyre of marine debris particles in the central North Pacific Ocean. Considering such devastating effects on marine habitats, the updated regulation is a much-needed change that will help in reducing marine waste. The Regulation applied to all the EU Member States from July 03, 2021. It requires marking to be added as a sticker to all packaging of 'Wet Wipes' placed on the market before July 03, 2021.

In a nutshell, 2021 has been a great comeback and has been quite far-reaching in terms of developing stringent regulations. The developments made many of the manufacturers and stakeholders align with the regulations for the best of compliance, and successful and quick market entry of the products.

As a pioneer in offering end-to-end Regulatory services, Freyr has offered customized assistance to many global customers in fulfilling their on-demand needs. In addition to expanding operations to new locations, Freyr has been with the industry to meet new age requirements and hence, has initiated service offerings like UKRP in-country representation and Swiss AR, along with a specialized focus on digital transformation and comprehensive software solutions. Freyr has given a facelift to technological services in the Regulatory arena with the introduction of Freyr Digital.

With a strong foothold in the industry and with advanced service offerings, Freyr is looking forward to stepping into 2022 to ensure that the world sees the best of compliant, safe, and effective medicinal products, devices, cosmetics, food and food supplements, and chemical products.

2022 and Beyond - Stay Ahead of the Compliance Deadlines

Thanks to the rapid development of vaccines and quick vaccinations in major parts of the world, there seem positive developments in all the business sectors towards the growth. However, the threat is persisting in terms of new waves and new variants of COVID. Let us hope we get over this soon and see the brighter side of the business. Even in these darkest times of humankind, few business sectors like Life Sciences are recording good business growth and taking quick strides forward.

The industry is expected to offer a lot to the researchers, innovators, and even regulators, with new scientific, operational, and technological workflows. As a leading Regulatory solutions and services provider committed to customers' compliant global market entry, here are a few upcoming Regulatory mandates or procedural changes we would want the industry to look up to. Let's take a closer look at the Life Sciences and MedTech segments.

Center of Excellence
Global Pharmaceutical Regulatory Services

EMA Releases New Guidance for Nitrosamine Detected Response Template

Per the EMA's new guidance for Nitrosamine detected Response Template, the Committee for Medicinal Products for Human Use (CHMP) has asked Marketing Authorization Holders (MAHs) to follow the latest pathway. For the first step of Risk Evaluation, the deadlines for new submissions to identify the presence of Nitrosamine levels in active substances and the finished products were set for March 31, 2021 (chemical medicines) and July 01, 2021 (biological drugs).

For the second step, named Confirmatory Testing, the MAHs need to conduct mandatory confirmatory testing in the presence of higher levels of Nitrosamine as compared to the approved levels. For marketing authorization modifications post the second step of testing, the MAHs are expected to change the Marketing Authorization Template and make the submissions to the EMA by September 26, 2022, for chemical products and July 01, 2023, for biological medicines.

Center of Excellence
Global Medical Device Regulatory Services

EMA Guidance: Quality Documentation for Drug-Device Combination Products

Given the continuous technological developments and wide range of medical devices or device parts that may be used with a medicinal product, it is essential to have appropriate guidelines on what type of information should be provided in a combination product's Regulatory submission. In August 2021, the EMA released a guidance document describing how qualitatively the dossiers (Marketing Authorization Application (MAA) or Post-authorization Application) should be presented for a medicinal product when used with a medical device or a device part. As the dossiers must be submitted following the Directive 2001/83/EC and/or Regulation (EC) 726/2004, the current guidance document focuses on the product-specific quality aspects of a medical device or device part that may have an impact on the quality, safety, and efficacy of a medicinal product. The new guidelines will came into effect from January 01, 2022.

SFDA Announced UDI Requirements and Deadlines for Medical Devices

It is well-known that a Unique Device Identification (UDI) is critical, and if implemented accurately, it will garner major and long-term benefits for medical device manufacturers, healthcare providers, and consumers. The major benefits of UDI include accurate reporting, reviewing, and analyzing of adverse event reports, reducing medical errors with rapid and precise identification of device characteristics, reduction in counterfeiting, better assessment of device performance, informed patient treatment, and providing a standardized identifier that facilitates efficient management of medical device recalls. However, the key element to achieving these benefits is to follow the specific guidelines issued by various Health Agencies. Recently, Saudi Arabia's medical device regulator, the Saudi Food and Drug Authority (SFDA), released a guidance document stating the revised UDI requirements and compliance timelines for Class B&C (effective from February 01, 2022) and Class A devices (effective from February 01, 2023).

US FDA Published Medical Devices Guidance Documents for Fiscal Year (FY) 2022

The FDA's Center for Devices and Radiological Health (CDRH) has published a list of medical devices guidance documents for the fiscal year 2022. This list of guidance documents conveys a degree of transparency (in terms of where the regulator plans to commit resources and potentially increase scrutiny over the coming year and how manufacturers may be impacted in terms of compliance) for the medical device applicants and registrants who are willing to enter the USA market. The FDA CDRH has divided its list of guidance documents into three (03) sections. The A-list consists of a list of prioritized device guidance documents the FDA intends to publish during FY2022. The B-list consists of a list of device guidance documents the FDA intends to publish as resources permit during FY2022, and the third one, which is the Retrospective Review List, consists of a list of final guidance documents issued in 1982, 1992, 2002, and 2012.

Center of Excellence
Chemicals Safety and Regulatory Affairs

EPA Revises LCR and Mandatory Timelines - Here is Everything You Need to Know

Recently, the U.S. Environmental Protection Agency (EPA) revised the Lead and Copper Rule (LCR) to protect children and communities from the risks of lead exposure. EPA aims to get lead out of the drinking water and empower communities through correct information.

Mandatory Timelines

Effective date: This final rule was going to be effective from December 16, 2021.

Postponed Effective Date: Previously, the effective date of the final rule was published on January 15, 2021, and then delayed in a rule published on March 12, 2021, in which it was postponed until December 16, 2021.

Compliance Date: The compliance date for the final rule is delayed until October 16, 2024.

EU REACH Chemicals Registration Requirements

The European Commission has updated the information requirements for chemicals registration under the EU REACH, intending to make the European Chemical Agency (ECHA) evaluation practices more transparent. The updates of the EU REACH annexes describe the information requirements for the companies that must be submitted during the chemical's registration. The law came into effect on July 08, 2021, and will be is effective from January 08, 2022.

Registration of Chemical Substances in South Korea

Chemical regulations in South Korea are managed by various Ministries such as the Ministry of Environment, Ministry of Employment and Labor, Ministry of Health and Welfare, Ministry of Agriculture, etc., under numerous laws based on the uses and hazard properties of chemical substances. All the Authorities aim to protect human health and the environment from the toxicity of chemicals. The K-REACH amended Act was published in March 2018 and came into force on January 01, 2019. Any company with an intent to import or manufacture a new chemical substance or an existing chemical substance must register under K-REACH.

Based on the amended K-REACH, new substances must be registered before December 31, 2024, to manufacture or import the existing chemical substances manufactured or imported up to 100-1000 tonnes per year, and December 31, 2030, for existing chemical substances manufactured or imported up to 1-100 tonnes per year.

Poison Centre Notification and Relevant Deadlines

Poison Centres take the responsibility to collect relevant information about hazardous mixtures and provide medical advice during health emergencies. With various notification systems and information requirements across different countries in the EU, ANNEX VIII of the CLP Regulation was implemented. It aims to harmonize the hazardous information and the format that must be submitted to Poison Centres to improve emergency responses.

Article 45 of the CLP Regulation describes the notification obligations for importers and downstream users who want to place hazardous chemical mixtures in the EU market. Mixtures intended for industrial use must comply with the new regulations from January 01, 2024. Mixtures that are already placed in the market and notified under the national legislation must comply from January 01, 2025.

EPA to Develop New Approach Methods (NAMs) to Reduce the Chemical Testing on Animals

The Environmental Protection Agency of the US is prioritizing attempts to develop and use New Approach Methods (NAMs) for chemical testing. This new approach will help in reducing the usage of animals as subjects in chemical testing while ensuring the protection of human health and the environment. NAMs are equivalent to "alternatives" to animal testing. This action shows how the EPA is trying to achieve the goal of eradicating the use of animals in chemical testing by 2035. Hence, stakeholders must keep abreast of the upcoming guidelines on animal testing and act accordingly.

Center of Excellence
Global Food and Food Supplements Regulatory Services

FSSAI Revises Nutraceutical Regulations

The Food Safety and Standards (Health Supplements, Nutraceuticals, Foods for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations 2016 was implemented on January 01, 2018. Recently, the FSSAI, with the previous approval of the Central Government, made the first amendment in the above regulations.

These regulations cover eight (08) categories of functional foods listed below:

- Health Supplements
- Nutraceuticals
- Food for Special Dietary Use
- Food for Special Medical Purpose
- Specialty Food Containing Plant or Botanicals
- Foods Containing Probiotics
- Foods Containing Prebiotics
- Novel Foods

All the Food Business Operators (FBOs) need to comply with these regulations' provisions from April 01, 2022.

Center of Excellence
Global Cosmetics Regulatory Services

European Green Deal and Its Impact on the Cosmetics Industry

Maintaining optimal climatic health is one of the major concerns for every individual, and many revolutionary changes have been adopted across various parts of the world to slow down the effects of climate change. To align with the same, Europe, as a continent, has initiated the European Green Deal. The proposal is supposed to directly generate a new growth strategy and transform the EU into an eco-friendly and competitive economy. Per this new proposal, there would be no net emission of greenhouse gases by 2050. The main intention of the European Green Deal is to make the European economy sustainable by focusing on climate neutrality by 2050. To sum it up, the year 2022 promises a gamut of opportunities for the Life Sciences and MedTech industries. It is crucial for the industry stakeholders to abide by the updated regulations and have a keen eye on the nuances of each Regulatory procedure, right from strategy to submissions, for the successful market entry.

Having been in the industry for over ten (10) years, Freyr, with a team of 1200+ Regulatory experts, has successfully assisted 850+ global customers in meeting their compliance requirements across 120+ countries. Would you like to know how we achieved this? The pleasure is ours to take you through the journey and multiple Regulatory scenarios we have been dealing with. Let us initiate the conversation now. Reach out to us.

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Global Medical Device
Regulatory Services

Streamlining your ANDA Submissions

Profound research with poor documentation may not achieve Regulatory approvals. Documenting each section of the ANDA demands attentive preparations by medical writers, else the entire development and marketing strategy will be derailed. Besides research protocols, the regulations, restrictions, and legalities that govern scientific and medical information play a vital role in ANDA submissions. Knowledge of Regulatory intricacies, efficient planning, and documenting data in the right way will lead to successful submissions.

ANDA submissions demand stringent timelines. To curb costly delays, it is required to employ proficient medical writers to develop the ANDA modules. Medical writers significantly contribute to the development of the following sections of the CTD.

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- **Module 5** – Bioequivalence Studies – The complete bioanalytical study methods and reports used in BE studies.
- **Module 2.7** – Clinical Summary – Develop the Data on Bioequivalence (DBE) tables and provide the safety and efficacy summaries including Biowaiver justification, wherever applicable.
- Apart from clinical modules development, specific writers need to be employed for CMC, labeling, and patent & exclusivity related documents.

Takeaways for Successful ANDA Submission

Every nook and corner of clinical and nonclinical research data relies on medical and scientific documentation. Here are the important takeaways every medical writer should inculcate in the ANDA application, as guided by the FDA.

Overviews and Summaries: Referred to as Module 2 documents in the ANDA eCTD format. Module 2 contains the Quality Overall Summary (QOS - providing an overview of the Chemistry, Manufacturing, and Controls) and Clinical Summary (providing bioequivalence data, safety, and Pharmacokinetic parameters). This module should represent the integrated and critical assessment of the pharmacologic, pharmacokinetic, and toxicologic evaluation of the pharmaceutical. Generally, Nonclinical Overview, Nonclinical Summary, and Clinical Overview are not required for ANDA.

Nonclinical Study Reports: Generally, the ANDAs do not require data for Module 4. But, if any nonclinical study reports or safety assessments are submitted supporting proposed specifications like toxicology studies to qualify impurities as per the ICH guidance for industry Q3A and Q3B(R2), residual solvents, leachables, or excipients; these reports or assessments should be included as part of the submission in Module 4.

Clinical Study Reports: The data derived from all the clinical studies (Bioequivalence) supporting the ANDA will be part of Module 5. The tabular listings of all clinical studies, biopharmaceutic and bioequivalence studies, and the literature references are included.

Conclusion

Conclusively, adhering to the FDA recommendations, medical writers must monitor the compliance of the ANDA as per the applicable guidelines, alongside articulating and documenting the essence of clinical and nonclinical (as applicable) research outcomes in a clear and concise manner. Submitting inconsistent, inaccurate, or incomplete information in CTD modules lead to refusals based on Refuse to Receive (RtR) guidelines. Refer to an expert Regulatory medical writer for gap analysis and compliant submissions. Stay informed. Stay compliant.

Center of Excellence
Regulatory Affairs

An Overview of Clinical Overview

Clinical Overview is a document presenting a critical analysis of Pharmacology, Efficacy, and Safety of the pharmaceutical agent. This document is developed for multiple objectives like product registration, justification for labeling document, and so on. A clinical overview helps the reviewer to understand the objective of the application and clinical development plan for a product in scope.

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A Clinical Overview is an integrated document intended to provide critical analysis of the pharmacology, efficacy, and safety of the pharmaceutical agent in humans. It is one of the important documents of Module 2 of the Common Technical Document (CTD) i.e., Module 2.5, which refers to the data provided in the comprehensive clinical summary, the individual clinical study reports presented in Module 5, and other relevant reports. It provides concise information about the conclusions and the implications of the clinical data provided in the dossier with a conclusive interpretation on the benefit-risk assessment of the medicinal product in scope.

The main sections of a Clinical Overview include product development rationale, overview of biopharmaceutics, overview of pharmacology, overview of efficacy, overview of safety, benefits and risks conclusions, and applicable references. The CTD enables the customisation of the subsections based on the requirement, purpose of the clinical review, and the data available for the specific product in scope.

A Clinical Overview provides a brief discussion and interpretation of safety and efficacy findings related to the product, along with other relevant information (e.g., pertinent animal data or product quality issues that may have clinical implications), based on the findings from the clinical studies and/or published literature. Providing the strengths and limitations of the development program and study results help in analyzing the benefits and risks of the medicinal product for its intended use. It serves as a reference to the overall clinical assessment of the product and supports the information provided in the prescribing information.

The Clinical Overview is developed for a variety of requirements in today's scenario. Accordingly, there are two (2) types of Clinical Overviews: The Prospective and Retrospective Clinical Overviews. A Prospective Clinical Overview can be solely developed based on studies conducted by the innovator (for a new drug application to get the product registration), or data from studies conducted by the innovator and published literature data (for a hybrid application or 505b2 type of submissions, wherein the applicant rely on some of the safety and efficacy information derived from the Clinical Studies conducted by the Original Innovator), or solely developed by using data from published literature references (for Generic submissions or other submissions such as "Well Established Use" or "Bibliographic Submissions"). In all the above situations, the purpose of the Clinical Overview is to support the application as a part of marketing authorisation.

With regards to Retrospective Clinical Overview, this document is generally not submitted to Regulatory agencies as a part of registration dossiers. However, it is developed as a substantiation/justification for the core labeling documents (e.g., Company Core Data Sheet (CCDS) or Company Core Safety Information (CCSI)) developed by the innovator, to showcase the company's standpoint on the information related to safety and efficacy of a particular medicinal product in scope.

When a Marketing Authorisation Holder (MAH) has multiple registrations for a product across the globe, the format and extent of content (volume and depth of information) of the product information available in each country's labeling document vary significantly. This creates an ambiguity to when considering what is the actual safety and efficacy information of the product in scope. In these situations, the MAH can select one of the registered country's labeling documents as Reference Safety Information (RSI) or create core labeling documents (CCDS or CCSI).

Most MAHs prefer to develop the core labeling documents to represent the company's standpoint on the safety and efficacy of a particular medicinal product by using all the relevant information already available with them for that Product. Hence, the term used is retrospective development. The process would not end by developing only core labeling documents, it is required to develop the justification or substantiation document for the information available in the core labeling documents. This is the beginning of the development of a retrospective Clinical Overview to have the evidence for the safety and efficacy information available in the core labeling documents. This process is evolving and every time there is an update to core labeling documents (life cycle management), the Clinical Overview also needs to be updated to provide evidence to the changes made to core labeling documents.

The update to core labeling documents can be either safety or non-safety related. The trigger to update can be internal or external. Internally driven changes are based on safety monitoring, resulted from post-marketing studies or post-authorization safety studies, and may be due to open signals,whereas the externally driven changes include the changes suggested by Regulatory agencies. Whether the safety changes are internally driven or externally driven, post-validation of the changes, the update to core labeling documents, country labeling documents (in case of Agency driven) along with the justification document (Clinical Overview) is required. As the Clinical Overviews developed for internally driven or externally driven safety

changes are related to specific safety information and safety section these are termed as Abbreviated Clinical Overviews.

Additionally, these simpler versions of the Clinical Overviews are developed and submitted to Regulatory agencies as a part of life cycle management activities and/or market extension for a particular medicinal product. These overviews are used to substantiate the labeling changes during the post-approval part of the medicinal product's/drug's life cycle. Apart from internally or externally triggered safety changes, these overviews can focus on the specific update to the labeling documents related to efficacy, pharmacology, or any other information. These overviews are termed as Abbreviated Clinical Overviews (ACO), Addendum to Clinical Overviews (ACO), Tailored Clinical Overviews (TCO), Customised Clinical Overviews (CCO), etc., as these documents are confined to specific information updates related to the medicinal product. Although the terminologies may differ based on the company's specific processes, the purpose it serves is the same.

Irrespective of the type of Clinical Overview and the time of its submission, the level of evidence is very important. When the Clinical Overview is developed solely based on the clinical studies conducted by the sponsor for a new chemical entity, it is the first consolidated document that talks about the product's safety and efficacy. In this scenario, the Clinical Overview should reveal the strengths and limitations of the clinical development program and study output. It should also provide the benefits and risks of the product for the intended use.

When the Clinical Overview is developed for hybrid applications or the evidence comes from the studies conducted by both the sponsor and the literature data, the purpose and development-strategy of the Clinical Overview should be clearly presented to help the reviewer. Development of a hybrid Clinical Overview may trigger by introducing some novelty to the existing approved product. This may be a change in indication, new indication, new dosage form, new strength, new route of administration, new combination, new presentation, new target population (introducing paediatric indication), etc. The pros and cons of the change must be mentioned with the available evidence.

In a scenario where the Clinical Overview is developed entirely based on literature data (for generic or bibliographic or well-established use submissions), it is very important to consider the level or quality of evidence (hierarchy of evidence) to identify the literature articles. It is recommended to take help from medically qualified personnel in this process. In general, the well-accepted quality of evidence can be presented based on preference as follows.

- Clinical Practice Guidelines
- Meta-analysis and/or Systematic reviews
- Randomized Controlled Trials
  - Active Treatment Controlled Trials
  - Placebo Controlled Trials
- Uncontrolled Trials
- Cohort Studies
- Retrospective Studies
- Case Series
- Case Reports
- Expert Opinions
- Narrative Reviews
- Editorials

In cases where a lot of information is available, the literature with high-quality evidence would be preferred to use to develop the Clinical Overview. It is acceptable to omit the lower level of evidence when a significant amount of data is available with a high level of evidence. A few other points to consider while identifying the information for Clinical Overview are the impact factor of the journal, relevance of the information, the objective of the article, statistical parameters used, results of the trials or meta-analysis, statistical significance, power of the study, subset of the population enrolled, efficacy or safety parameters used, and precision of analytical methods used (but not limited to).

The information mentioned in each subsection of the clinical overview should be relevant to the subsection with the proper flow of the information. This helps the reviewer to understand your case and the objective of the document. Below is the information that can be covered in each subsection of the Clinical Overview. Product Development Rationale section should provide the details on pharmacological class of the product, give details on the pathological conditions in which the product is intended to be used, describe the existing therapeutic options available for the current condition in scope, how the product in scope is superior with regards to safety and/or efficacy or improve the condition/compliance (once daily versus multiple administrations, oral administration versus parenteral administrations), etc. This section should also cover the clinical development programme with details like completed, ongoing, and planned clinical studies and the basis for the application. A summary of the scientific advice received (if any) from the Regulatory agency can be provided.

An overview of biopharmaceutics should represent the critical analysis of the problems related to bioavailability or bioequivalence of the product that might directly or indirectly affect the safety or efficacy of the product in scope. In case of generic submissions with bioequivalance studies are part of the submission, a summary on the bioequivalence parameters and how the marketed formulation is equivalent to reference products (90% confidence intervals for Cmax, AUC 0-t and AUC0-inf) can be provided. If there is any study conducted to show the influence of food on the product's rate, the extent of absorption can be provided.

An overview of pharmacology should cover the information related to pharmacokinetics and pharmacodynamics of the product. This section should address pharmacokinetics in healthy subjects, patients, and special populations (paediatric, geriatric, pregnant women, lactating mothers, patients with renal impairment, patients with hepatic impairment, obese patients, cancer patients, patients with human immune deficiency virus, etc.). It also covers intrinsic factors (age, sex, race), extrinsic factors (diet differences, smoking, concomitant drugs), and pharmacokinetic interactions and their output. Details on rate and extent of absorption, distribution details, information related to metabolism and metabolites, and excretion are included. With regards to pharmacodynamics, mechanism of action, receptor binding, onset of action, pharmacokinetics/pharmacodynamics relationships, and pharmacodynamic interactions can be covered.

An overview of efficacy should provide the critical analysis of the efficacy of the product in intended use in the intended population. The analysis should cover the relevant data and should explain why and how the information supports the proposed use and the data in prescribing information. The quality of evidence should be considered and if there are any issues with efficacy parameters employed in the study or premature termination of the studies, they can be described with proper reasons. If there are any studies conducted in special populations, they should be clearly mentioned and if there are no studies conducted, support should be provided to extrapolate the efficacy data from the general population to the special population.

Overview of safety should cover the critical analysis of the safety data with regards to adverse effects (details on common, non-serious, and serious), warnings and precautions, drug interactions, safety in special populations, overdose, and its management. The adverse events data should be provided in detail with relevant tabulations and frequency of the adverse events, nature of patient population, and extent of exposure to be provided.

The benefits and risks conclusions section should provide the succinct, integrated, and properly explained assessment of the product for the intended use. If multiple indications are proposed, the benefits and risks conclusions should be provided for each indication. This section should be developed based on the proper weighing of key benefits and the key risks without any ambiguity. Finally, a list of references used in developing the Clinical Overview is to be included.

This article was first published by:

PHARMA FOCUS ASIA

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All You Need to Know About the Conformity Assessment Bodies (CABs) for Your Device's Malaysian Market Access

The Conformity Assessment Body (CAB) plays a vital role in issuing various certifications and carrying out technical assessments required for successful registration and distribution of your medical devices and IVDs.

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This part of the blog series introduces the Medical Device Authority (MDA's) requirement for CAB certification. The series will take you through the role of CABs in device registration and approval in Malaysia.

The CABs are entitled to perform the assessments under the below regulations -

- Medical Device Act 2012 (Act 737)
- Medical Device Regulations 2012
- Circular Letter of the MDA No.2/2014 on Conformity Assessment by way of Verification
- ISO 13485, Medical Device – Quality Management Systems (QMS) – Requirements for Regulatory purposes

The entities should be registered as Conformity Assessment Body (CAB) with the Medical Device Authority (MDA), Malaysia, to evaluate the device manufacturers or other stakeholders involved in a device supply chain. The CAB must be a registered entity in Malaysia, evaluated and approved by the MDA, and is continuously monitored by the Agency. The person responsible for the management and operations shall be a Malaysian citizen.

The MDA clearly defines the requirements for an entity to act as a Conformity Assessment Body (CAB) in Malaysia. The requirements are defined in relation to:

- The structure and composition of the organization acting as a CAB
- The resources of the CAB and the technical competency of the personnel
- Independent and impartial nature of the operations - procedures, liabilities, and confidentiality
- The required Quality Management Systems for carrying out conformity assessments
- Product testing, in case the CAB also carries out testing as a part of conformity assessment
- Process of how the CAB would carry out conformity assessment
- Communication of CAB changes with the clients and the MDA
- Communication arrangements between the client and the MDA on changes that may impact the compliance

The entity intending to obtain the CAB registration shall submit the application through the online system available at the MDA portal, www.mda.gov.my, Medical Device Centralised Online Application System (MeDC@St) along with the application fee. Any request from the MDA to submit missing or additional information shall be submitted within thirty (30) days from the date of such a request, or the application will be considered as withdrawn. The applicant must make a new application unless an extension to the timelines for submitting additional information is granted by the MDA.

The Agency may inspect the premises the applicant intends to use. If the applicant is approved by the MDA, a registration fee shall be paid. Only after the registration fee is received by the MDA, a registration certificate would be issued.

Once registered, the CAB can start accepting the applications from various stakeholders for certifications and registering their devices in Malaysia.

Are you aiming to launch your medical device or IVD in the Malaysian market? Reach out to a Regulatory expert. Stay informed. Stay compliant.

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Best Practices For Writing An IVDR-Compliant Performance Evaluation Report

Do you know? A non-compliant IVDR performance evaluation report poses risks during the authorization process and risks patient safety. This paved the path for strict and robust IVDR requirements on the performance evaluation of IVDs.

What Is Clinical Evidence?

As per the new European regulation 2017/746 on in vitro diagnostic devices (the EU-IVDR), "'Clinical evidence' means clinical data and performance evaluation results, of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s) when used as intended by the manufacturer."[1]

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In short, clinical evidence is the data that supports the use of the device, which is required for all IVDs irrespective of the class, based on assessed data used to demonstrate compliance with the general safety and performance requirements (GSPRs) laid out in Annex I of the regulation. As the IVDs are classified in accordance with the rules set out in Annex VIII of the regulation in a risk-based approach, the amount and quality of the clinical data varies among the device classes.

How To Gather Clinical Data For An IVD

The building blocks of the clinical evidence are based on three integral pillars for an in-vitro diagnostic device, namely:

- Scientific validity
- Analytical performance
- Clinical performance

Scientific Validity: Scientific validity means the association of an analyte or marker with a clinical condition or a physiological state. This can be demonstrated through a literature search if enough information with adequate quality can be found to establish the validity.[2] Additionally, consensus expert opinions result from proof of concept, and clinical performance studies may be utilized as sources of data. The scientific validity of the analyte or marker is documented in the scientific validity report.

Analytical Performance: Analytical performance is the ability of a device to correctly detect or measure a particular analyte. The analytical performance of the device shall be demonstrated in relation to the following parameters (unless any of them can be justified as not applicable): analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off (including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference), and cross-reactions.

Generally, analytical performance is demonstrated based on analytical performance studies and is demonstrated and documented in the analytical performance report.

Clinical Performance: Clinical performance is the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state, in accordance with the target population and intended user. The clinical performance of the device shall be demonstrated using the following parameters (unless any of them can be justified as not applicable): diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, and expected values in normal and affected populations.

Demonstration of clinical performance must be based on the clinical performance studies, scientific peer-reviewed literature, and/or publishing experience gained by routine diagnostic testing. Clinical performance studies should always be performed unless it can be justified that a demonstration based on other sources of clinical data is sufficient. The clinical performance should be demonstrated and documented in the clinical performance report.

The gathering of clinical evidence from these elements occurs throughout the lifetime of the device, which results in a rule of thumb as depicted below:

Performance Evaluation Plan

A Performance Evaluation Plan or PEP consists of the procedures and methods to correctly perform and appropriately report the performance evaluation. According to the EU-IVDR, the PEP should cover at least the following:

- The intended purpose of the IVD
- Description of the analyte
- Target population
- Description of the state-of-the-art
- Steps for demonstrating the scientific validity, clinical performance, and analytical performance
- Determination of the acceptability of the benefit-risk ratio

Performance Evaluation Report (PER)

The Performance Evaluation Report is an output of the process of performance evaluation activities populated from the results of applying the PEP. Annex XIII, Part A (1.3.2) of the IVDR outlines the specific components of the PER and specifies that it must include:

- The scientific validity report
- The analytical performance report
- The clinical performance report
- An assessment of all these reports supporting that the demonstration of the clinical evidence is sufficient to decide on the benefit-risk ratio.

Performance evaluation reports for Class C and D devices 3, 4 must be updated at least annually, whereas PERs for Class A and B5 devices should be updated as needed, although at least a three (03)-year review cycle is recommended. Along with the above-mentioned elements of the performance evaluation, this should include continuous planning and gathering reports of post-market surveillance, as well as identifying and assessing any new/upcoming/residual risks as per the risk-mitigation activities.

The practical considerations to be taken into account while preparing a PER include:

- The reasoning behind the clinical evidence gathering methods used, including literature searches (related protocols and reports)
- A description of the technology behind the IVD
- The intended purpose and associated claims
- The actual scientific validity and the analytical and clinical performance data that have been evaluated
- The clinical evidence supporting the use of the device when assessed in the context of the current state-of-the-art
- Any new conclusions coming from post-market performance follow-up or other sources

Conclusion

The impact of European In-Vitro Diagnostic Regulation 2017/746 (IVDR) on the device industry is more profound than the impact of European Medical Device Regulation 2017/745 (MDR). The majority of IVDs under the earlier IVD directives were self-certified and did not involve any notified bodies for conformity assessment. In contrast, around 90% of IVDs now require the involvement of notified bodies. Also, new requirements for establishing the performance of an IVD have been introduced in the EU IVDR, adding a significant volume of Regulatory work for IVD manufacturers. Receipt of insufficient or irrelevant data will result in the issuance of major non-conformities by notified bodies. You should take into account all the practical considerations described above when building the performance reports for your IVDs.

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This article was first published by:

MED DEVICE ONLINE

FREYR CONNECT

FREYR REGULATORY ARTWORK SERVICES

Key Process Elements to Achieve Successful Artwork

What is an ideal workflow of artwork? What are the key process elements to achieve successful artwork? Get a clear-cut understanding on some of the pressing artwork challenges and the implementation of key process elements.

Key process elements to achieve successful artwork

Pharma and life sciences companies are governed by the global Health Authorities with stringent quality norms. With years spent on innovating new drugs, life sciences organizations may not have have sufficient time available for artwork design processes, which may result in an incompliant product presence. In such scenarios, a company's well-defined artwork management system plays a key role in curtailing the possible compliance setbacks. With defined Regulatory artwork processes, organizations can sustain such critical situations, especially in time-bound pressures.

Introduction

Being an intrinsic part of the pharma product supply, the artwork process always goes through constant pressure to deliver accurate output in a compressed time frame. Even minuscule errors (such as misplacement of a decimal point) can be costly, damaging, and put companies at risk owing to the threat of product recalls, Health Authority warnings, and fines. According to the data by the US Food and Drug Administration (USFDA) over a six (06)-month period, there were a total of four hundred and fifty-five (455) recall notices, of which 51 per cent were attributed to mislabeling and 13 per cent to faulty packaging, which sometimes root back to artwork inefficiencies.

Due to tough Regulatory requirements and heavy investments in innovative or generic products, pharmaceutical and life sciences companies across the world must have established and defined artwork processes in place that guarantee zero errors and secure timely approvals for quick market entry of the products. These can truly be possible by implementing technology-driven robust processes that help to efficiently integrate the areas of repository management, data management, label Regulatory control, authoring, and design control.

Artwork Process Challenges

It is quite evident that when it comes to artwork management, there are certain challenges. If these challenges are not addressed timely, there is a risk of Regulatory fines and recall, increased time-to-market, loss of competitive position, and damaged brand equity. Here are a few of them:

1. **Compliance burdens:** Artwork and labelling compliance is probably the biggest challenge for pharma companies of any size. From keeping abreast with the ever-evolving local or regional Regulatory authority updates to adapting to the new market requirements, it is a huge and complex task. For a company whose core focus is to innovate medicinal products, it is challenging to track the Regulatory updates.

2. **Recall risks:** Product recall is a terrible experience for a manufacturer. As per research, it is believed that more than 50 per cent of product recalls are due to labeling or artwork packaging, and more than 60 per cent of all recalls are caused by human errors. The consequences of product recalls are dire. Also, such errors may cause serious risks to patient safety, which may result in fines, reputational damage, and even job losses.

3. **Multiple artwork revisions:** Reworks can be costly, time-consuming, and ultimately cause delays in the artwork review and approval process. When a job card is initiated without much information on the drug, there will be delays and errors, resulting in rework. Also, reactive and poor communication are the major reasons that cause unnecessary revision cycles that consume resources' bandwidth and delay the artwork design output.

4. **Poor tracking of the process:** The artwork process flows across many facilities and regions globally makes it difficult to track. Hence, it is challenging to track accurate information and report and measure performance. It calls for a necessity for process centralisation to enable visibility throughout the product lifecycle for identifying any bottlenecks and process inefficiencies.

5. **Difficulty integrating with partners:** Integrating with partners and global expansion will be highly difficult to achieve without a standardised artwork workflow. Also, improper communication with the partners results in more reworks that delays the entire process, which in turn may cost much to a partner.

6. **Delayed time-to-market:** Poor stakeholder visibility, inefficient processes, and difficulty in ensuring the completion of mission-critical tasks along with all the challenges mentioned above can put the artwork creation and approval process at a source of risk, resulting in delayed market entry. The consequences of delays can be significant and costly.

An Ideal Artwork Process Workflow

To secure a compliant marketplace, manufacturers must follow an ideal workflow for artwork. It can be like as follows:

Implementation of Key Process Elements for Successful Artwork

Pharma artwork is a complicated and lengthy process similar to developing the product itself. Implementation of standardised process elements and automation can protect organizations from vulnerabilities and accelerate their existing workflows. Here, we discuss some of the key elements to achieve successful artwork.

Aligning unstructured data: Many pharma and life sciences companies are still using traditional methods such as spreadsheets to manage their artwork and approval processes. It necessitates routing of printed documents, which host a lot of risks and inefficiencies through emails and folders. These documents can easily be lost, damaged, or misplaced, costing valuable time and resources. Also, in such cases, it becomes difficult to find out which document is the most recent. Without a proper version, it is never clear that your spreadsheet has been routed to the right parties for approval.

A well-established document management system working in a closed-loop can save the day. It helps to keep track of all the required documents and provide the right version at the right time with proper electronic signatures validated, and drives a higher level of accountability.

Streamline artwork process: Pharma must have an ideal artwork process to come up with error-free artwork with quick time-to-market. Therefore, organizations must move towards standardising and harmonising the existing processes. It helps in creating and developing artworks under a common platform in a standard way.

Standard Operating Procedures (SOPs) also play an important role in regulating and operating processes and workflows. Creating result-driven SOPs can outweigh the challenges, monitor the entire lifecycle, improve overall performance, and provide right-first-time artwork.

Transform to automated/digital artwork management: The traditional artwork management process has been cumbersome. There are still many companies using the old manual processes for artwork management. Incorporating an automated artwork approval process into your product lifecycle can help you deliver on-time, quality work consistently. Automation acts as an aid for manual work. An automated tool can help teams apply their attention to moving the projects forward and speeding up time-to-market.

From original documents to graphics and design layouts to finished materials, automation can quickly verify the diverse components. Text verification tools can ensure error-free documents. Such automated solutions are readily available and easily leveraged to transform productivity and optimise outputs.

Enable Regulatory compliance: There are various regional compliance standards, language differences, and consumer needs that make the artwork process increasingly difficult. It is crucial to keep track of the ever-changing regulations with an audit trail of all projects with the help of a digital tool to ensure compliance with regulations such as ISO certifications and 21 CFR Part 11. Hence, the tool should maintain a permanent record of the entire project, including all approval points, statuses, dates, and users involved in any critical route. It helps users to monitor output and streamline processes within their divisions, as well as with their supply chain partners and consumers.

Conclusion

In a nutshell, product artwork and packaging play a critical role in the market entry of medicinal products. With quicker time-to-market, a product's influence on consumers and brand recognition can be maximised. It indeed is highly recommended to implement the process elements in a structured way.

This article was first published by:

EXPRESS PHARMA

Center of Excellence
Global Cosmetics Regulatory Services

EC's New Regulation and Mandatory Deadlines for Plastic in Wet Wipes

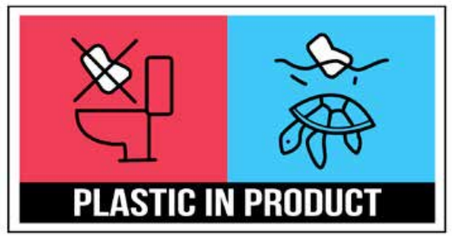
Labeling and packaging are the two (02) important stages in the product lifecycle. They allow the consumers to know more about the product and understand its appropriate usage. From a manufacturer's point of view, correct labeling helps in achieving compliance with the Regulatory bodies, defining the quality, and providing statutory warnings to consumers. In this regard, it is quite crucial for a manufacturer to keep track and be cognizant of the changing Regulatory requirements across the globe.

In December 2020, the European Commission published the Regulation (EU) 2020/2151, which sets out harmonized marking requirements for single-use plastic products. Plastic and plastic products have been a constant threat to the marine environment and have far-reaching consequences on marine life. One such example is the Pacific Trash Vortex - a gyre of marine debris particles in the central North Pacific Ocean. Considering such devastating effects on marine habitats, the updated regulation is a much-needed change that will help in reducing marine waste.

Key Points from the Updated Regulation

1. The product that contains plastic should never be washed off due to its potentially harmful nature to the marine environment.

2. The Regulation applies to all the EU Member States from July 03, 2021.



3. The marking may be added as a sticker to all packaging of Wet Wipes placed on the market before July 04, 2021.

4. I would switch point three (03) and five (05) to retain chronology.

Conclusion

The Regulation came into force in January 2021 and the required marking should be applied to all the EU Member States from July 03, 2021.

In the light of the updated requirements, Wet Wipe manufacturers should ensure that their products conform to the EU laws within the stipulated deadlines and therefore face no restrictions in the EU market. How precise is your knowledge of the updated Regulation? Consult a Regulatory expert to keep abreast of the defined deadlines. Stay informed. Stay updated.

FREYR CONNECT

Center of Excellence
Chemicals Safety and Regulatory Affairs

EU CLP Regulation: Requirements for Labeling & Packaging

The chemicals industry plays a pivotal role in producing petrochemicals, polymers, basic inorganics, specialities, and consumer chemicals in Europe. The European Chemicals Agency (ECHA) implements the EU's chemicals legislation to protect health, safety, and the environment. Classification, Labeling and Packaging (CLP) regulation helps in identifying hazardous chemicals and informs users throughout the EU about their hazards. The regulation ensures a good understanding of the chemical substances and mixtures, and facilitates free flow of goods.

Recently, the ECHA released a guidance on labeling and packaging requirements for hazardous chemical substances, intending to assist suppliers of chemical substances and mixtures. According to the guidance, the following suppliers must ensure that their substances and mixtures are labeled and packaged as per the CLP regulation:

- Importers of substances and mixtures
- Manufacturers of substances
- Distributers of substances and mixtures, including retailers
- Downstream users of mixtures and substances, including formulators

Labeling Rules for Substances and Mixtures

According to the guidance, any substance or mixture classified as hazardous substances under the CLP Article 17 must display a label with the following elements:

- Name, address, and telephone number of the supplier
- Quantity of the substance or mixture
- Product identifiers
- Hazard pictograms
- Hazard statements
- Relevant signal word
- Appropriate precautionary statements
- A section for supplemental information

For mixtures falling under the scope of CLP Article 45 and Annex VIII, a Unique Formula Identifier (UFI) must also be added/printed/affixed to the label.

According to the CLP Regulation, the label must be written in the official language/languages of the Member States where the substance/mixture is going to be placed. Suppliers can either provide multi-language labels covering all the official languages of the respective countries where the substance or mixture is/going to be supplied or can provide separate labels for each country aligning with the regional language standards.

Packaging Rules for Substances and Mixtures

The requirements for packaging of hazardous chemical substances/mixtures are provided in the CLP Article 35, which include the following:

- The packaging must be designed, constructed, and fastened in such a way that the contents do not escape.
- The materials of the packaging and fastening must not be damaged by the contents. Also, when in contact, they should not be liable to form hazardous compounds with the products.
- Strong and solid packaging to ensure that they will not loosen.
- Packaging must be fitted with replaceable fastening devices to allow repeated fastening without the misplacement of contents.
- The packaging must not attract children or mislead the consumers.
- Do not use similar packaging designs for foodstuff/animal feed/medicinal/cosmetic products which may mislead the consumers.

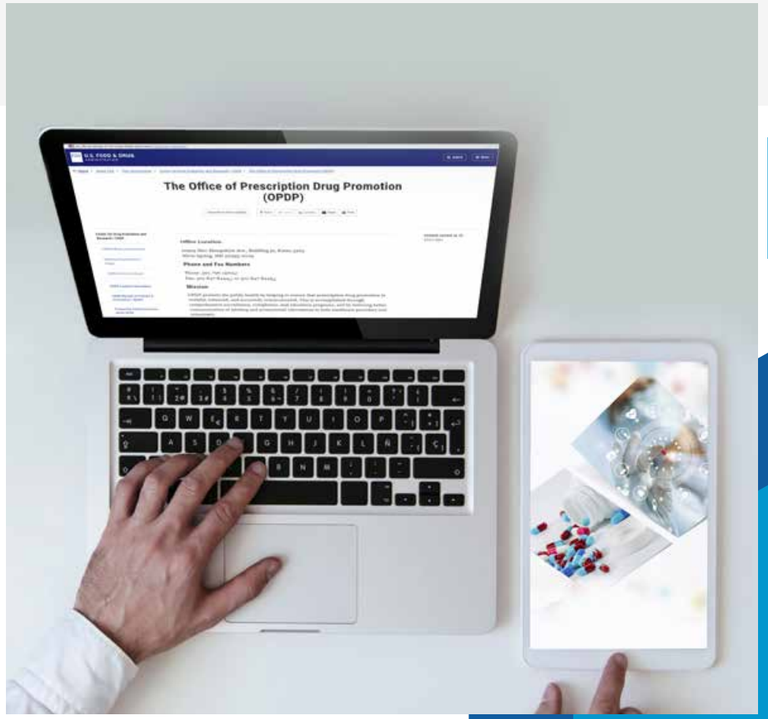
For substances and mixtures that are supplied to the general public, the packaging must:

- Use child-resistant fastening (CRF), also called child-resistant closure
- Use tactile warnings of danger (TWDs)
- Provide additional safety measures based on the product

Conclusion

In a nutshell, the European chemicals industry provides excellent opportunities to the suppliers of chemical substances and mixtures. Therefore, to enter the EU market, it is essential to understand every aspect of the regulations under the ECHA's chemical legislation such as the EU REACH, CLP, and BPR. Get in touch with Freyr for a smooth Regulatory sail. Stay informed. Stay updated.

Center of Excellence
Regulatory Medical Writing



The New Normal of "Pharmaceutical Ad Promo Material"

In an era of Type-Backspace-Enter, relying on the Ink-Paper-Print model especially amidst the global pandemic can be worrisome. Traditional brand communication becomes a difficult affair due to social distancing measures and hence, the society is adapting to the 'New normal'. Brands across the globe have already adopted changing trends in communication aligning with various pandemic norms. Industries across nations have, therefore, proven their agility in a true sense.

In a whirlpool of changing dynamics, the quality and authenticity of communication mustn't be compromised. Serious medical information, written briefly in the most concise manner of spacing, requires stringent regulations for compliance.

Reduced frequency of Medical Representative (MR) visits to doctors have made it difficult for brands to stay in touch with the prescriber. As a result, innovative ways and languages to position your brand correctly, seem necessary. Along with miscellaneous strategies and diverse mediums available for promotions, monitoring and reviewing brand communication is of essence. When it comes to brand communication and material surrounding the brand image, it can get overwhelming, specifically for medical practitioners, to absorb information arranged in a fashion that increases cognitive load. Projecting fancy jargons and creative medical terminologies won't ensure proper positioning in traditional as well as remote modes of advertising.

The dynamic nature of changing regulations requires dynamic brands, functioning at the same octave to understand the needs & expectations of the customer. Understanding your brand needs and portraying them in just the way what you believe along with remaining compliant standards is what Freyr's expertise is. Pioneer towards healthcare 4.0 negating the Regulatory hindrances.

Irrespective of the campaigning trends, catching up with the velocity of advertising & promotional growth in pharma requires brands to blend the following in their strategy:

Patient centricity

Clear understanding of what is to be conveyed and to whom should it be conveyed

- **Accelerated deliverability of information**
  Integrating marketing efforts to deliver brand-related information in a better and accelerated way
- **Enhanced awareness**
  Informed patients in the digital era constantly seek out brands to understand the information available at the right place in the right manner
- **Weighing success/failure of campaigns**
  Involving ad promotional activities ensures brand presence in the marketplace
- **Reducing cognitive load**
  Concise and appropriate information that help your audience to recall the communication while making an informed choice

Center of Excellence
Global Medical Device Regulatory Services

Ordinance Update for INMETRO Certification: New Changes in Conformity Assessment Requirements

The Brazilian Medical Devices Market is growing significantly and is expected to reach USD 1.8 billion by 2023. Medical devices in Brazil are regulated by the National Health Surveillance Agency (ANVISA). Some medical devices require additional safety certification and accreditation by the National Institute of Metrology, Standardization and Industrial Quality (INMETRO) before the registration at ANVISA. The manufacturers should conduct testing and must obtain INMETRO certification through an accredited Certification Body (CB).

The Brazilian INMETRO certification is a mandatory requirement for all classes of electro-medical devices under IEC 60601. Other non-electrical products such as Dental Handpieces (ISO 14457:2012), hypodermic needles, gloves, syringes, etc., also require INMETRO Certification for selling the devices in Brazil. The INMETRO certification requirements have been in place for a long time. On December 18, 2020, INMETRO updated the conformity assessment requirements under the new INMETRO Ordinance No. **384/2020, which has replaced the previous Ordinance No. 54/2016. The new ordinance has brought changes in the validity of the certificate and requirements for renewal, on-site inspections and test reports.**

Earlier, the validity of the INMETRO Certificate was of five (05) years and required renewal of certification before expiry. Under Ordinance No. **384/2020, the INMETRO Certificates do not have an expiry. The validity of certificates is maintained by carrying out regular audits every 15 months, or at least once annually.**

On-site inspections were carried out earlier for the process of INMETRO Certification of medical devices. These on-site inspections are no longer a requirement for all the certification processes after the publication of Ordinance No. 384/2020. The certification bodies will review the results of previous audits performed as per the standards of MDSAP or ISO 13485 and decide whether an on-site inspection is necessary. A desktop audit will be carried out for the INMETRO process if the certification bodies decide that an on-site inspection is not required.

Earlier, test reports issued within two (02) years were required for the process of INMETRO Certification. Since the publication of Ordinance No. 384/2020, the test reports older than two (02) years (for small and medium-sized equipment) and older than four (04) years (for large equipment) are acceptable for the INMETRO Certification process. However, the manufacturers should conduct new testing if any changes are made to the device after the issuance of test reports.

The INMETRO certification is issued by the INMETRO itself or by an INMETRO-accredited Certification Body (CB). Before applying for necessary certifications and approvals, Brazil Registration Holder (BRH) must ensure that the products comply with all the necessary INMETRO Certification requirements.

INMETRO Certification is a mandatory requirement prior to the registration of electro-medical devices and some non-electrical medical devices by ANVISA. INMETRO Certification by accredited Certification Body (CB) provides assurance that the product complies with the Regulatory framework and meets safety standards.

Conclusion

To gain comprehensive insights on the INMETRO certification process and requirements, consult a proven Regulatory expert. Stay informed. Stay compliant.

FREYR CONNECT

Center of Excellence
Regulatory Affairs

RAPEX:
EU's Rapid Alert System for Identifying Unsafe Consumer Products

FREYR CONNECT

It is crucial for Regulatory bodies to monitor the vast range of consumer products available in their market. With new products entering the market regularly, this task becomes increasingly complex for Regulatory Authorities. However, it is important to detect potentially harmful products to ensure product compliance and consumer safety. The Rapid Exchange of Information System (RAPEX) is the European Union's rapid alert system to identify unsafe consumer products to ensure consumer well-being.

The RAPEX system encompasses consumer products like cosmetics, clothing, jewelry, and toys, and excludes food, pharmaceutical products, and drugs. It facilitates quick exchange of information on measures like repatriation or product recalls. Along with the picture of the product, RAPEX also displays the brand, name, and risk associated with the unsafe product. This provides clarity about the concerned product across the entire value chain. The system covers the measures taken by the national authorities and the voluntary actions of manufacturers and distributors. The call-to-action time is reduced with the instant notification of unsafe products. The product can be quickly recalled/ repatriated and necessary actions can be taken across all the EU Member States.

The RAPEX was established on the basis of the General Product Safety Directive 2001/95/EC (GPSD), an EC Directive on general product safety. It aims to detect consumer products that have:

1. Potentially harmful ingredients
2. Inferior quality
3. Technical faults
4. Hazards during use (e.g., electric shocks and ignition hazards of electric appliances)

The Directorate-General for Justice and Consumers of the European Commission publishes a weekly report containing the latest RAPEX alerts.

In addition to the manufacturers and distributors, the RAPEX system is also accessible to the public. The RAPEX system has greatly helped Regulatory authorities increase vigilance and detect unsafe consumer products across the EU countries.

Conclusion

Are you looking for guidance on RAPEX and other Regulatory developments taking place in the EU? For Regulatory assistance in the EU market or to avail Responsible Person (RP) services, consult a Regulatory expert. Stay informed. Stay compliant.

Center of Excellence
Global Pharmaceutical Regulatory Services

TGA's Black Triangle Scheme - A Complete Perspective

Health Authorities worldwide are initiating various programs to strengthen Adverse Drug Events (ADE) reporting of new prescribed medicines every day. An Adverse Drug Event (ADE) can be defined as any unfavorable and unintended sign, symptom, or disease associated with the use of a medicine. The safety and efficacy of new prescribed medicine is usually decided based on clinical trials. And as the clinical trials are subjected to a restricted number of participants, it is highly possible for a new side effect - ADE - to be identified when a larger population uses these drugs. While some ADEs may be minor, some may be fatal, and hence it is crucial to report them.

FREYR CONNECT

The Black Triangle Scheme is one such initiative by the Therapeutic Goods Administration (TGA), Australia, which provides a simple means for practitioners and patients to identify certain types of new prescription medicines or those being used in significantly different ways and improve the currently-low ADEs reporting.

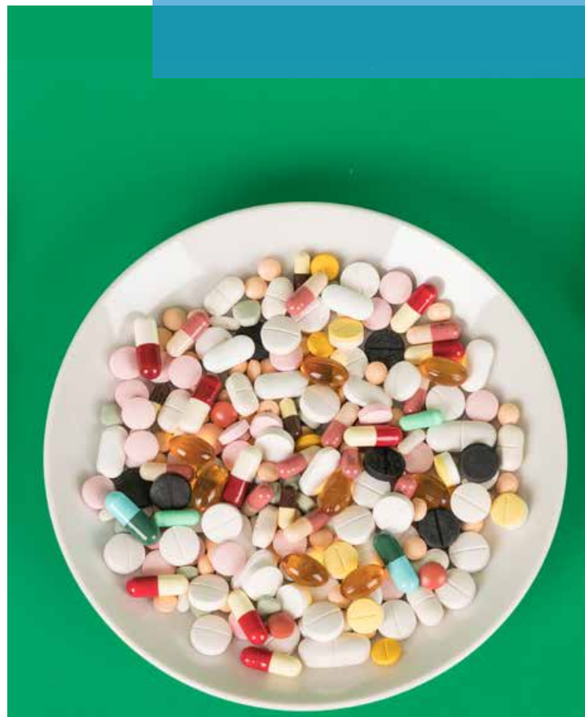
Under this program, a list of medicines is provided, which has a black triangle inscribed on them, indicating that they are subjected to additional monitoring. The black triangle symbol and accompanying text will appear on the Product Information (PI) and the Consumer Medicines Information (CMI) of products included in the scheme.

The Black Triangle Scheme commenced in January 2018 to encourage the health professionals and the consumers to report any possible adverse reactions observed with the medicines.

Before the scheme's commencement, TGA conducted time series analysis with segmented regression to analyze the quantity of ADE reports pre and post the scheme for a year. The analysis showed an increase of 0.41 reports per medicine (95%CI, 0.02-0.80, p = 0.039) post the scheme.

The black triangle scheme applies to certain prescribed medicines only and does not mean that the medicine is unsafe. Based on the criteria given by the TGA, a sponsor should mention in the application that the drug is to be added in the scheme.

This scheme facilitates the TGA in post-market monitoring of the safety and efficacy of the drugs circulating in the Australian market. The ADE reports help the TGA analyze the performance and characteristics of a new drug and identify a potential emerging threat.



Conclusion

It is necessary for Pharma manufacturers to be fully aware of the TGA regulations to apply for inclusion in the scheme. To know more about the functioning of the Australian Health Authority and drug registrations, reach out to an expert for Regulatory consultations and solutions; stay informed and stay compliant.

FREYR REGULATORY ARTWORK SERVICES

The Importance of Color Palette Conquests in Brand Building

> Colors, like features, follow the changes of the emotions.
>
> *- Pablo Picasso*

FREYR CONNECT

From paintings to artifacts and literature, the significance of colors and shade palette cannot be overlooked. The challenge lies in how we can use colors effectively to communicate brand perception. For example, symbols like the red cross signs, green cross signs, etc., portray essential information about places where medical help is provided and where you can buy medicines. Further addressing the importance of colors, we found that recent studies have shown that certain colors invoke subconscious emotions within people. This itself is a testimony of how the audience perceives certain elements subconsciously.

Brand perception starts before the end consumer purchases the commodity. Companies make major brand-building investments to convey exactly what the brands want to portray through their products. Sensory stimuli are significant, and studies have been conducted to understand the impact of the color scheme on successful brand communication. According to statistics, colors are associated with brand recognition by eighty percent (80%) of the consumers. However, all art visualizations and templates can be successfully envisioned only if the said designs are scalable.

Often, decisions on the shade and color palette are based on 'What looks good together?' rather than 'What feels right?'. One can achieve the correct fit for an indication and a brand with the right tools and a tailor-made approach that offer optimal outputs with designated inputs.

Color branding is a technique used to differentiate one brand from another. Various platforms where colors are used for effective communication are:

- **Logos**
- **Website**
- **Advertisements**
- **Packaging**

Conclusion

Creating a positive impact of colors on a majority of platforms requires effort and consistency in communication. Over the years, experts have established that uniformity and color combination establish brand identity in the minds of consumers. The ideal brand strategy is to build a successful brand image with the right aesthetics and an aligned vision to conquer the perceiver's mind.

Reach out to an expert to design your brand campaign with an optimum blend of micro & macro elements and for a quality review of your ad-promo material for your promotional activities.

Center of Excellence
Publishing & Submissions

Regulatory Submission Software
Key Considerations to Choose

As many of the Health Authorities transitioned from paper documentation format to the eCTD format, it is time for organizations to define key measures to submit documents in the electronic format to remain compliant.

The eCTD publishing and submission is a cumbersome process that requires the cooperation of multiple individuals from various departments within the organization. Also, it is paramount that Standard Operating Procedures (SOPs) and clear expectations are established to streamline the process, which requires ample time and proper planning.

The quick path to simplify such Regulatory processes is to choose a Regulatory submission software with an integrated document management system and dossier publishing solution. The software streamlines the submissions process with the utmost possible data accuracy. Selecting the best software in a huge pool of resources can be challenging.

Here are a few basic considerations one must look into while choosing a Regulatory submission software. The software must:

- be a lightweight, easy-to-use web-based application
- be able to create, track, validate, view, publish and manage the entire document life cycle, including pre-clinical/clinical research data
- support region-specific submission formats under strict eCTD guidelines and compliance timelines
- have an inbuilt eCTD validator to check compliance
- have an inbuilt viewer to review the region-specific submission lifecycle
- have end-to-end tracking traceability
- have Health Authority query management system
- provide alerts for submission due dates and Health Authority activities to mitigate the risks of missing deadlines

Apart from the features mentioned above, the software must have a seamless workflow from creation to publishing.

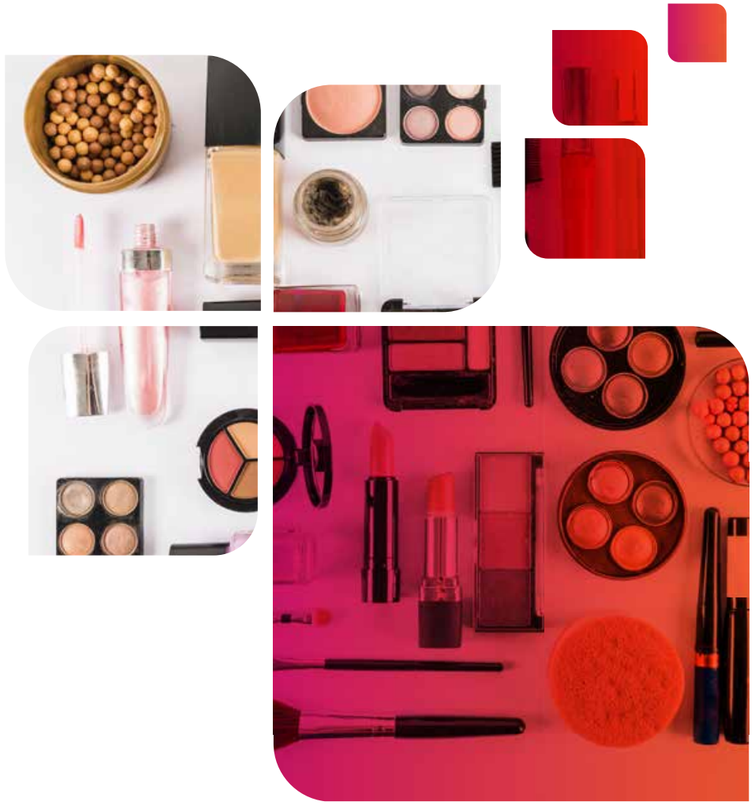
In a nutshell, it is crucial for manufacturers in the life sciences industry to streamline the submission process with the best Regulatory publishing software to manage the multitude of Regulatory submission requirements. Here is an opportunity to go through a proven software - Freyr SUBMIT PRO.

Request a demo

FREYR CONNECT

Center of Excellence
Global Cosmetics Regulatory Services

DTAB Advises Voluntary Specification of Veg/Non-Veg Symbols on Cosmetic Products



FREYR CONNECT

The use of red/brown- and green-colored dots to classify vegetarian or non-vegetarian is a mandated practice for food products in India. These dots are labeled on the food products' packaging. However, there is no such system for cosmetics in India that declares their vegetarian or non-vegetarian nature.

In this regard, a new voluntary indication for specifying the origin of cosmetic products was advised by the Drug Technical Advisory Board (DTAB) on September 10, 2021. The DTAB is the highest statutory decision-making body of the Central Drug Standard Control Organization (CDSCO).

CDCSO is responsible for regulating imported beauty and personal care products in India. Over the years, the DTAB had received several proposals and VIP references for an indication to classify products as per their vegetarian or non-vegetarian origin. After detailed deliberation, the Board has given an official notice concerning the indication. The notice specifies that manufacturers may indicate red/brown or green dots on beauty care products to indicate their non-vegetarian or vegetarian nature, respectively. This labeling method is applicable for packaging tubes of toothpaste, shampoos, soaps, other cosmetics, and toiletries. The indication, however, would be voluntary for cosmetic manufacturers.

This new indication will allow consumers to gain more information about product ingredients and make an informed decision as per their individual preferences.

Conclusion

To achieve compliance for cosmetics in India, it is necessary to be cognizant of the latest developments taking place in the Indian cosmetic market. Reach out to a regional Regulatory expert like Freyr for Cosmetic Regulatory assistance in India.

Center of Excellence
Global Pharmaceutical Regulatory Services

EMA Releases New Guidance for Nitrosamine Detected Response Template

After the initial discovery of nitrosamine impurities in drugs and Active Pharmaceutical Ingredients (APIs) by the USFDA in mid-2018, the EU Regulatory bodies have also joined many other countries in a bid to prevent the risks involved. They have re-called several medicines that post health perils from the substance. Known for its carcinogenic properties, Nitrosamine may prove to be harmful when ingested above the accepted levels by humans. The substance, N-nitrosodimethylamine (NDMA), has an acceptable limit of 96 ng/day and anything above this is objectionable in drugs and APIs.

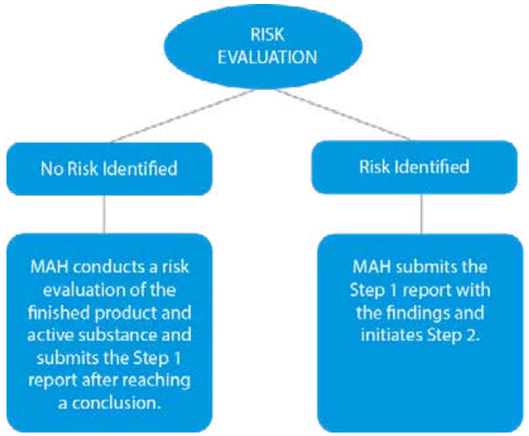
Nitrosamines are formed when secondary, tertiary, or quaternary amines react with a nitrosating agent. All the drugs that have chemically synthesized active ingredients are being checked for impurities. The Committee for Medicinal Products for Human Use (CHMP) has reviewed and created an assessment report. It has asked Marketing Authorization Holders (MAHs) to follow the latest guidance for reviewing all the chemical and biological medicines currently available in the market for human consumption.

MAHs are responsible for making sure that the manufacturing process of all the biological and chemical products is reviewed periodically to identify any contamination. Once identified, the relevant steps must be taken to allay the risks they pose. Though the chances of such contamination are less during the manufacturing of chemical and biological medicines drugs, the European Medicines Agency (EMA) is not taking any chances there. Pharmaceutical companies need to ensure that the relevant manufacturing protocols are in place as per the latest EMA guidelines. They are also responsible for checking the levels of nitrosamine in drugs that are available in the market and keeping them within the acceptable limit.

Post finalizing a review under Article 5(3) of Regulation (EC) No 726/2004 (call for review) last year; the EMA has issued new guidance for the avoidance of the presence of nitrosamine contamination in human medicines. The process is the same for nationally authorized and centrally authorized products. The EMA, along with the European Directorate for the Quality of Medicines & HealthCare (EDQM), will be implementing the CHMP Article 5(3). Here is the process that should be followed to remain compliant with the modifications.

The three-step guidance for MAHs

- **Risk Evaluation** - Manufacturers need to conduct a risk evaluation process to identify the active substances and the finished product to check the nitrosamine levels. If there are any instances of cross-contamination, the same should also be included in the outcome report. The deadlines for submissions at this stage were set for March 31, 2021, for chemical medicines, and July 01, 2021, for biological drugs.



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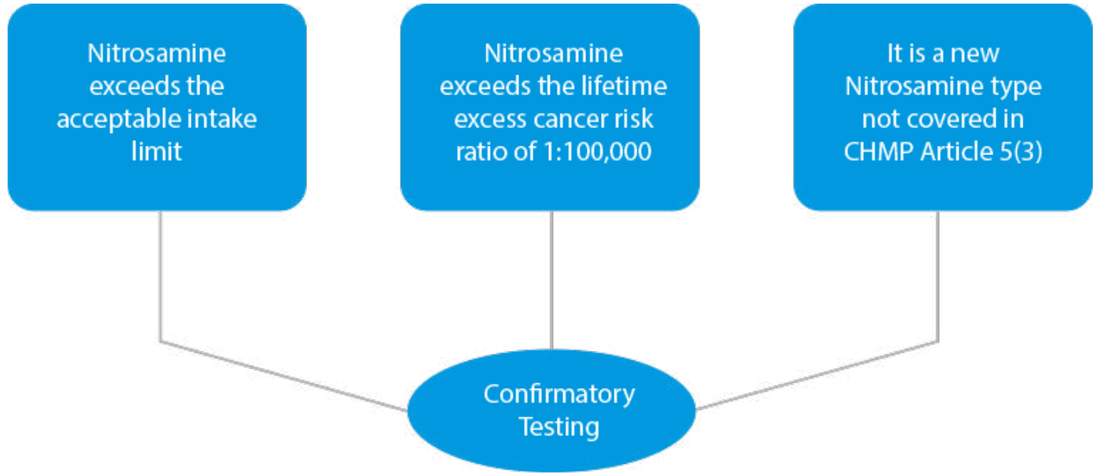
- **Confirmatory Testing** – In case of any cross-contamination findings or if products are identified as risky due to the presence of higher levels of Nitrosamine, confirmatory testing needs to be performed. Confirmatory testing is mandatory in three (03) instances.



- **Marketing Authorization Modifications** - When the presence of nitrosamine is detected, two (02) confirmatory tests need to be performed to report the correct readings to the EMA. Based on these, the MAHs must apply for changing the manufacturing process. This is done by using the standard Regulatory procedures with the help of a variation to the Marketing Authorization template. The timelines for these are September 26, 2022, for chemical products, and July 01, 2023, for biological medicines.

Ideal Way Forward for MAHs to Deal with the New Nitrosamine Level Compliance

Since this is the latest development that the EMA has proposed to mitigate the risks involved with Nitrosamine levels in drugs and a cross-contamination situation, the whole process can be quite overwhelming for MAHs and API manufacturers. Whether it is submitting the Response Template when contamination is detected at Step 1 or conducting consequent testing, every phase has to be compliant with the new rules. MAHs need to collaborate with Regulatory experts who are up to date with all the latest changes and ensure compliance with the new guidance. Choose the right partner like Freyr to avoid any delays and errors.

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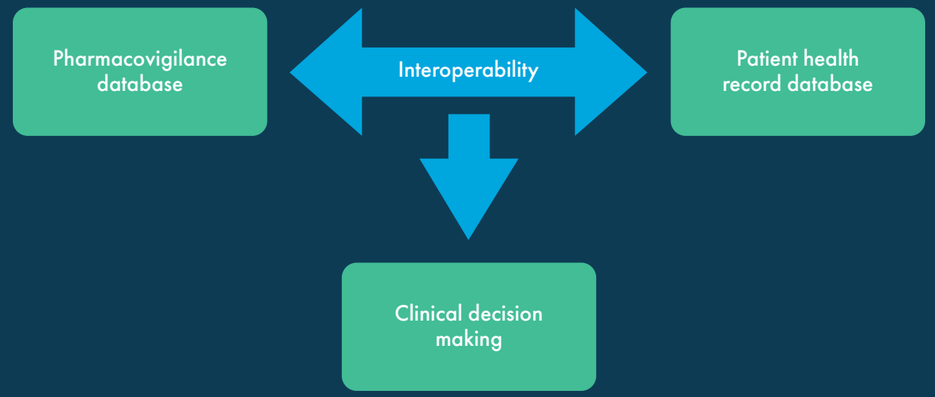
ICH and SNOMED Collaborate to Evolve Clinical Decision Making

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is an international non-profit organization that strives to maintain an updated database to summon Regulatory agencies and pharmaceutical manufacturers to discuss scientific and technical aspects of the industry on a single platform.

Medical Dictionary for Regulatory Activities (MedDRA), owned and developed by ICH, is a distinct and standardized Regulatory dictionary that facilitates the communication of Regulatory information across the globe, seamlessly. Similarly, pioneering in clinical terminology, Systematized Nomenclature of Medicine (SNOMED) International is a not-for-profit organization that maintains the world's most comprehensive terminology database, Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED CT) which includes over 350,000 concepts ranging across diagnosis, signs, and symptoms.

In a study published in 2009, the feasibility of using SNOMED CT as an entry point for coding adverse drug reactions and mapping them automatically to MedDRA for reporting purposes and interoperability with legacy repositories was analyzed. Understanding the scope of such a collaboration, ICH and SNOMED as a joint effort, announced the release of important new maps in Regulatory, and clinical space. Collaborative efforts under the project WEB-RADR 2, led to the release of two (02) important roadmaps (MedDRA to SNOMED CT and SNOMED CT to MEDRA), which have been structured around repeatability of term usage and additional key pharmacovigilance MedDRA terms identified by the European Medical Agency (EMA). To promote drug safety, interoperability among the Pharmacovigilance database (MedDRA) and Electronic health records (SNOMED CT) can help identify possible side effects and activate adverse events reporting simultaneously. The data collected through such reports can be useful for conducting epidemiological research in patient demography. Key elements associated with MedDRA adverse event reporting could be used to associate adverse drug events while providing "aid in clinical decision making".



The production version of the two (02) maps is being made available to licensed SNOMED CT and MedDRA users from April 30, 2021, onwards and will be based on the January 2021 version of SNOMED CT and the September 2020 version of MedDRA. It has been decided that the maps will be released annually in April.

To access the maps:

- Licensed MedDRA users, visit the **Downloads** page on the MedDRA website
- Licensed SNOMED CT users visit **SNOMED International**

Recent updates regarding established interoperability between pharmacovigilance database and Patient health records may seem complex to navigate through. However, Freyr's experienced Regulatory professionals can function as a single point of contact to provide technical support across patient health database and enhanced clinical decision-making needs. To enhance the quality output of your Pharmacovigilance requirements, we provide assistance across; ICSR, Aggregate reports, Qualified Person Responsible for PV (QPPV) Services, the US Agent services, Signal Detection & Evaluation, Database Migration, Adverse Event Reconciliation, Local Affiliate Services, and much more. To explore Freyr's end-to-end Pharmacovigilance capability, **contact us now!** Stay informed. Stay compliant.

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ANATEL Certification for **Medical Devices in Brazil**

The Brazilian Medical Devices market is growing significantly and is expected to reach USD 1.8 billion by 2023. Medical devices in Brazil are regulated by the National Health Surveillance Agency i.e., ANVISA (Agência Nacional de Vigilância Sanitária). Medical devices using functionalities such as Bluetooth, Wi-Fi, Radio Frequency (RF), and other wireless interface require ANATEL certification and homologation as a pre-requisite for ANVISA registration. ANATEL (Agência Nacional de Telecomunicações) is the National Telecommunications Agency responsible for regulating all the telecommunication products marketed in Brazil.

ANATEL Homologation refers to granting of approval by the ANVISA's compliance with Brazilian regulations and ensuring that the medical device is safe to use. The requirements for Brazil ANATEL Certification are defined in Resolution 715/2019. ANATEL Homologation plays an important role in completing the registration process of telecommunication products with the ANVISA. Medical devices with wireless technology aid in monitoring patients remotely or transferring patient data from the medical device to another platform such as a cell phone.

Classification of Telecommunication Products

ANATEL classifies telecommunication products into three (03) categories such as Category I, II, and III.

- Category I includes end-user products such as mobile phones, satellite phones, VOIP phones, mobile phone batteries, mobile phone charging cables, etc.
- Category II includes products requiring radio frequency such as TV and radio antenna, receivers, and transmitters, Wi-Fi equipment, and RF automation devices.
- Category III includes products such as optical fiber cables, mobile network signal transmitters and cable connectors.

Medical devices using RF wireless technology such as wireless cardiac monitors, implanted cardiac pacemakers and defibrillators, as well as neuromuscular stimulators, Radio Frequency Identification (RFID) wireless systems, and Handheld TENS (Transcutaneous Electrical Nerve Stimulation) devices fall under Category II of Telecommunication products. Each category must comply with different requirements for ANATEL Homologation.

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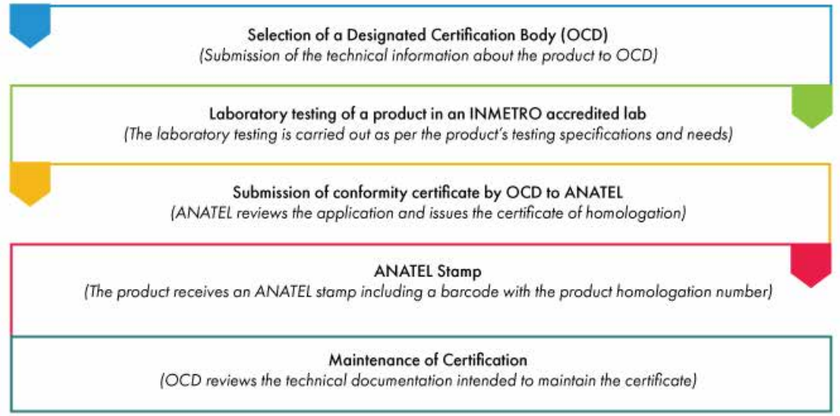
Medical devices using RF wireless technology such as wireless cardiac monitors, implanted cardiac pacemakers and defibrillators, as well as neuromuscular stimulators, Radio Frequency Identification (RFID) wireless systems, and Handheld TENS (Transcutaneous Electrical Nerve Stimulation) devices fall under Category II of Telecommunication products. Each category must comply with different requirements for ANATEL Homologation.

- The Category I products must go through laboratory testing at an INMETRO accredited laboratory followed by an annual re-evaluation for maintenance of certification. The re-evaluation also involves laboratory testing.
- The Category II devices, like Category I products, must undergo laboratory testing at an INMETRO accredited laboratory followed by a bi-annual re-evaluation for maintenance of certification. The re-evaluation, in contrast to category I products, involves document verification and does not require laboratory testing. This is applicable to the wireless medical devices.
- The Category III products must undergo laboratory testing for certification, but there will be no periodic re-evaluation.

Step by step Process of ANATEL Certification and Homologation

The conformity assessment and ANATEL approval of Telecommunication products involve various stakeholders, including entities such as medical device manufacturers and Brazilian Registration Holder (BRH), assessment agencies such as testing laboratories and Designated Certification Body (OCD) and authorities like ANATEL.



The duration for the entire ANATEL approval process is largely dependent on the type of the telecommunications product along with the time required for the completion of laboratory tests. ANATEL Brazil Certification is a mandatory requirement for the registration of telecommunication products with ANVISA. The ANATEL certificates do not have an expiry once issued by the OCD. However, the certificates are maintained periodically by the OCD for any change in the requirements of testing specifications.

For more information on the ANATEL certification and its process, kindly reach out to a regional Regulatory expert. Stay informed. Stay compliant.

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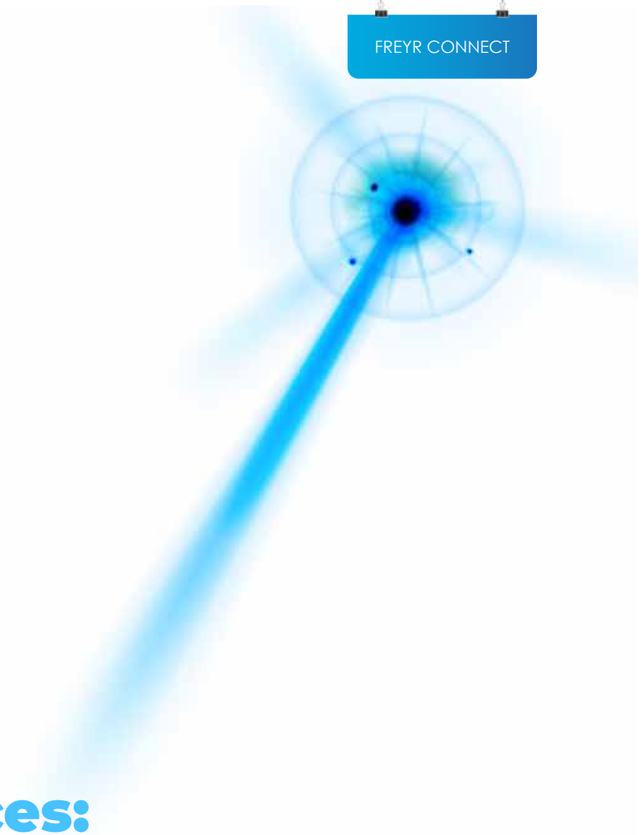

Laser based devices: Key regulatory considerations

Light Amplification by the Stimulated Emission of Radiation, widely known as Laser technology, was first introduced in 1960 and it has far-flung applications in various industries including the medical field.

The laser-based products, available in various sizes, shapes and forms, have a laser system that stores and releases the energy from sources such as electrical charge or optical illumination or chemical reaction as light. Laser light in contrast to ordinary light has a specific wavelength, amplification of this specific wavelength and is a narrow beam of light focussed in one direction. All these features result in a light that is concentrated in a small area and can create a very high intensity light at farther distances from the source.

Its use in the medical industry varies from diagnosis of an underlying health condition for the treatment to life-threatening cancer disease. Its application in the fields of ophthalmology, cosmetics and dentistry has been resourceful for practitioners. Medical lasers are medical devices that use precisely focussed light sources to treat or remove tissues.

In the US, both medical and non-medical lasers are regulated by the FDA. The non-medical laser products are categorized and regulated under the radiological products category. Medical lasers are considered as medical devices and they comply with the requirements of both radiology products as well as devices. FDA recognises four (04) major hazard classes (I to IV) of lasers, including three (03) subclasses (IIa, IIIa, and IIIb). This nomenclature is different from the International Electrotechnical Commission (IEC) classification system. However, in either of them, the higher class corresponds to a more powerful laser and has greater potential to pose serious injury, if not used properly. Hence, the labeling of Classes II-IV must include a warning symbol stating the class and output power of the LASER product. The medical lasers are categorized under Class IV and they are considered as high-risk radiological products by the US FDA.

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Class FDA	Class IEC	Laser Product Hazard	Product Examples
I	1, 1M	Considered non-harardous. Hazard increase if viewed with optical aids, including mangnifiers, binoculars, or telescopes.	• laser printer • CD players • DVD players
IIa, II	2, 2M	Hazard increases when viewed directly for long periods of time. Hazard increases if viewed with optical aids	• Bar code scanners
IIIa	3R	Depending on power and beam area, it can be momenterily hazardous when directly viewed or when staring directly at the beam with an unaided eye. The risk of injury increases when viewed with optical aids.	• laser pointers
IIIb	3B	Immediate skin hazard from direct beam and immediate eye hazard when viewed directly.	• laser light show projectors • industrial lasers • research lasers
IV	4	Immediate skin hazard and eye hazard from exposure to either the direct or reflected beam; may also present a fire hazard.	• laser light show projectors • industrial leasers • research lasers • medical device lasers for eye surgery or skin treatments

Table 1. *The US FDA Classification of LASER Products as a Radiological Product*

Various laws, regulations, and standards are applicable to the laser devices and mandate the manufacturer to ensure certain engineering controls and risk communication methodologies are applied to manage and mitigate possible biological hazards. The end-users must ensure proper use of the device as per the device labels issued by manufacturers as the failure of the same can lead to a lack of safety and effectiveness of the product.

Medical lasers have diversified applications and are used in various types of surgical procedures such as:

- **Cosmetic surgery:** To remove tattoos, scars, stretch marks, sunspots, wrinkles, birthmarks, spider veins or hair
- **Refractive eye surgery:** To reshape the cornea to correct or improve vision as in LASIK or PRK
- **Dental procedures:** Inclusive of endodontic/ periodontic procedures, tooth whitening, and oral surgery
- **General surgery:** Inclusive of tumour removal, cataract removal, breast surgery, plastic surgery and most other surgical procedures

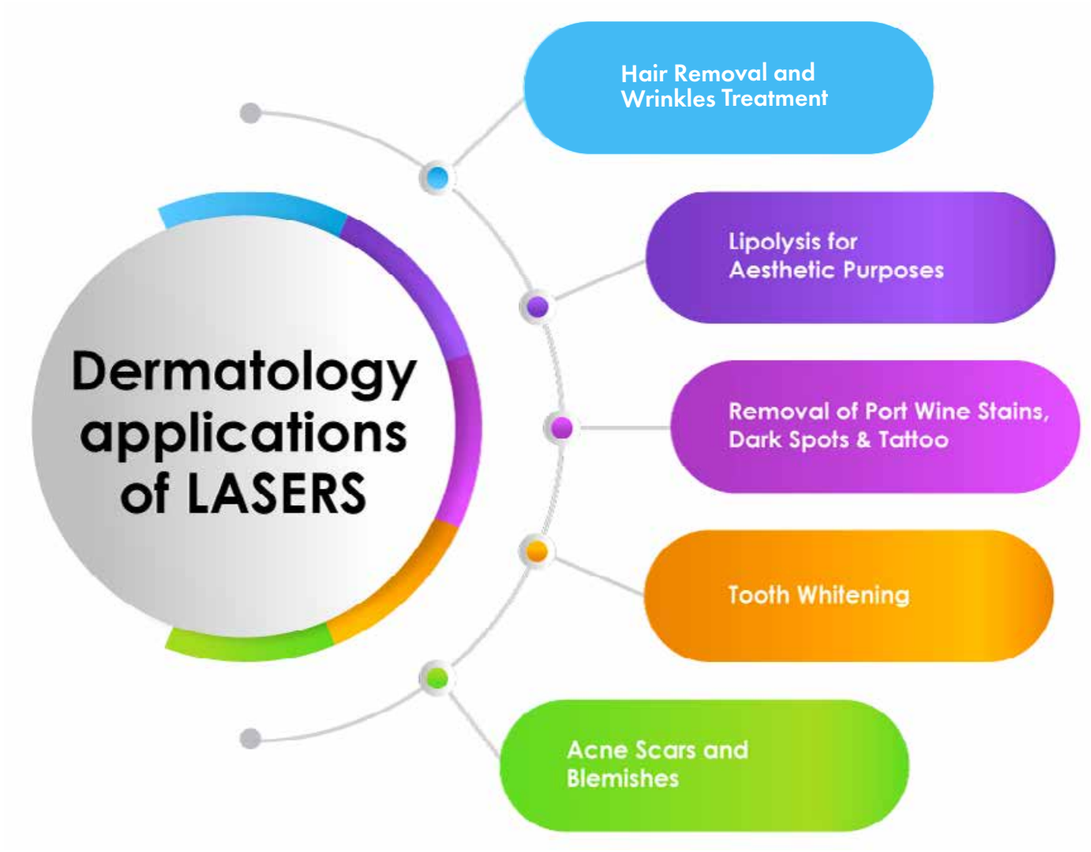

Figure 1. Aesthetic Applications of LASER Devices

The laser surgical devices used in dermatology for general and plastic surgeries are regulated under 21 CFR Part 878.4810. There are various laser devices under different product codes used for aesthetic purposes.

Regulation Number	Device Name	Device Class	Product Code
§878.4810	Laser Assisted Lipolysis	Class 2	ORK
§878.5400	Laser for Disruption of Adipocyte Cells for Aesthetic Use	Class 2	PKT
§878.5400	Fat Reducing Low Level Laser	Class 2	OLI
§878.4810	Laser, Cellulite Appearance	Class 2	OYM

§878.4810	Light-based, Over-the-Couner Wrinkle Reduction	Class 2	OHS
§878.4810	Light-based, Over-the-Couner Hair Removal	Class 2	OHT
§878.4810	Massager, Vacuum, Light Induced Heating	Class 2	NUV
§878.4810	Over-the-Counter, Power Light-based Laser for Acne	Class 2	OLP
§878.4810	Powered Laser Surgical Instrument	Class 2	GEX
§878.4810	Powered Laser Surgical Instrument with Microbeam\Fractional Output	Class 2	ONG
§878.4810	Powered Light-based, Non-laser Surgical Instrument	Class 2	ONE
§878.4810	Powered Light-based, Non-laser Surgical Instrument with Thermal Effect	Class 2	ONF

Table 2. *Product Codes for Aesthetic LASER Medical Devices*

Manufacturers of aesthetic laser medical devices must comply with the regulations for Radiological Health i.e., Title 21 CFR (Subchapter J, Radiological Health) Parts 1000 through 1005 and the medical device regulations.

Regulation	Aspects
21 CFR Part 1000	General
21 CFR Part 1002	Records and reports
21 CFR Part 1003	Notification of defects or failure to comply
21 CFR Part 1004	Repurchase, repairs, or replacement of electronic products
21 CFR Part 1005	Importation of electronic products
21 CFR Part 1010	Performance standards for electronic products: General
21 CFR Part 1040.10	Performance standards for electronic products - laser products
21 CFR Part 1040.11	Performance standards for Light-emitting products - Specific purpose laser products

Table 3. *Applicable Regulations for Radiological Health*

The aesthetic laser medical devices with medical applications must, in addition to the above regulations, comply with the device regulations and consensus standards applicable for a given device product code.

Title		ORK, OYW, OHS, OHT, NUV, OLP	GEX, ONG, ONE, ONF	ONF*
12-102 ANSI IES RP-27.2-00/R17	Recommended Practice for Photobiological Safety - Measurement Technique	X	X	NA
12-249 IEC 62471 First Edition 2006-07	Photobiological Safety of Lamps and Lamp System	X	X	NA
12-297 ANSI IES RP-27.1-2015	Recommended Practice for Photobiological Safety - Measurement Technique	X	X	NA
12-321 ANSI IES RP-27.3-17	Recommended Practice for Photobiological Safety for Lamps - Risk Group Classification and Labeling	X	X	NA
12-273 IEC 60825-1 Edition 2.0 2007-03	Safety of Laser Products - Part 1: Equipment Classifications, and Requirements [Including: Technical Corrigendum 1 (2008), Interpretation Sheet 1 (2007), Interpretation Sheet 2 (20070]	NA	X	NA

Table 4. *Consensus Standards for LASER Devices*

The majority of Laser devices used for aesthetic purposes are considered as moderate-risk devices, requiring compliance with special controls and a 510(k) clearance from the FDA for importing and marketing the device in the USA. Very few devices fall under Class I requiring compliance with general controls and few devices falling under Class III require a Pre-Market Approval (PMA) from the FDA. The labels of medical laser shall comply with 21 CFR 801 and 21 CFR 1040.10 & 1040.11, Performance Standard for Light Emitting Products.

It is critical to evaluate the intended use of the device and map them to the right regulations. For example, when not labelled or represented as sterile, laser for disruption of adipocyte cells for aesthetic use, classified under PKT, is GMP exempt and 510(k) registration. The device, however, shall comply with general requirements concerning records (820.180) and complaint files (820.198).

The fat reducing low-level laser systems for aesthetic use are classified under product code OLI and regulated under 21 CFR 878.5400. They fall under Class II and shall comply with the special controls issued by the FDA for assured safety and effectiveness of the device and shall obtain the 510(k) approval for importation and distribution of the device within the US market. These are low-level laser systems for the disruption of adipocyte cells within the fat layer for the release of fat and lipids from these cells for non-invasive aesthetic use. The US FDA requirements for this device have been detailed below.

The manufacturer shall identify all the components of the device systems including system software and accessories. photograph or drawing of the device, functional block diagram of the device along with its accessories, predicate comparison sheet; risk profile of the device covered in the risk assessment document shall be submitted to the FDA as a part of the 510(k) technical file. The ocular injury, electrical shock and unintended cell damage and use errors are the common risks involved

in these devices used for fat reduction. The manufacturers can choose to justify the risk profile by adopting various mitigation measures such as bench testing, software validation, clinical testing, biocompatibility testing, labeling, and ensuring that the device is in compliance with IEC 60601-1 and IEC 60601-1-2.

Mitigation Strategy	Types of Risk	Objective
Bench or Preclinical Testing	• Ocular injury • Unintended cell damage	• It shall meet all design specifications and performance requirements • Assesses the probability of system failure, and possible mitigation measures, risk communication to the user
Software Validation	• Ocular injury • Unintended cell damage	• The software shall be developed in compliance with IEC 60601-1-4; "General Requirements for Safety; Collateral Standard: Programmable electrical medical devices or equivalent methods • 510(k) content shall be in line with the US FDA's "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" • The 510(k) shall detail the anticipated risks, level of concern for each of the identified risks
Electromagnetic Compatibility	• Electrical shock • Unintended cell damage	• The electromagnetic testing of the devices shall be conducted in compliance with IEC 6061
Clinical Testing	• Ocular injury • Unintended cell damage	• The clinical studies or trials, if required for establishing the substantial equivalence, shall comply with IDE, IRB and informed consent regulations defined under 21 CFR 812, 21 CFR Part 56 and 21 CFR Part 50 respectively
Biocompatibility Studies	• Unintended cell damage	The studies shall be conducted either as per • ISO 10993-1, Biological Evaluation of Medical Devices Part 1: Evaluation and testing for intermittent external contact with intact external body surfaces or • Shall compare with the predicate device the identical material of construction and material processing
Labeling	• Ocular injury • Electrical shock and unintended cell damage and use errors	• The labeling components of the 510(k) shall comply with 21 CFR 807.87(e) and the device labels shall comply with general labeling requirements defined under 21 CFR 801 • The device label must include directions for use, indications for use, contraindications, storage conditions, warnings, precautions as required by 21 CFR 801.109 • The device user manual shall include details on the device and all accessories; interconnectivity between the device and the other components or accessories; all features, functions, output modalities, and specifications; all user-accessible controls, indicators, markings, and/or labels on the device that provide information regarding the function or meaning of each control, display output jack, etc; illustrations of the device and accessories; summary of clinical testing

Table 5. *Risk Mitigation Strategies for Fat Reducing, Low-level, Laser Aesthetic Device*

Once the FDA approval/clearance is obtained, all the electronic products are subjected to achieve compliance for 21 CFR 1000-1050. Accordingly, the manufacturers of all the different classes of lasers must submit "Product Reports" (Also called as Radiation Safety Product Report) to the FDA, as per 21 CFR 1002, before the product is introduced into interstate commerce. Once a product report is submitted to the FDA, an accession number is issued by the FDA for the device. Including the accession number is mandatory in the Customs Clearance Form and is usually verified by the US Customs during the importation of the product. If your product is made in another country for import into the United States, the import clearance process requests identification of the accession number on the import affirmation form, FDA 2877.

It is recommended by the FDA to submit the "Periodic Safety reports" at least one month before the product is imported into the US. The manufacturers have varied options to compile and submit the product reports. Product reports can be compiled using Form 3632 /one can compile the product reports using the e-submitter software available on the FDA website. Once an e-copy is generated, the e-copy of the file is usually exported as an XML document that can be submitted to the CDRH directly through ESG Gateway/alternatively the e-submitter can load the XML file onto a CD and can be mailed to CDRH or emailed to Rad Health Customer Service @fda.hhs.gov for processing and issuance of accession number. Reports prepared and submitted using e-submitter software may be acknowledged significantly faster than a traditional report submitted on paper. For faster acknowledgement of the receipt of the product report within 48 hours, the ESG Gateway can be used for product report submission.

In addition to product reports, the manufacturers shall submit duly filled Form 3636/use e-submitter tool to compile the annual reports on radiation safety testing of the devices by September 1st of each year.

Furthermore, EU MDR has broadened the definition of medical devices and more products such as epilation lasers are classified as medical devices. Products listed under Annex XVI make aesthetic claims or other non-medical purposes, but they are very similar to medical devices in terms of safety and risk profile. High-intensity electromagnetic radiation emitting equipment such as lasers and intense pulsed light equipment intended for skin resurfacing, tattoo or hair removal or other skin treatment are considered as medical devices. This might be overwhelming for the companies with medical device portfolios, as the EU MDR requirements could be all new to them. Such companies can start by appointing a Regulatory outsourcing partner and finding the right Notified Body for certification. The laser surgical instrument falls under Class IIb as per the classification rules defined in Chapter III rule 9 of the EU Medical Device Regulations (MDR). The manufacturers shall develop the EU MDR compliant device documentation, comply with ISO 13485:2016 followed by conformity assessment of the device by the Notified Body and for CE certification of the device.

In China, powered laser surgical instrument used in dermatology and surgery and intended to remove unwanted brown spots, sun freckles, or tattoos from the skin is classified as Class III.

In a nutshell, the Laser products intended for medical use fall under the purview of multiple regulations and will be under the vigilance of various offices. Navigating through the regulations and framing the right Regulatory strategy requires a thorough understanding of the device technologies as well as applicable regulations.

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FDA's Safety And Performance-based Pathway: An Alternative to Substantial Equivalence for 510(k) Submissions

What is FDA's safety and performance-based pathway? Why is it an alternative to substantial equivalence for 510(k) submissions? Why should medical device manufacturers opt for this approach? How is it beneficial to access the US market?

Since the inception of the 510(k) program, the 510(k) clearance of medical devices has been based on their proven substantial equivalence with claimed predicate device(s). In concert with the goal of adopting the least burdensome approaches, the FDA provides an alternate pathway based on proven safety and performance characteristics, instead of devices' equivalence to other predicates. This pathway is an expansion of the abbreviated 510(k) pathway, applicable to some well understood low to moderate-risk class II device categories. The FDA has released and continues to release device-specific guidelines to encourage manufacturers to opt for this approach for their device approvals. The FDA also conducts webinars and workshops to assist industry stakeholders understand the pathway.

The pathway is voluntary and is not mandated by the FDA. Though the manufacturer is not required to prove substantial equivalence of its device with a predicate device, the manufacturer is still required to identify a predicate device in the scope of the submission. Manufacturers can opt for the safety and performance-based pathway if the device has the same indications for use as the identified predicate, its technological characteristics do not raise any different safety and

effectiveness concerns than the identified predicate, and it meets all the FDA-identified performance criteria for the given device. If any of the above factors are not met, the manufacturer can opt to submit a traditional, special, or abbreviated 510(k).

The FDA has so far identified performance and safety criteria and testing methodologies for spinal plating systems, orthopedic non-spinal metallic bone screws and washers, magnetic resonance receive-only coils, cutaneous electrodes for recording purposes, and conventional foley catheters, and the final guidance is in effect for each. The draft guidance for soft (hydrophilic) daily wear contact lenses has been released, with the final guidance not yet available. For each type of device, the guidance includes the description of the device, the types of devices included and excluded under the purview of the safety and performance-based pathway, applicable performance criteria that are to be met by the device, and the recommended testing methodologies. A brief outline of these device categories is detailed in the table below.

Table 1: *Safety and Performance-based Pathway Device Categories*

Device	Device Class	Regulation	Product Codes	Device Types	Intended Use / Device Description	Out of Scope
Orthopedic Non-spinal Metallic Bone Screws and Washers	II	21 CFR 888.3040	HWC	Screw, fixation, bone	• Bone screws: orthopedic non-spinal fracture fixation, osteotomy, or small joint fusion or arthodesis	• Bone screws and washers inteded for mandibular, maxillofacial, cranial, and orbital fracture fixation or for use in spine • Devices intended for use with suture or chord components as part of implant system
	II	21 CFR 888.3040	HTN	Washer, bolt, nut	• Washers: intended for use with bone screws only to aid in load distribution at the screw head/bone interface	
Cutaneous Electrodes for Recording Purposes	II	21 CFR 882.1320	GXY	Electrode, cutaneous	• Non-invasive, single use electrodes intended to be used on normal, healthy, clean, intact skin for recording	• Dry electrodes • Reusable cutaneous electrodes • Cutaneous electrodes intended for stimulation or for use in MR environment • Electrodes regulated under other regulations • Electro-conductive media devices and needle electrodes
Spinal Plating System	II	21 CFR 882.3060	KWQ	Applicance, fixation, spinal	• Anterior cervical or anterior/ lateral thoracolumbar spinal plating systems intended for fixation of vertebral bodies for purpose of stabilizing the spine for fusion	• Plating systems attaching to the posterior spine or the occiput

Conventional Foley Catheters	II	21 CFR 876.5130	EZL	catheter, retention type, balloon	• Drainage is accomplished by inserting the catheter through the urethra into the bladder • The catheter is retained by use of a balloon inflated in the bladder, which is attached to the distal end of the catheter	• Three (03) lumen catheters, catheters treated to enhance their lubricity, suprapubic catheters, and antimicrobial catheters
Magnetic Resonance Receive-only Coils	II	21 CFR 892.1000	MOS	Coil, magnetic resonance, specialty	• MR receive-only coils are intended for hydrogen/ proton imaging, have no patient contact with intact skin to ptoduce images of human anatomy for general diagnostic use by trained clinicians • only air-cooled MR coils • Receive-only radio-frequency (RF) coils	• MR coils intended for specific clinical conditions • Water-cooled and cryogen cooled electronics
Soft Hydrophilic Daily Wear Contact Lenses	II	21 CFR 886.5925	LPL	Spherical or toric lense	• Intended to be worn directly against the cornea and adjacent limbal and scieral areas of the eye for the optical correction of ametropia (myopia or hyperopia with or without astigmatism) • The lenses are designed to be frequent replacement or daily disposable lenses	• Lenses to correct presbyopia, to enhance or alter the apparent color of the eye, to act as a bandage or therapeutic lens • Lenses for the management of keratoconus or irregular corneal conditions • Lenses with special optical performance beyond that of correcting ametropic (e.g., blue light filtering), with special physical performance (retains moisture, lubricates, reduces depoits) and with special health performance characteristics (e.g., relieves dry eye)

The performance criteria defined in these guidelines ensure that the new device is at the least equivalent to legally marketed devices, in terms of safety and performance. The safety and performance can be demonstrated based on the FDA's recognized consensus standards, the FDA guidance, special controls, scientific literature, or submission of historical data. While opting for this pathway, the manufacturer should not use performance criteria suggested in standards that are not recognized by the FDA. Some tests would require complete test protocols and all test reports and the summary of test results and declaration of conformity would be sufficient for submission, as a part of 510(k) application.

When the performance criteria are included in the FDA recognized consensus standard and the manufacturer uses the same testing methodology included in the FDA recognized consensus standard, submitting a declaration of conformity would suffice under this pathway. When the performance criteria are established by the FDA in the safety and performance guidance for a given device category and the test methodology from the FDA recognized standard is adopted by the manufacturer, a summary of results should accompany the declaration of conformity. In cases where the performance criteria are established by the FDA in the safety and performance guidance for a given device category and the test methodology is recommended or specified by the FDA, a testing protocol

is required. If the test methodology is neither included in the recognized standard nor recommended by the FDA, or if the manufacturer uses its in-house test method as an alternative, the manufacturer shall submit the complete test report. However, manufacturers should note that the FDA does not consider performance criteria that are not included in the device-specific safety and performance-based guidelines.

The table below shows the data that should be included in the submission under various possible scenarios.

Table 2: *Data Required Under Various Possible Scenarios*

Type of Performance Criteria and Methodology the FDA identified for Safety and Performance-based Pathway		
Performance Criteria	**Testing Methodology**	**Safety and Performance-based Pathway 510(k) Submission Should Include**
FDA-recognized standard	FDA-recognized standard	Declaration of Conformity
FDA-established	FDA-recognized standard	Results Summary and Declaration of Conformity
FDA-established	FDA-recommended or specified	Results Summary and Testing Protocol
FDA-established	None specified/recommended or alternative to the FDA-specified methodology used	Complete Test Report

The submission process, cover letter, Refuse To Accept (RTA) checklist requirements, the review process, e-copy requirements, and MDUFA fees remain the same as for other types of Pre-Market Notification pathways like traditional 510(k), abbreviated 510(k), and special 510(k). The timeline for the FDA to review and make a decision on a 510(k) submitted under the safety and performance-based pathway is 90 FDA days.

To comply with the RTA policy guidance, the manufacturer shall include the sections listed below in the same order. Where a particular section is not applicable for a given device category, the manufacturer can retain the section heading and include the statement, "This section does not apply" or "N/A" for ease of review by the FDA staff. The statement should provide the rationale for why a particular section is not applicable for the device.

Table 3: *Required Sections for Safety and Performance-based Pathway*

1. Medical Device User Fee Cover Sheet (Form FDA 3601)	10. Device Description
2. CDRH Premarket Review Submission Cover Sheet (Form FDA 3514)	11. Executive Summary/Predicate Comparison
3. 510(k) Cover Letter	12. Substantial Equivalence Discussion
4. Indications for Use Statement (Form FDA 3881)	13. Proposed Labeling
5. 510(k) Summary or 510(k) Statement	14. Sterilization and Shelf Life
6. Truthful and Accuracy Statement	15. Biocompatibility
7. Class III Summary and Certification	16. Software
8. Financial Certification and/or Disclosure Statement (Forms FDA 3454 and FDA 3455)	17. Electromagnetic Compatibility and Electrical Safety
9. Declarations of Conformity and Summary Reports	18. Performance Testing – Bench
	19. Performance Testing – Animal
	20. Performance Testing – Clinical
	21. Other

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The manufacturer shall demonstrate the device's compliance to a standard through the declaration of conformity to the standard, results summary, or a summary report, if recommended in any relevant device-specific guidance, testing protocols, and/or a complete test report demonstrating that the new device meets the FDA-identified performance criteria. The manufacturer shall identify a predicate and provide a trade name, model number, name of the 510(k) submitter/holder, and 510(k) number, if available. Though the safety and performance-based pathway does not require the manufacturer to compare performance specification testing with a predicate device, the manufacturer shall provide a comparison with predicate device in terms of indications for use and technology. For other sections of the 510(k) technical file, i.e., proposed labeling, sterilization and shelf life, biocompatibility, software, electromagnetic compatibility and electrical safety, and performance testing, the data shall be submitted in terms similar to a typical 510(k) technical file, though it is not a direct comparison with the predicate device.

Below is an example of the test methodologies, performance criteria, and data submission requirements defined for MR coils.

Table 4: *MR Coil Requirements as per the Safety and Performance-based Pathway*

Test	Test Methodology	Submission Requirement	Performance Criteria
Image Signal to Noise	• IEC 62464-1 Magnetic resonance equipment for medical imaging - Part 1: Determination of essential image quality parameters • National Electrical Manufacturers Association (NEMA) MS 1 Determination of Signal-to-Noise Ratio (SNR) in Diagnostic Magnetic Resonance Imaging • NEMA MS 6 Determination of Signal-to-Noise Ratio and Image Uniformity for Single-Channel, Non-Volume Coils in Diagnostic Magnetic Resonance Imaging (MRI) • NEMA MS 9 Characterization of Phased Array Coils for Diagnostic Magnetic Resonance Images (MRI)	Summary of results and Declaration of Conformity	• >130 (for 1.5T coils) • >215 (for 3T coils) (using the lowest SNR measure over all imaging coils, planes, and anatomical regions)
Image Conformity	• IEC 62464-1 Magnetic resonance equipment for medical imaging - Part 1: Determination of essential image quality parameters • NEMA MS 3 Determination of Image Uniformity in Diagnostic Magnetic Resonance Images • NEMA MS 6 Determination of Signal-to-Noise Ratio and Image Uniformity for Single-Channel, Non-Volume Coils in Diagnostic Magnetic Resonance Imaging (MRI) • NEMA MS 9 Characterization of Phased Array Coils for Diagnostic Magnetic Resonance Images (MRI)	Summary of results and Declaration of Conformity	• Worst-case non-uniformity < 50% (e.g., without any optional software correction algorithms applied)
Surface Heating	• NEMA MS 14 Characterization of Radiofrequency (RF) Coil Heating in Magnetic Resonance Imaging Systems	Summary of results and Declaration of Conformity	• Temperature criteria as defined by ANSI/AAMI ES 60601-1: <41°C for both normal use and single fault (coil not plugged in) condition

Acquired Image Quality	• Sample clinical images from all target anatomical locations are reviewed to determine that the images produced by the device are of sufficient quality for diagnostic use	Statement from a U.S. Board Certified or international equivalent qualified physician	• Statement from a U.S. Board Certified or international equivalent qualified physician (e.g., radiologist, radiation oncologist) that images are of diagnostic quality and sample clinical images to support the ability of your coil to generate diagnostic quality images
Decoupling Circuit	• Inspection of circuit diagrams	Circuit diagrams and description of decoupling mechanism	• Presence of decoupling mechanisms
Immunity, Electrostatic Discharge	• IEC 60601-1-2 Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests	Summary of results and Declaration of Conformity	• Pass at ±8 kV contact, ±2 kV, ±4 kV, ±8 kV, ±15 kV air
General Electrical/ Mechanical Safety	• AAMI/ANSI ES60601-1 Medical electrical equipment - Part 1: General Requirements for Basic Safety and Essential Performance • IEC 60601-2-33 Medical electrical equipment - Part 2- 33: Particular requirements for the basic safety and essential performance of magnetic resonance equipment for medical diagnosis	Summary of results and Declaration of Conformity	• Demonstration that the device performs safely and as anticipated in its intended use environment

The safety and performance-based pathway offers a cost-efficient way for device manufacturers to gain market access in the U.S., as the number of samples that are required to be tested are reduced by half. The FDA is expected to issue a draft and final guidance(s) for additional device types that qualify for the safety and performance-based pathway.

This article was first published by:

MED DEVICE ONLINE

Center of Excellence
Global Food and Food Supplements Regulatory Services

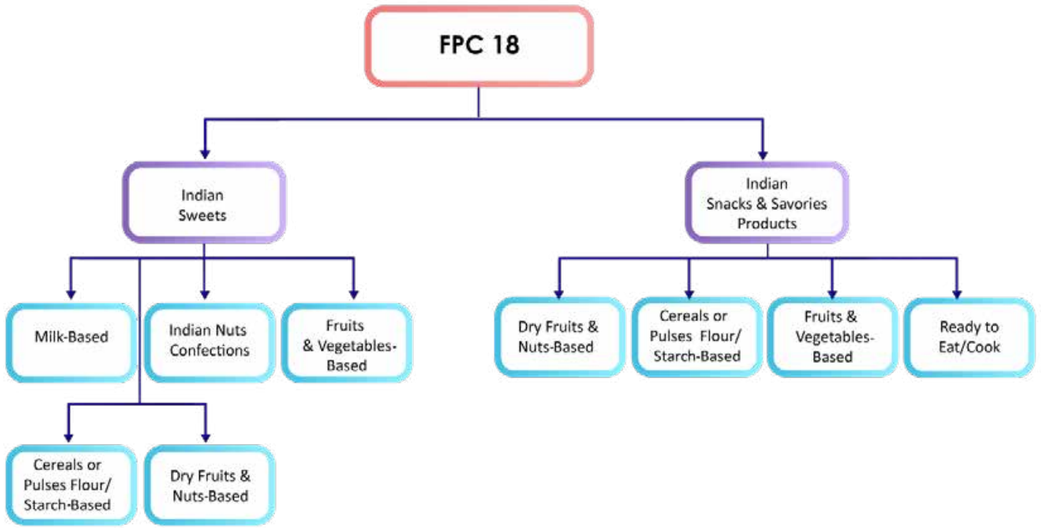
FSSAI Announces New Category for Sweets & Savouries

India has a rich tradition of sweets, snacks and savories with a difference in taste, texture and ingredients. Traditional milk-based sweets are mostly prepared from Khoya, Chhena, sugar and other ingredients such as maida, flavors, and colors, e.g., Peda, Barfi, Milk Cake, Gulab Jamun, Rasgulla, Rasmalai, etc. In addition, there are sweets containing cereal, starch or grain as the main ingredient, e.g., Suji Halwa, Moong Dal Halwa, Jalebi, Boondi Laddoo, Motichoor Laddoo, Gujiya, Balusahi, Soan-papdi, etc. There are also sweet snacks like Chikki, Gajak, Murrunda, Gudchana coated with jaggery, sugar, honey and other ingredients.

As there are no specific regulations proposed by the FSSAI, there are many challenges in the manufacturing and selling of sweets, snacks and savory food. The packaging and labeling requirements are often neglected. Moreover, there are issues like no proper category for sweets, snacks and savory food due to the unavailability of standards of these products under the Food Safety and Standards Regulations. As a result, such small and medium food business operators are required to obtain a central license under the proprietary food products, which is costly and entails numerous compliance requirements. Hence, the FSSAI has come up with a new food category to imply standard procedures for the mentioned food categories.

Below is a quick guide that explains the New Order in brief

1. Detail Categorization of Food Product Category 18



2. Important Point to be Noted

FSSAI stated that the above-mentioned Food Product Category (18) should not be applicable to those products whose standards have already been defined by the FSSAI and mapped in Food Safety Compliance System under the Food Products Category (01-14).

3. General Requirements for these Regulations While Applying for the FSSAI Registration/License

The FBO, when applying for registration/license for the above-mentioned food categories/products, should take a note of the following:

1. License/Registration rules imply as per the standards applicable.
2. Manufacturers can use additives as applicable.
3. FBO must follow GMP guidelines laid down under the applicable category.
4. Already licensed FBO, which falls under the new category, can continue its business with the current license and require no further modification.
5. Caterers, restaurants & other food services serving fresh foods can continue with their existing license as per the eligibility.
6. Contaminants including heavy metals and pesticide residue standards will imply as per the "Foods not specified" category.
7. Microbiological requirements and standards may imply as per the regulations specified for the base product used in the preparation. For e.g., major raw materials – milk in milk-based sweets, and nuts used in the preparation of snacks.

Conclusion

To begin manufacturing/processing, packaging, or holding the food products under Category 18 for consumption in India, FBOs must follow the regulations laid by the FSSAI. Failure to do so will result in heavy penalties and suspension of the license of your facility.

To get more insights on the FSSAI's food regulations, consult a Regulatory expert who can assist you in compliance requirements.

FREYR CONNECT

Center of Excellence
Regulatory Labeling

Pharma Labeling: An Overview of Compliance Issues and HA Audit Findings

As the use of pharmaceuticals can have a substantial impact on a patient's health and well-being, the information on the label must be clear and correct. It is particularly true when it comes to usage directions, expiration dates, and component lists. Thus, an audit of pharmaceutical labeling operations is required.

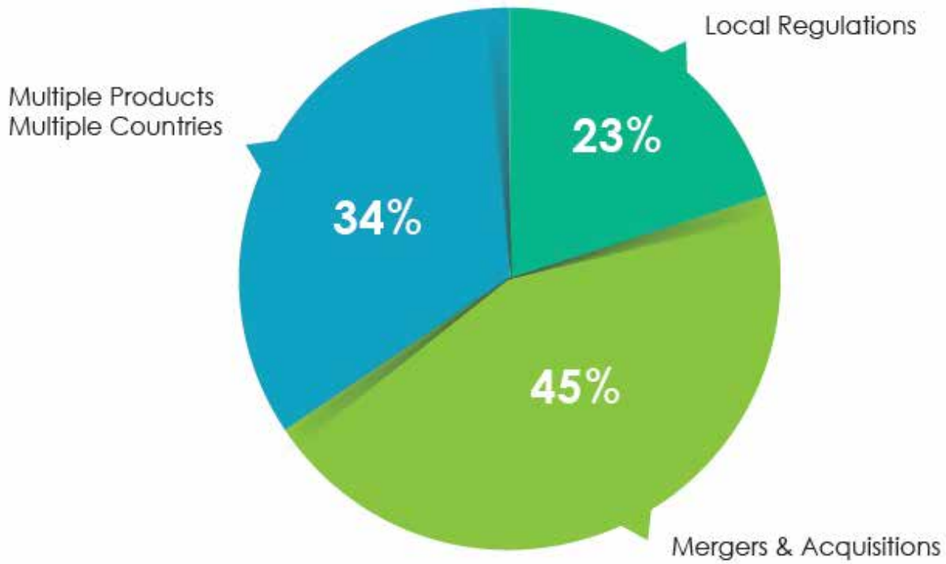
As a significant aspect of Regulatory compliance, data accuracy stands as one of the most critical criteria in medicine labeling. According to the FDA and MHRA studies, roughly 51 percent of auditing issues are associated with labeling-related documents.

The five (05) most common audit issues that were highlighted by the major Health Authority label audit findings are as follows:

- Deviation from SOPs
- CCDS & CSI Information
- Version Control
- Ineffective Tracking
- Decentralization

The above-listed issues may arise at the time of mergers and acquisitions, multiple products approved in multiple countries, and changes in local labeling.

Top Reasons for Pharma Labeling Audit Issues



Source: www.ddismart.com

Failure to fulfill the requirements of Regulatory standards to disclose product safety information, or sharing such information can:

- **Put the patient safety at risk:** Any inaccuracies in labeling could result in the misuse of a drug, resulting in negative effects and, in some cases, may be fatal.
- **Be costly to organizations:** Recalling a product due to a labeling error is a costly process that can harm a company's bottom line either the profitability or brand image.
- **Be time consuming:** When there is a labeling information gap, investigating a labeling issue may be time consuming for Health Authority.
- **Damage the reputation:** Once the product is recalled from the market, it may even impact the brand image and subsequently can have a detrimental impact on an organization's reputation.

In such scenarios, how do you ensure that your pharmaceutical product labeling procedure will meet the required criteria?

Adopting Automation for Labeling Compliance

Automation, like it does in so many other fields, is critical in ensuring global labeling compliance. In addition to this, automation reduces human intervention and ensures the development of high-quality deliverables that significantly reduce overall operational costs and improve the time-to-market of organizational product lines.

Today, the best method to successfully meet Regulatory labeling compliance is to invest in a comprehensive label life cycle management tool. By contracting out global labeling operations to specialized end-to- end label management software vendors, pharmaceutical manufacturers can bank on effective and streamlined label management.

FREYR CONNECT

Freyr What Is..?

What is Wireless Technology Licensing?

The healthcare industry is drastically changing with the advancements in digital technology. With the virtue of this technological progress, the global medical device industry is now exploring new areas like wireless medical devices to improve care while lowering treatment costs. Manufacturers of such wireless devices have to follow a dual line of regulations (approval required from telecommunication authority and Regulatory Authority), and many countries have specific requirements concerning the medical device wireless technology licensing.

The Thailand Food and Drug Administration (TFDA) has issued certain rules for Thailand's foreign and local manufacturers who wish to sell medical devices involving wireless technology. For the importation of wireless technology devices with cellular, Radio Frequency Identification Devices (RFID), WiFi, or Bluetooth connectivity into Thailand, manufacturers have to get approval from the National Broadcasting and Telecommunications Commission (NBTC). The NBTC is the telecommunications commission of Thailand that requires all the wireless medical devices to obtain the approval certificate, an important customs clearance document. Manufacturers must note that even if NBTC provides the approval certificate for the device, the TFDA holds the ultimate authority to decide on whether to sell the device in Thailand.

NBTC classifies telecommunication devices into three (03) categories

Class A devices: These devices must be tested only in the NBTC accredited laboratories. Manufacturers must provide all the data required for approval and must also note that samples must be provided along with the application for some products. On approval of the application, the device will receive the login number and certification.

Class B devices: The same applicable products as Class A, and can accept foreign reports such as Radio Equipment Directive, FCC, Electro Magnetic Compatibility (EMC), application by using Conformity Assessment Body (CAB).

Supplier Declaration of Conformity (SDoC) compliance statement mode: The product requirements are voluntary. A local representative in Thailand makes an application. An SDoC form is required. Technical documents can be sent to the NBTC for inspection; samples are not required.

Obtaining NBTC Certificate:

The wireless medical devices falling under Class A and Class B require an NBTC Certificate for customs clearance. The manufacturers must ensure that the NBTC certificate is in place before the device is imported into Thailand. The foreign manufacturers must appoint a local representative with a commercial license issued by the NBTC for submitting the applications, customs clearance facilitation to the NBTC on behalf of the manufacturer.

The manufacturers can start their certification by identifying an NBTC accredited testing laboratory. Usually, the testing laboratories require the manufacturer to fill their standard test application (request) forms, submit product manuals and instruction manuals along with the device samples. The manufacturer is also required to share the list of testing standards (in a bottom-up test). The testing laboratories issue stamped reports for the devices that clear all the testing requirements.

The manufacturers must submit the application for NBTC certification along with the technical product documentation and test reports issued by the NBTC accredited laboratories. The technical product shall include product instructions, adapter safety report, list of key components, key component certificates, and certificate numbers for key component model manufacturers. The submission package shall include the product label, packaging picture, user instructions, and temperature requirements. The application should accompany 1-2 pieces of device prototype as well.

The NBTC requires 30 to 45 working days to review the application. The import license will be valid for 180 days from the authorization date and can be multiple times within the validity period. The NBTC application review fees vary with the device class as detailed in the below table -

Device Type	Technology Covered	NBTC Fee (excludes 7% VAT)
Class A	RFID, WLAN, WPAN	ThB 1,000** (29.58$)
Class B	Cellular	ThB 5,000** (147.89$)
SDoC	Bluetooth, WIFI	None

This medical device wireless technology licensing in Thailand is a slightly lengthy but effective way to ensure that the medical devices imported and sold in Thailand are of good quality and do not pertain to any risk to the end-users. This seamless collaboration between the NBTC and the TFDA helps manufacturers place their wireless medical devices in a hassle-free way into the Thailand market.

To know more about wireless technology licensing of medical devices in Thailand, reach out to a Regulatory expert like Freyr. Stay informed. Stay compliant.

Freyr
What Is..?

Who is a PRRC?

PRRC stands for Person Responsible for Regulatory Compliance. With the new EU Medical Device Regulation (MDR) and In-Vitro Diagnostic Regulation (IVDR), the EU regulators want to ensure that companies have a qualified Regulatory expert- a PRRC at their disposal to ensure that the company complies with the Regulatory requirements.

What are the requirements for a PRRC?

The medical device and IVD manufacturers shall have within their organization, a Person Responsible for Regulatory Compliance (PRRC) whereas the small and micro manufacturers may not have a PRRC within the organization but must have one such person permanently and continuously at their disposal. For the Authorized Representatives (AR), they shall have one PRRC permanently and continuously at their disposal. The PRRC should have proper expertise and qualification in the field of medical devices or IVDs, whichever is applicable.

What should be the qualification of a PRRC?

The Article 15 of MDR and IVDR clearly mentions the required qualifications and professional experience that a Person Responsible for Regulatory Compliance (PRRC) should possess which are:

- A diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree or of a course of study recognized as equivalent by the Member State concerned, in law, medicine, pharmacy, engineering or another relevant science, and a minimum of one year of professional experience in Regulatory affairs or in quality management systems concerning medical devices

- any qualification acquired outside the EU, including any university diplomas or certificates, should have been recognized by an EU Member State as equivalent to the EU corresponding qualification
- four years of professional experience in Regulatory affairs or in quality management systems relating to medical devices and the EU requirements in the field

Who should appoint a PRRC?

- Manufacturers: The manufacturers shall have at least one PRRC within their organization with accurate expertise in the field of medical devices in the EU. This is valid when the organization has at least 50 employees in the company. The PRRC appointed by the large manufacturers should be the employee of the company.
- Distributors and Importers: The distributors and importers who modify an existing device, change the intended purpose of existing device or make available a device on the European market is considered as a manufacturer and should appoint a PRRC.
- Other persons acting as manufacturer: Any legal or natural person who modifies an existing device, changes the intended purpose of existing device or makes available a device on the European market is considered as a manufacturer and should appoint a PRRC. This is because the person assumes the obligations that the manufacturer is responsible for.
- Assembler of systems and procedure packs: The companies who assembles devices into a system or procedure pack using the devices which do not bear the CE marking, or the sterilization is not performed as per the protocols or the combination of devices is not compatible, then such system or packs are considered as medical device and hence such organization has to appoint a PRRC.
- Authorized Representatives: They should have permanently and continuously at their disposal a PRRC who has required expertise.

Where can the PRRC be located?

It is very important to have a close linkage between the manufacturer and the PRRC. Considering this fact, it is assumed that for a manufacturer based outside the EU, the PRRC will also be located outside the EU and for a manufacturer based inside the EU the PRRC will be located inside the EU, the PRRC. Whereas in case of the micro and small manufacturers located inside the EU, the PRRC should be permanently and continuously available at their disposal and hence the PRRC should be located inside the EU. Considering that the authorized representative is located inside the EU, it is assumed that the PRRC should be permanently at its disposal and hence should be located inside the EU.

What are the roles and responsibilities of a PRRC?

- Conformity of the devices should be checked and should be in accordance with the QMS
- The technical documentation and the declaration of conformity should always be up to date
- The post marketing surveillance obligations should be complied
- The reporting obligations should be fulfilled by the PRRC

Can a company have more than one PRRC?

Yes, more than one PRRC can be appointed by the companies and the responsibilities can be divided, as long as the qualification requirements are met and the division of responsibilities is documented in writing.

How many PRRC should an organization with more than one legal manufacturer have?

If a parent company has more than one legal manufacturer, then it is necessary to ensure that each legal manufacturer has a PRRC appointed.

Can one individual be the PRRC for a manufacturer and its authorized representative?

The PRRC for an authorized representative and for a manufacturer based outside EU cannot be same. In the regulations for Authorized representative, it is clearly mentioned that PRRC will be an additional level of scrutiny. Therefore, if the same person acts as PRRC for both, the additional level of scrutiny would be compromised. For EAR and PRRC services, reach out to us at sales@freyrsolutions.com

Awards & Recognitions - 2021

ELEMED FEATURED FREYR AS THE "BEST SUPPLIER TO THE INDUSTRY" OF THE YEAR 2021

INTERNATIONAL - REGULATORY SOLUTIONS PROVIDER OF THE YEAR, FREYR

INTERNATIONAL - GAMECHANGER OF THE YEAR CEO, FREYR

INTERNATIONAL - NICHE TECHNOLOGY COMPANY OF THE YEAR (PHARMA AND LIFESCIENCES), FREYR

USA-9 TECHNOLOGY MAGAZINE LISTED FREYR IN THE "10 BEST TECHNOLOGY SOLUTION PROVIDERS OF 2021"

GHP AWARDS 2021 HONORED FREYR FOR "INNOVATIVE GLOBAL REGULATORY SERVICES AND SOLUTIONS FOR LIFE SCIENCES"

ANALYTICS INSIGHT FEATURES MD, FREYR AS "THE 10 MOST IMPACTFUL WOMEN IN TECHNOLOGY - 2021"

Freyr Webinar Series

Upcoming Webinars

Simplified Authorization of Biocides in the EU

Food and Food Supplements Indian Market and FSSAI Regulatory Scenario

Past Webinars

Swixit - Regulatory Impact for Medical Devices & MedTech Industry

IDMP is Real: Redefine RIMS With the EMA's SPOR Operating Model

Medical Devices in the UK & UKRP: Latest Industry Updates

Know More

CPHL WORLDWIDE 2021

Freyr Attended CPhI Worldwide 2021

We were glad to attend CPhI Worldwide 2021, held between November 9-11, 2021. We want to extend our sincere gratitude to CPhI for making this event possible and look forward to participating in more such events.

Also, a big thanks to all the industry thought leaders for sharing their inputs on global regulations, best practices, and practical solutions.

FREYR CONNECT

Infographic

EMERGENCY USE AUTHORIZATION (EUA): HIGHLIGHTS

Country Product EUA Guidelines

	Turkey	Mexico	South Africa	India	Brazil
Central Regulatory Authority	Republic of Turkey Ministry of Health	Cofepris – Comisión Federal para la Protección contra Riesgos Sanitarios	SAHPRA – South African Health Products Regulatory Authority	CDSCO – Central Drugs Standard Control Organization	ANVISA
Emergency Authorized Use	Yes	Yes	Yes	Yes	Yes
HA Approval Timeline	3-5 Months	3-5 Months	3 Months	3-5 Months	1 Months
Involvement of Local Population for Phase III CT	Not Mandatory Possibility to get a waiver	Yes, the MoH requires the Mexican population to be included in the Phase III study	Not Mandatory, if but MoH can expect Phase III data on the new variant and co-morbid condition (HIV and TB)	Not Mandatory, if safety and efficacy are established	Not Mandatory to involve the Brazilian population
Reference Approval from "Primary" Markets for the EUA	Not Mandatory	Not Mandatory (But highly advantageous)	Not Mandatory	Required	Not Mandatory
Scientific Advice from the HA	Yes	Yes	Yes	Yes	Yes
Current Manufacturers	1 (Sinovac)	2 (Sputnik and Sinopharm)	2 (AstraZeneca and J&J)	3 (Sputnik, Covishield, Covaxin)	3 (AstraZeneca, J&J and Butantan)
Government Responsibility for Procurement	-	Yes	Yes	No	No, Sponsor is responsible
PV Responsibility	MA Holder's responsibility	MA Holder's responsibility	MA Holder's responsibility	MA Holder's responsibility	Local
MA Holder	Yes	Yes	Yes	Yes	Yes
"Rolling Submission" Availability	Yes (But the term is not used)	Yes (But the term is not used)	Yes	Yes (But the term is not used)	Yes
Freyr Timeline (Gap Analysis, Dossier Compilation & Submission)	4-6 Weeks	4-6 Weeks	4-6 Weeks	4-6 Weeks	4-6 Weeks

THE WAY FORWARD WITH MICHAEL LAMBELL

In the dynamic field of Regulatory Affairs, quite a few factors shape a leader – commitment, innovation, hard work, and discipline. These qualities build a persona that leads by example and creates the best work-space environment for everyone. In this volume's Leadership CONNECT, let us know more about one such person who has been an exemplary for leading Regulatory Affairs of medicinal products at Freyr. He is Michael Lambell, the Vice President of MPR RA, who, with his pleasant demeanor, is an inspiration to many.

1. **Hello Michael. Firstly, we are incredibly happy for the opportunity to know you better. Thank you for interacting with us.**

   You're very welcome. It's great to have the opportunity to connect with you in these times when most of us are working remotely. It's even more important to stay in touch when we have the opportunity.

2. **As you are aware, Freyr has completed ten (10) years in the Regulatory Services and Solutions realm and has established itself as an industry leader. What, according to you, has made this possible for Freyr?**

   I think that the flexibility and responsiveness that Freyr shows when engaging with its customers is a clear strength. Additionally, the desire to thoroughly understand what a customer's specific needs are and what those needs might develop into sets the foundation for a relationship that can flourish.

   These, coupled with the expertise and willingness of the team we have in Freyr, have played a significant part in the first 10 (ten) years of the journey.

3. **Due to COVID-19, we are witnessing many initiatives in the Regulatory fields of Life Sciences and MedTech industries. How has the post-COVID 'new normal' situation affected the Health Authorities' decision-making regarding medicinal products Regulatory Affairs?**

   As one would expect, Health Authority decision-making follows a science-based approach. Regulatory submissions of all types need robust justifications and are well-supported by appropriate data. In my view, this reflects one of the main aspects of the support which Freyr provides to our clients; ensuring the submissions meet the standards required for a successful application.

   As we are all aware, the pandemic has resulted in companies developing products to treat the disease. We have supported some of them with their Regulatory needs. Sometimes, this means assisting them with Emergency Use Applications procedures, which some Health Authorities follow to streamline the process of making urgently needed medicines available in the market as soon as possible.

4. **Can you share a few thoughts on Brexit and the areas of opportunity that it opens up?**

   Brexit has significantly changed many aspects of the Regulatory landscape as it relates to the UK. As such, it has resulted in a range of new areas where Freyr can offer support to clients with new products to register or to those with existing products wishing to maintain and ensure compliant supply lines.

   As is the case with most new market entries, it is important to receive good advice at the right time. With this in mind, I would suggest that a conversation with the relevant experts in our team is the best place to start so that a customer's needs can be fully understood, taking into account Brexit-related factors.

5. **CMC RA is a dynamic sector in the pharmaceutical industry. You are at the helm of MPR RA at Freyr, and your decisions, for obvious reasons, make an impact. How do you keep up with the ever-changing industry on any given day?**

   CMC RA is certainly an area that attracts a wide variety of projects, and each customer requirement is different. Keeping up to date with relevant guidelines (and ensuring visibility of forthcoming changes) is key to this, providing ongoing opportunities to learn and to broaden the experience.

   A significant factor for success relies on the professionalism, diligence, and dedication of my colleagues working in the Regulatory organization. Their experience and desire to stay up to date make Freyr's expertise available to support a wide range of client inquiries and needs.

6. **What has been the biggest challenge you faced in your stint with Freyr? What kind of measures have enabled you to overcome them?**

   Being in a leading global Regulatory services company at a time of change is always exciting. Freyr has expanded to pass the milestone of 1000 employees, and as it continues to grow beyond this, ensuring our teams are set to grow accordingly is an ongoing challenge.

   However, it's a challenge that will continue to provide scope for us to grow our existing skill sets and to broaden our experiences. In my view, knowing this helps make the challenge more of an opportunity.

7. From all our interactions with fellow Freyrians so far, we have understood that Mick always prefers to be punctual and deliver a project on time. Could you please brief us on your focus on time?

I think the conscientious influence of my fellow Freyr colleagues helps to maintain a focus on time, including the following aspects:

- ensuring we set challenging (but achievable) timelines,
- planning our time in a way that helps us to achieve as much as possible in what we have,
- communication of any potential risks in the agreed timelines

These points (among others) can also help to ensure that we achieve an appropriate balance between the time we spend focussing on our work and the time which we need to dedicate to our personal lives.

8. What if you were not into CMC Regulatory Affairs? Which field/career pathway would you have opted for?

I think I would always have followed a path related to a technical/scientific field.

The way digital technologies continue to transform our lives is fascinating (and sometimes, to me at least, a little daunting as well). So, perhaps a path related to this area would have been an interesting one to follow. Overall, a career related to healthcare is where I think I would have found myself, even if I had followed another route.

9. Who do you look up to for inspiration?

We all can derive inspiration from many sources. Within Freyr, I think we are fortunate to have many colleagues who inspire us to stretch ourselves and try to be the best we can be.

I think it's also good to keep in mind that we can be inspired by people at all stages of their careers – whether it is a colleague who is well experienced in their field or someone in the earlier stages of their career journey which provides a new and unexpected insight in tackling a challenge.

10. What are the essential qualities of successful leaders?

A variety of attributes contribute to different extents in successful leaders. I think the key attributes include a willingness to listen to different viewpoints and to take various competing factors into account when making decisions. Of course, encouraging an environment where colleagues can express their opinions and make suggestions is also necessary for this to work.

FREYR CONNECT

HA Updates

All Devices and IVDs Marketed in India Now Have to be Listed with SUGAM portal by

October 1, 2023

- Import/manufacturing license for Class C & Class D medical devices

October 1, 2022

- Import/manufacturing license for Class A / Class B medicaldevices & IVDs

October 1, 2021

- Mandatory Listing of all devices
- All foreign manufacturers to appoint Indian Authorized Agent (IAA)

Have You Listed Your Devices Yet?

Consult Us Today

Client Wins

The Customer: Germany-based, Pharmaceuticals & Personal Care Products Company

Project Details: Formulation Assessment for India, UAE and KSA Markets

The Customer: US-based Ammonia-Free Hair Dye Products Company

Project Details: PIF Compilation for the USA Market

The Customer: France Based, Pharmaceuticals Manufacturing Company

Project Details: GAP Analysis and eCTD Publishing Services for Saudi Arabia

The Customer: US-based, Food Supplements Company

Project Details: Product Compliance Support for Australia

The Customer: Israel Based, Leading Multinational Pharmaceutical Company

Project Details: Regulatory Support in Saudi Arabia, UAE, Nigeria, Ghana, Kenya and Morocco

The Customer: Russia based, Personal Care and OTC Manufaturing Company

Project Details: Label & Claims Compliance Support As Per the EU regulations

The Customer: US-based, Global Largest Pharmaceutical Company/US-based, Multinational Pharmaceutical Company

Project Details: Labeling, Artwork & RA support

The Customer: Japan-based, Beauty and Wellness Brand Development Company

Project Details: Food Supplement Product Compliance Services

The Customer: Israel-based, Leading Multinational Pharmaceutical Company

Project Details: eCTD Publishing Services

The Customer: Canada-based, Leading Biotechnology Company

Project Details: Registration Holder Support in India and Mexico

The Customer: US-based, Leading Consumer Products Company

Project Details: Trademark Registration

The Customer: US-based, Leading Disinfectant Products Company

Project Details: Labeling & IFU Compliance Support

The Customer: Korea-based, Leading Medical Device Manufacturing & Distribution Company

Project Details: Product Registration in the USA and Canada

The Customer: US-based, Leading Food and Beverages Company

Project Details: Novel Foods Approval Support

The Customer: US-based, Leading Sterilization Products Company

Project Details: License Transfer& RP Support

The Customer: Japan-based, Beauty and Wellness Brand Development Company

Project Details: Food Supplement Product Classification

The Customer: Canada-based, Innovative Medical Devices Company

Project Details: Indian Authorized Representative Support

The Customer: Spain based, Leading Cosmetics Products Company

Project Details: Cosmetic Product Notification Services in Canada

The Customer: US-based, Cosmetics Manufacturing Company

Project Details: Product Classification in Japan

The Customer: Spain-based, Global Pharmaceuticals Company

Project Details: Regulatory Support For the EMA and the FDA Dossiers Submission

The Customer: Croatia-based, Leading Generic Pharmaceuticals Company

Project Details: Product Registration in the USA Market

The Customer: Italy-based, Leading Healthcare Products Manufacturing Company

Project Details: Food Facility Registration (FFR) & USA Agent Services For FFR

The Customer: Indonesia based, Leading Consumer Goods Company

Project Details: Cosmetics Regulatory Services in India

The Customer: Denmark-based, Leading Specialty Pharmaceuticals Company

Project Details: Labeling, Artwork and LR Support in 35 Countries

The Customer: UK-based, Leading Health Supplements & Beauty Products Supplying Company/UK-based, Leading Consumer care Products Supplying Company

Project Details: Regulatory Gap Analysis For the EU Region

The Customer: UK based, Multinational Consumer Goods Manufacturing Company

Project Details: Regulatory Formulation Assessment For 8 Personal Care Formulations

The Customer: US-based, Leading Oncology Therapeutics Manufacturing Company

Project Details: Publishing and Submission Support for INDs, BLAs & LCM submissions in the USA and Canada

The Customer: Israel Based, Leading Multinational Pharmaceutical Company

Project Details: Regulatory Support in the UAE

Case Study 1

FREYR REGULATORY ARTWORK SERVICES

Implementation of CDPM Functions for 395 CRRs with 50% Cost Savings and Zero Recalls

Client
Global top 5 Pharma Company

Health Authority
US FDA, EMA

Freyr CoE/Product
Regulatory Artwork

Service Offering
End-to-end Artwork Services

Industry
Pharmaceutical

Service Region
North America and EMEA Regions

Client Location
USA

Therapeutic Area/Indication
Skin care, baby care, oral care, wound care

BENEFIT HIGHLIGHTS

- Centralized, error-free, and round-the-clock services and execution
- Reduced artwork reworks from multiple cycles to single iteration
- Over **50%** savings in cost of compliance

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Business Imperatives

- The client was looking for end-to-end centralized artwork services for the CDPM (Copy Development Project Management) functions for various products
- The CDPM must own the entire process from initial manuscript routing until the final completion and release of marketing material

Challenges

- Client took up multiple activities, hence was unable to strengthen CDPM function
- Client was facing delays in task execution due to CDPMs working in different locations
- CDPM metrics are behind 24-hour SLA (Service Level Agreement) on significant percentage of (Change Request Record) CRRs
- Delays in managing wide range of product portfolios

Freyr Solutions and Services

- Strengthened CDPM function by assigning the roles and responsibilities to a dedicated team
- Centralized approach for in-house training and fast-paced task execution
- Developed and implemented critical checklist to avoid business critical errors in artwork
- For time efficiency, developed of a single point of contact team to manage wide range of product portfolios

Client Benefits

- **Zero recalls**/critical incidents in artwork errors
- Round-the-clock coverage, hence **reduced overall (turnaround time) TAT** of artwork process
- Clarification for product related queries at single contact point
- Error-free rapid task execution resulted in improved metrics
- Overall cost savings of nearly **50%**
- A total of **395** CRRs (Change Request Record) have been completed through the system by the CDPMs over last six months

Case Study 2

Center of Excellence

Pharmacovigilance

Authoring 70+ PADER Reports with Considerable Cost Benefits

Client
US-based Pharmaceuticals Company

Health Authority
US FDA

Freyr CoE/Product
Pharmacovigilance

Service Offering
PADER

Industry
Pharmaceutical

BENEFIT HIGHLIGHTS

- Streamlined process with submission ready documents
- Timely delivery of the PADER reports
- Significant cost benefits

Service Region
USA

Client Location
USA

Therapeutic Area/Indication
Multiple

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Business Imperatives

- A US-based global Pharma company was looking for Regulatory support in authoring and finalizing the Periodic Adverse Drug Experience Reports (PADERs) for marketed drugs
- Freyr has supported 70+ PADERs
- Freyr has supported all PADERs related activities

Challenges

Ambiguity

- To provide a real time conclusion, based on the limited information provided
- Stringent timelines
- Health Authority specific timelines
- Complex/tedious review process

Freyr Solutions and Services

- Freyr Expertise and Approach followed
- The domain expertise team in Freyr decided to avoid the rework/reading of case narratives again and again, started providing a summary
- Efficient planning during authoring and review process
- End-to-end Regulatory support for 70+ PADERs
- Experienced Medical Writers with good domain knowledge
- **Meeting Stringent Timelines**
- Internal QC and medical review
- Proper planning and execution

Client Benefits

- Avoiding rework, which in turn saves time
- Streamlined process with submission ready documents
- Timely delivery of the PADER reports
- Significant cost benefits

Client Testimonials

Thank you so much Freyr for the help on this project. You provided outstanding customer service!

RA Specialist
A Pharmaceutical Company

Thank you so much for sending the assessment reports. The reports are presented in very structured and clear way. We highly appreciate your support.

Leiter Regulatory Affairs / Head of Regulatory Affairs
A Cosmetic Manufacturer

Thank you Freyr. This is excellent and will be super helpful.

Global Director, Regulatory Affairs
A Utah-based multi-level marketing company

I am sure you have heard by now that we have received its first ever approval from the FDA for our Brands division. This is a major milestone for us as well as for my team. I would be remiss if I did not point out that we would not have been able to do this without the help of Freyr's dedicated team. From the original filing, then the following year of responses, Freyr's team has helped us to get to final approval.

Thank you Freyr team for a job well done!"

Sr. Director, Head of Regulatory Operations and Strategic Business Solutions,
A Global Specialty Pharmaceutical Company

FREYR CONNECT

All people involved in this project were very helpful, knowledgeable and fast. Freyr performed more than we expected. Outstanding service!"

A Swiss-based Nutraceuticals Company

Thank you very much for a nice closure! It has been a pleasure working with you all. I want to take this opportunity to thank you for all your support with our newsletter's projects during the past 2.5 years, the excellent collaboration, and communication. The dedication and professionalism of your team were greatly appreciated. All the projects were delivered on time and were compliant with our quality standards.

The team followed attentively and patiently addressed all the changes in our IT systems and processes and acted as a true partner providing valuable comments to draw attention to some points or issues about the content. I enjoyed working with the team and hope we will have new opportunities to continue our collaboration in the future.

THANK YOU and Season's Greetings!!

Regulatory Consulting Manager
A global leader in providing trusted insights and analytics

Thank you Freyr for the strong support thus far in 2021. We are so excited to grow our partnership in the months and years ahead.

Freyr truly exceeded all our expectations and went above and beyond of what we asked. Most remarkable is the staff's quick response time, as they literally seem to be working around the clock. It was an unexpected surprise to have a global partner that was responsive at all hours of the day to our questions and concerns.

Equally impressive is that Freyr's delivery team was very clear in setting expectations and explaining the project's process. We appreciated that they were always truthful about lead times for queries, submissions, and document review. Freyr always delivered when promised and frankly, the process was easier than we thought. Their document exchange portal was easy to use, and our points of contact were very strong communicators.

Lastly, I am sure that Freyr represents larger and more influential firms. However, I would never get this impression for my interactions with them. Our dedicated account representatives are so welcoming every time we speak and make us feel like the only client in their portfolio. It is very refreshing to feel Freyr's personal touch, compared to the transactional nature of other consulting partners we have worked with in the past.

Regulatory Specialist
An American Global Manufacturer of Electronic Instruments and Electromechanical Devices

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

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

About Freyr

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

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