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LEAD STORY

2021 and Further -
A Regulatory Preview

FURTHER 2021

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What's **INSIDE?**

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FOREWORD

Dear Patrons,

Greetings and Good Wishes!

We really hope and trust that you and your family are staying safe and healthy. It's our pleasure to bring forth the brand new Issue of Freyr CONNECT Volume 8.

As you may know, the global Regulatory landscape is unconventional in nature, triggering the need for industry to keep abreast with the ever-evolving regulations and to decode Regulatory best practices for compliance. Missing out any of the updates may incur huge loss of capital and time for industry. Therefore, with this Issue we bring you the latest Regulatory information and best practices for compliance.

What do we cover in this Issue? Here is a glimpse. Commencing with a lead story depicting the Regulatory preview of the year 2021 and further, we will take you through the insights on how Brexit finalization will change the European medical device compliance. Moving ahead, we have detailed the ideal features of SPL & SPM software that can help you align with both the US FDA and Health Canada mandates. In addition, this Issue also covers Regulatory updates from various Health Authorities like Health Canada, SFDA, the US FDA, ANVISA and many more. Finally, the Issues highlights Freyr's proven Regulatory expertise in terms of case studies and insightful webinar sessions (Cosmetics and Medical Devices).

All in all, we hope this newsletter will help you understand the status-quo of Life Sciences Regulatory landscape and walk the right Regulatory pathway to achieve compliance.

Happy Reading!

Suren Dheenadayalan
CEO

2021 and Further - A Regulatory Preview

The year 2020 has been unpredictable for all the industries across the globe, including lifesciences industry. With the outbreak of COVID-19 pandemic, the industry and the global Health Authorities (HA) faced various challenging scenarios, which in turn affected their long-term Regulatory plans.

The global Health Authorities (HA), along with various healthcare providers, were pushed to transform their operational models overnight to deal with the on-going crisis. The industry transformed its regulations to ensure that demand for essential medical and medicinal products, such as PPE kits, surgical masks, hand sanitizers, etc., was met successfully. The global Health Authorities also introduced expedited pathways for vaccines to help them reach the markets in a shorter time.

However, due to the chaos ensued, the year 2020 has well-prepared the industry for the upcoming year 2021. Right from amending existing regulations to bringing in new regulations, the global Health Authorities are working continuously to release new guidance documents, pathways, regulations and rules for medical devices, pharmaceuticals, cosmetics, food supplements, chemicals, etc., to improve the overall Regulatory scenario. In addition to this, there are a few Regulatory updates, such as EU MDR, that are going to come into effect in 2021, which were earlier postponed due to the COVID-19 pandemic. Thus, to help you get acquainted with these upcoming regulations, we have decoded and collated some of the Regulatory updates to help you strategize better. Let's take a look at them.

Regulatory Updates 2021

Pharmaceuticals

MHRA Post-transition Guidance for PV, QPPV and PSMF

Medicines and Health Regulatory Authority (MHRA) of the United Kingdom (UK) has published guidance for pharmacovigilance procedures and post-transition requirements for Qualified Person Responsible for Pharmacovigilance (QPPV) and Pharmacovigilance System Master Files (PSMF) for the UK authorized products. The MHRA announced that the responsibility for pharmacovigilance will be retained across the UK, and all the Marketing Authorization Holders (MAHs) must have a QPPV residing and operating in the EU/UK permanently from January 1, 2021.

Water for Pharmaceutical Use - EMA's Revised Guidelines

To enhance the quality of the Pharmaceutical water, the European Medicine Agency (EMA) has updated the two-decades-old EMA's 'Note for Guidance on quality of water for pharmaceutical use'. The new set of guidelines will come into effect from February 2021.

The major concern behind the revision of the guidelines is to control the microbial quality of water, which is a key resource for the development and maintenance of water purification systems. The European Pharmacopoeia signifies quality standards for grades of water for pharmaceutical use that includes water for injections (WFI), water for preparation of extracts and purified water.

Post-Brexit Compliance with Clinical Trial Rules

The European Commission (EC), along with the European Medicines Agency (EMA), released a notice to remind clinical trial sponsors to comply with the EU clinical trial rules following the Brexit transition period that is going to expire on December 31, 2020.

As there is no possibility for further extension of the Brexit transition period, the EC has released a Brexit readiness notice for clinical trials. The sponsors are expected to abide by the following rules to ensure smooth operation of their ongoing clinical studies:

- They must have a qualified person established in the EU or EEA or a legal representative established in the EU
- Investigational medicinal products used in clinical trials must be imported to the EU only after the qualified person certifies the batch-release
- Sponsors of all ongoing trials must also establish a qualified person in the EU

Regulatory Updates 2021

Chemicals Safety and Regulatory Affairs

Rising Demand for Chemicals and The Need for Best Practices

Based on the infographic provided by the American Chemistry Council (ACC), explaining the contribution of chemicals to cleaning products and medical equipment, chemicals contribute:

- 75% - in cleaning compounds
- 27% - in medical equipment
- 25% - in medical supplies

This clearly shows the high demand for chemicals in the industry. With the increasing demand, there are best practices chemical manufacturers must follow both from the Regulatory and operational perspectives, such as:

- Adherence to the Dynamic Regulations
- Management of Manufacturing and Operational Data
- Minimizing Formula Costs to Create New Efficiencies
- Recalls and Quality Audits

Biocidal Products & Authorization in Europe

Biocidal Product Regulation (BPR) aims to ensure a high level of protection for humans and the environment and improve the functioning of the Biocidal products' market in the European Union (EU). All Biocidal products must require authorization to enter the European market. Also, the active substances present in that Biocidal product must be previously approved. The European Commission has provided several authorization processes that are as follows:

- National Authorization and Mutual Recognition
- National Authorization and Mutual Recognition Renewal
- Union Authorization
- Simplified Authorization
- Same Biocidal Product Authorization

Regulatory Updates 2021

Medical Devices

Role of MHRA and Post-Brexit Scenario for Medical Devices in the UK

As you may know, the Brexit transition period has ended on December 31, 2020, and the UK's Regulatory Authority, Medicines and Healthcare Products Regulatory Agency (MHRA) has taken over the current EU responsibilities for medical devices and In vitro diagnostics (IVDs), from January 1, 2021. Accordingly, the MHRA published a guidance on the new rules that will govern the regulation of medical devices and IVDs placed in Great Britain (England, Wales and Scotland), Northern Ireland and EU market, post the transition period (however, different rules will apply to Northern Ireland). The MHRA guidance provides information on how the UK system will operate for device certification, conformity assessment and registration with the MHRA.

Medical Devices Labeling Requirement for the EU MDR Compliance

As the EU MDR transition deadline is inching closer, i.e., May 2021, manufacturers must execute the labeling requirements with utmost priority and caution and must ensure high standards of quality and safety for compliance. Prior to execution, understanding the new labeling requirements and accurate implementation is of paramount importance. Any labeling errors can impede the progress, and cause product recalls, which may lead to costly delays. Therefore, the key is to carefully prepare the medical devices labels aligning with the EU MDR labeling requirements.

Regulatory Updates 2021

Food Supplements

Changes of FDA's New Nutrition Facts Label

In 2016, the United States Food and Drug Administration (USFDA) published final rules for Nutrition Facts Label for packaged food. The FDA established the rule to align the nutrition fact label of food products with the current food habits and practices. According to the final rules published by the US FDA, for food product manufacturers entering the US market, with an annual sale of less than USD 10 million,

the labeling changes are mandatory from January 1, 2021.

The major changes in the labeling rules are related to the list of food nutrients that are required to be declared on the label of the food product, along with updating the serving size requirements and a change of design.

Regulatory Updates 2021

Cosmetic Products

NMPA's Final Version of CSAR

In 2020, the National Medical Products Administration (NMPA) of China published the final version of the Cosmetic Supervision and Administration Registration Regulation (CSAR), which has come into effect from January 1, 2021. The aim of the updated CSAR is to ensure that the products manufactured and distributed in China are safe and effective for use. The key aspects of the CSAR are:

- Manufacturers are entirely responsible for the efficacy claims mentioned on the product label
- Cosmetic manufacturers are required to align by the regulations of the CSAR
- The CSAR includes a few changes in terms of classification and scope of cosmetics
- Cosmetic products will soon be regulated based on their associated risk factors

In conclusion, the year 2021 promises a plethora of opportunities for life sciences industry manufacturers to explore. However, the above mentioned updates are just a glimpse of the upcoming changes in the global Regulatory landscape. Manufacturers must be on a constant look out for Regulatory updates to ensure compliance with the latest regulations and to overcome any possible challenges. Till then, be game for 2021. Stay compliant. Stay safe.

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Brexit Finalization: How Will Medical Device Compliance Change In Europe In 2021?

The UK left the European Union (EU) earlier this year with an 11-month transition period ending on December 31, 2020.

Given that the UK has been a member of the European Union for almost 46 years, the bilateral interactions are deeply rooted and the mechanisms to ensure hassle-free interactions between the UK and the EU after the exit is crucial. Post the Brexit transition period, high import tariffs, duties, and taxes have increased the cost of the device, The Medicines and Healthcare products Regulatory Agency (MHRA), which regulates medical devices marketed in the UK, released new guidelines in September 2020 detailing how devices will be regulated beginning January 1, 2021, with varied compliance dates for different device classes. The new rules will be applicable for placing medical devices in Great Britain, Northern Ireland, and the EU. Medical device and In Vitro Diagnostic (IVD) manufacturers will need to register medical devices with the MHRA, identify a UK Responsible Person, obtain proper device certification, and include proper device marks and labels.

The location of the manufacturer, the risk classification of the device, and the market of interest determine the Regulatory requirements for device manufacturers to place a new device into the market and for continuity of existing device distribution. The enforcement powers of the MHRA are derived from the four main regulations noted below. The Medicines and Medical Devices Bill is currently under

Regulation	***The MHRA Rights***
Medical Device Regulations, 2002	• Compliance notice • Restriction notes • Clinical investigation notifications • Notified Body designations
General Product Safety Regulations, 2005	• Recall notices
Consumer Protection Act 1987	• Prohibition notices to ban the supply of any unsafe goods • Notices to warn in case of unsafe goods • Suspension notices to suspend the supply of any unsafe goods for up to six months • Forfeiture orders • Notice to obtain information, wherein the MHRA requires a person to furnish information or to produce records to help decide whether to serve, vary, or revoke a prohibition notice or a notice to warn
Consumer Rights Act 2015	• Inspection of premises • Examination of manufacturing procedures • Request for documents • Detention or seizure of records/goods

Table 1: Regulations that entitle rights to the MHRA

review by the House of Lords and would be in effect after the Royal Assent. To support the medical device industry after the transition period, more regulations and guidelines are expected to be released from time to time. The UK cannot be a part of the EU decision-making group.

Prior to Brexit, device manufacturers in the UK were currently complying with Directive 90/385/EEC on active implantable medical devices (EU AIMDD), Directive 93/42/EEC on medical devices (EU MDD) and Directive 98/79/EC on IVD medical devices (EU IVDD) in order to place devices in the UK market. The MHRA regulations also required the manufacturers of all class I devices manufactured, refurbished, or re-labelled with manufacturer name; any system or procedure pack containing at least one medical device; and custom-made devices and IVDs manufactured and/or undergoing performance evaluation to register with the Health Authority. All other devices falling into any other device class are required to have the conformity assessment carried out by the Notified Bodies (NBs) located in any of the EU countries (known as the EU 28 before Brexit, now the EU 27) in order to place the device in the market.

The geographies are grouped as Great Britain, Northern Ireland, and the EU 27 to assess the impact of Brexit on the medical device industry and to create an action plan for various stakeholders. The geopolitical scenarios in Northern Ireland require the regulations to be different from those to be implemented in Great Britain.

Device Registration with the MHRA

As of January 1, 2021, all devices, irrespective of device class, must be registered with the MHRA. This enforcement has a grace period of varying duration, based on risk class of the device.

- High-risk Class III and Class IIb implantable devices must be registered within four months of the date of enforcement
- Moderate-risk Class IIa and other Class IIb devices have a grace period of eight months.
- Low-risk Class I devices have varied implementation timelines in the UK and Northern Ireland. These devices are required to be registered immediately from January 1, 2021, to be marketed in Northern Ireland, whereas a grace period of 12 months is available for devices to be marketed in the UK. This grace period in the UK does not apply to the Class I, IVD, and custom-made devices that required registration with the MHRA even before the decision to exit the EU was taken.

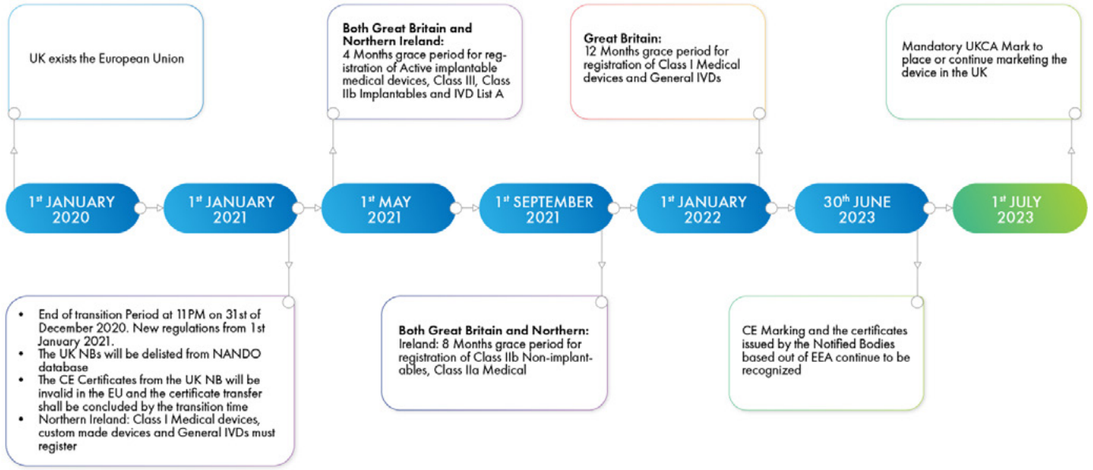

Figure 1: Post-Brexit Compliance Timelines for varied device classes in Great Britain and Northern Ireland

Identifying and Appointing a UK Responsible Person

Non-UK medical device manufacturers need to appoint a UK Responsible Person (UKRP), who must register with the MHRA. The manufacturer shall have a registered place of business in the UK to register the devices with the MHRA and to take responsibility of the device being placed in the UK. Importers or distributors representing the manufacturers can act as UKRPs and can liaise with the MHRA. As detailed in the UK MDR 2002, the roles and responsibilities of the UKRP are:

- To ensure that the technical documentation is available and updated in a timely manner
- To ensure the conformity assessment of the device is successfully concluded
- To ensure the Declaration of Conformity (DoC) is in place
- To have all the technical information about the device and to produce the details and device samples whenever requested by the MHRA. In case of non-availability of samples, the UKRP may coordinate with the manufacturer and ensure that the samples are submitted.

The UKRP will also be playing a critical role in the post-market surveillance of the device and should work with the manufacturer and the MHRA to implement corrective action and preventive action associated with complaints and related safety issues.

The European Authorized Representatives (EARs) based out of the UK will no longer be recognized by the EU and the manufacturers shall appoint a new EAR from one of the EU 27 countries or Northern Ireland. Manufacturers from countries other than the UK and the EU need to appoint an EAR (with roles and responsibilities defined in the MDR and IVDR) to market the device in Northern Ireland.

Manufacturer Location	Pre- Brexit Scenario			Post Brexit Scenario		
	EU 27	UK-GB	UK - NI	EU 27	UK-GB	UK - NI
EU – 27	No EAR			No EAR	UKRP	EAR
UK – GB	No EAR			EAR from EU 27 countries or NI	NA	EAR from NI or EU 27 countries
UK – NI	No EAR			NA	NA	NA
Other Countries	Single EAR based out of any of the EU 28 countries			EAR from EU 27 countries or NI	UKRP	EAR from EU 27 countries or NI

Table 2: Authorized Representative Requirements in the EU and the UK

Changes to NBs and CE Certifications

Prior to Brexit, owing to the single market concept, CE certification issued by any of the NBs based out of any EU country was recognized across the UK and the EU. After Brexit, manufacturers intending to place the device or market the device in the EU 27 need the CE certificate issued by the NB based in the EU 27. The MHRA continues to recognize CE marking and the certificates issued by the NBs located in the European Economic Area (EEA) until June 30, 2023. Devices certified by the UK NB should transfer its certificates to the NBs based out of the EU 27 in order to continue marketing in the EU. The majority of the NBs based in the UK are partnering with NBs based in the EU to facilitate smooth transfer of certifications.

Notified Body Location	MDD/IVD/AIMD	MDR/IVDR
European Union	• Not valid after May 2021	• Valid • Issue ISO 13485:2016 and CE certificates • The certificate is valid in Northern Ireland and the European Union (EU 27) countries
United Kingdom	• Automatically recognized as Conformity Assessment Bodies (CABs) to issue certifications for the UKCA mark • Issues certification to claim the UKCA marking • The devices can be marketed in Great Britain only	• Not required, as MDR and IVDR will not be implemented in the UK • CE marking for Northern Ireland

Table 3: Brexit and Notified Body Considerations

Changes to Marks and Labels

By July 1, 2023, all devices marketed in Great Britain need to have UKCA marking. In Northern Ireland, the UKCA mark is not valid and the manufacturer may opt for either the CE mark (as per IVDR) or the CE UK(NI) mark.

The UK-based NBs approved under the MDD, IVDD, and AIMDD will be automatically designated as Conformity Assessment Bodies (CABs) for the UKCA from hJanuary 1, 2021. Beginning on that date, the MHRA will initiate designating the CABs. Manufacturers intending to market devices in Northern Ireland can get the conformity assessments from the NBs based out of either the UK or the EU 27. In Ireland, the marking on the label would depend on the location of the NB.

Type of Product Marking	Great Britain	North Ireland	European Union
UKCA	√*	X	X
CE Marking	X**	√	√
Both CE and UKCA	√	√	√
CE UK(NI)	X	√	X

Table 4: Different Marks and their Zone of Application

**The UKCA marking can be voluntarily used from January 1, 2021 to July 1, 2023 and is mandatory thereafter.*

***The CE marking will be recognized until June 30, 2023. Thereafter, only the UKCA mark will be recognized.*

The devices to be placed and marketed in the EU 27 and Northern Ireland must comply with the EU labeling requirements. Unlike the pre-Brexit market, in which a single CE marking was required, post-Brexit markets would have three markings (one for Great Britain, one for Northern Ireland, and one for the EU). The devices intended to be placed in Northern Ireland should have the CE(UK)NI mark (if using a UK-based CAB) or the CE mark (if using an EU-based NB).

Going Forward: 2021 and Beyond

Unlike in Great Britain, the EU MDR and EU IVDR will be implemented in Northern Ireland starting in May 2021 and May 2022, respectively, along with the other EU 27 countries. Distributors of UK-manufactured devices will be considered as importers in the European Union and would be subject to product liability requirements of the device, as per Product Liability Directive 85/374/EEC. The detailed regulatory requirements in each geographic area are summarized in the below table.

		Market in Scope		
		Great Britain	Northern Ireland	European Union
Manufacturer Location	Great Britain	• Manufacturer registration with the MHRA • Device registration with the MHRA • EU AIMDD, EU MDD, EU IVDD will be in effect after the transition period	• Comply with the EU MDR and the EU IVDR from May 2021 and May 2022 • Conformity Assessment by the Notified Bodies based out of EEA (CE Mark) or UK (UK(NI)) Mark • CE/UK(NI) marking of the devices • Appoint European Authorized Representative based out of Northern Ireland or any of the EU 27 countries	• Comply with the EU MDR and the EU IVDR from May 2021 to May 2022 • Conformity Assessment by the Notified Bodies based out of EEA • CE marking of the devices • Appoint European Authorized Representative based out of Northern Ireland or the EU 27 countries
	Northern Ireland	• Manufacturer registration with the MHRA • Device Registration with the MHRA • If registered with the MHRA for marketing in Northern Ireland, no separate approval is required for supply to Great Britain	• Comply with the EU MDR and the EU IVDR regulations from May 2021 and May 2022 respectively • CE mark of device either from EEA or the UK Notified Body • Manufacturer registration with the MHRA • Device registration with the MHRA	• Comply with the EU MDR and the EU IVDR from May 2021 to May 2022 • Conformity Assessment by the Notified Bodies based out of EEA • CE marking of the devices

Manufacturer Location				
European Union		• Appoint United Kingdom Representative Person (UKRP) based out of the UK • UKRP registration with the MHRA • Device registration with the MHRA • UKCA mark	• Comply with the EU MDR starting in May 2021 and comply with the EU IVDR starting in May 2022 • CE mark of device either from EEA or the UK Notified Body • Manufacturer registration with the MHRA • Device registration with the MHRA	• Comply with the EU MDR starting in May 2021 and comply with the EU IVDR starting in May 2022 • Conformity Assessment by the Notified Bodies based out of EEA • CE marking of the devices
All Other Countries		• Appoint United Kingdom Representative Person (UKRP) based out of the UK • UKRP registration with the MHRA • Device registration with the MHRA • CAB assessment and UKCA mark	• Comply with the EU MDR starting in May 2021 and comply with the EU IVDR starting in May 2022 • Appoint European Authorized Representative based in Northern Ireland or the EU 27 countries. • CE mark of device either from EEA or the UK Notified Body • Manufacturer registration with the MHRA • Device registration with the MHRA	• Comply with the EU MDR starting in May 2021 and comply with the EU IVDR starting in May 2022 • Conformity Assessment by the Notified Bodies based out of EEA • CE marking of the devices • Appoint European Authorized Representative

Table 5: Post-Brexit Compliance Requirement and Action Plan

Non-UK device manufacturers willing to launch their devices for the first time in Great Britain should comply with the EU MDD requirements and should initiate registration of Class I devices or perform conformity assessments for devices of other classes. Manufacturers with devices already being marketed in Great Britain can continue marketing their Class I devices, provided that the devices are already registered with the MHRA. Manufacturers of other device classes should initiate the discussion with their current NBs for any collaboration with their counterparts in the UK. If not, the manufacturers should find the UK-based CABs for recertification. In all the above scenarios, the first step is to identify and appoint a UKRP followed by the other activities as mentioned above.

Futuristic Approach to Regulatory Intelligence

The life sciences industry is governed by regulations, which are continuously evolving to help the industry players deliver nothing but the best. Staying current with these regulations on a continuous basis and keeping up with the exponentially changing Regulatory landscape can prove to be challenging for life sciences manufacturers.

Furthermore, understanding and interpreting all the updates available on the Health Authority (HA) websites, third party databases, and adapting to the new regulations can add additional burden on the company resources. To overcome these challenges and hurdles, organizations today, more and more, are relying on Regulatory intelligence tools and services to create a compliant strategy and execution plan to avoid mishaps throughout the product lifecycle. For more than a decade now, large and enterprise companies have been investing in a dedicated RI function. Despite the integration of Regulatory intelligence tools, solutions, or support, organizations are still facing difficulties in decoding the regulations and complying with them. It might be due to inefficiency of existing tools to tackle end-to-end Regulatory intelligence.

So, what should be the requirements for an ideal RI software? An ideal 360-degree Regulatory intelligence support must encompass and support Regulatory functions of global Regulatory affairs, CMC, submissions, labeling, artwork and packaging, supply chain, technology and IT, Regulatory policy, and even marketing.

Unmasking the gaps between Regulatory policy and Regulatory intelligence and paving way to synchronous functioning of an organization demands relentless efforts and support – both technological and functional. From a bird's eye view, the Regulatory intelligence process seems effortless – gathering data, analysing information, and creating Regulatory strategy (understand the detailed Regulatory Intelligence process). Regulatory Intelligence is the key to unlock superior Regulatory submission strategies and new market decisions. However, each step in this process includes a multitude of steps.

For instance, let's consider Product Development scenario from the perspective of an organization, Health Agency, and Regulatory Intelligence.

Organization Perspective	Health Agency Perspective	Regulatory Intelligence Perspective
Focused view on therapeutic segment of interest	Holistic view on developmental landscape	Understand new technologies and build internal capabilities
Regulatory Intelligence data pertaining to competitor /precedence molecules	New technological advancements in each therapeutic segment	Identify applicable regulations
To get it right-the-first-time of Regulatory approach	Monitor the advancements to understand need for more stringent regulations and data requirements	Track and keep updated on new advancements in regulations
	Identify need for new policies, laws, and directives	Understand and identify test requirements and optimum data requirement for Regulatory submissions

		Regulatory pathways for registration
		Optimize data and documentation for global registration

Bridging the Gap Between Regulatory Intelligence and Regulatory Policy

- Every organization should create an internal Regulatory policy to comply with the HA policies and laws
- The organizational policies need to govern internal procedures and processes
- Diversified outcome from each of the organization
- The RI data form the input for refining and betterment of existing policies

Comprehensive Approach to Regulatory Intelligence

A wholesome approach for Regulatory intelligence includes:

- Primary research that covers data across country updates, Regulatory updates, congress coverage, trade associations coverage, authority and ministry coverage, key opinion leaders, and key influencers
- Secondary research that encompasses data about Country/product Regulatory, landscape, ongoing literature review, Regulatory updates, clinical intelligence, HA updates, news and research, Regulatory precedent of, policy, Impact on policy, lead countries & follow up countries.
- Technology solution that is web-based, metadata driven Regulatory intelligence platform, real-time tracking and update, multiple information sources, actionable, auditable, collaborative, social, compare documents, regulations, requirements globally.
- **GRX Framework** – INSIGHT integrated with other technologies, in-house integration with DMS, PLM, submissions and other software, reusable content.
- Real-time distribution and action, real-time impact assessment of regulations and changes assign activities across departments for timely action.
- **Reporting and audit** – Country/product specific comprehensive analysis, Newsletters and periodic reports, real time news updates, on demand reports, audit actions for compliance with changing regulations.

Value Proposition of Regulatory Intelligence

RI Trends	Description	Value Proposition
Competitor Intelligence	Regulatory status or Regulatory evaluation of a competitor product	Determines likelihood of success of own strategy and gauges launch time if need to be 'first in line'
Environmental Intelligence	Existence, implementation and use of legislation, Regulatory frameworks, tools, or initiatives on a specific pharmaceutical topic	Enables identification of requirements, rewards, and incentives, as well as regulator acceptability and competence
Due Diligence Support	Scenario and risk management planning in relation to an in-licensing opportunity	Enables identification of potential risks that may impact Regulatory success. Aids go/no-go decision-making
Procedural Intelligence	Practical experience on the interpretation or application of Regulatory provisions that relate to a Regulatory procedure	Clarifies whether your situation falls within known instances. Shapes dialogue with regulators if need to justify position
Regulatory Precedents	Known instances of a novel Regulatory approach or deviation from normal practice (success or failure)	Helps determine likelihood of success and any key differentiators that might persuade regulators to accept your position
Metrics	Mathematical occurrence of a Regulatory event or time span for a Regulatory procedure	Aids submission and launch planning and internal benchmarking against industry standard

The Key Outcomes of Regulatory Intelligence

- Timely and Consistent Submissions Across Markets
  - » Effective approval process
  - » Uniform versions of documents
  - » Better planning for turnaround time and quality metrics
- Compliance
  - » Market specific process adherence
  - » Harmonized documentation and quality standards across markets
- Policy and Strategy
  - » Proactive product/market strategy
  - » Policy adaptation and internal/external influence
- Supporting Business as Usual
  - » Support day-to-day intelligence needs for micro and macro decisions
  - » Real time knowledge support
  - » Accelerated training
- Impact on Patient Safety and Brand Image
  - » Consistency across markets impacting brand image
  - » Accelerated response to changes in regulations
- New Regulatory Opportunities and Portfolio Maximization
  - » Market specific process adherence
  - » Harmonized documentation and quality standards across markets
- Centralized Intelligence Delivery Platform
  - » Global submissions, dossier preparation, CMC management, artwork and label management
  - » Global intelligence-driven approach
  - » Compliance monitoring and business risk management
- Productivity, Efficiency, and Cost
  - » Informed decisions
  - » Improved compliance
  - » Intelligence-driven approach
  - » Internal links
  - » Importance of Regulatory intelligence
  - » Regulatory intelligence in emerging markets

To conclude, the right approach to Regulatory intelligence will benefit in faster time to market, lesser cost for development, greater market potential, higher success rate, proactive Regulatory decisions, global implementation, and improved operational excellence. What is your approach towards RI? Define it carefully and in a compliant manner. Stay informed. Stay compliant.

FREYR CONNECT

Computer System Validation a Practical Risk-Based Approach

This whitepaper provides guidance on how to overcome the challenges associated with software validation and its compliance for Health care and Pharmaceutical Industries, who are looking to do Computer System Validation (CSV) for the first time.

It also elaborates on how the risk-based approach is important in developing systems by Quality by Design and thus helps the system to be robust throughout the Software Development Life Cycle (SDLC).

It also throws light on the risk management practices to be followed and the documentation required for the risk management for the entire life cycle of the system.

OVERVIEW

Definition:

"Computer system validation is the process of providing a high degree of assurance through documented evidence and that a computer system consistently meets its pre-determined or intended use or quality attributes such as accuracy, security, reliability and functionality."

Validation of a computerized system depends on the following criteria:

Medical devices and IVD manufacturers aiming for a Brazilian market-entry are obliged to adapt to the ANIVSA's new Regulatory framework as mentioned above for streamlined device registration. What is your adaptation approach for the new notification pathway? Chalk it out with a regional Regulatory expert to forgo last-minute challenges. Stay informed. Stay compliant.

The criticality of the system

The complexity of the system

part of SDLC based on the criticality, novelty and complexity of the system

Major challenges faced during validating computer systems are:

- Inadequate documentation of deliverables in the Software Development Life Cycle (SDLC)
- Inadequate definition of expected results
- The software does not meet its specifications
- Inadequate design of qualification documents like installation qualification, operational qualification, performance qualification and user acceptance testing
- Inadequate requirement for gathering the systems
- Inadequate knowledge of Regulatory expectations
- Inadequate risk assessment
- Inadequate knowledge on required deliverables as

The criticality of the system

The complexity of the system

The above-mentioned challenges may lead to the failure of SDLC and may not meet business and Regulatory requirements that may highly impact the business.

Expectations

The industry has set expectations to overcome these challenges efficiently to minimize the risks related to computerized systems and to increase resource utilization. A few of the methods used to overcome the challenges include:

- Quality risk management to be adopted throughout the product life cycle
- Able to assess the impact of business processes on the related regulations and quality attributes affecting patient safety, product quality and data integrity
- Proper understanding of the product and the business process involved
- Efficient use of change management during the entire process of the product life cycle
- Developing proper procedures and templates for evaluating the impact of regulations while allocating adequate effort to mitigate the risk
- Supplier involvement and documentation shall be leveraged with scalable life cycle activities

The Need for a Risk-based Approach to CSV

Minimizing the costs of rework, reducing unwanted costs and increasing focus on regulations will lead organizations to adopt the risk-based approach to validation.

Organizations must see this risk-based approach as a chance to integrate risk management with business improvement methods and cut back compliance prices by adhering to Regulatory expectations. The USFDA, MHRA, EMEA, Health Canada and other Regulatory agencies are insisting the industry to move towards the risk-based approach to CSV and compliance with ERES (Electronic Record/Electronic Signature) regulations.

The industry lacks clarity and has impro
per standards, weakly structured quality systems, lack of expectations, improper executions and failing project management, which are leading to failure of projects with limited value added to quality.

Major companies understand the theoretical part of the risk-based approach to validation regarding the methodologies, documentation, processes to be followed, but they lack clarity on how to apply risk management to CSV and how to get benefits from it.

Proper inputs on the business process, system components, along with a skilled resource, can yield positive results and benefits in reducing the costs and meeting the Regulatory requirements.

Industry Guidance to CSV for Risk-based Approach

The organizations mentioned below provide guidelines for a risk-based approach to CSV:

ICH (International Council for Harmonization)

ICH Q9 Quality Risk Management provides principles and ICH Q9 Quality Risk Management provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality.

It provides a systematic approach for a robust quality risk management system and suggests organized method for assessment, communication, control and application of risk management in the pharmaceutical and life sciences industries.

ISPE GAMP 5

The following GAMP 5 software and hardware categories are used to establish the validation approach and determine the deliverables:

The requirement of deliverables can be assessed by the categories mentioned above. The complexity of the system will be increasing from Category-3 to Category-5, accordingly, and the risks shall be identified and mitigated.

Practical Risk-based approach to CSV

GAMP 5 provides a basic framework for CSV process and the related activities that give an excellent approach for ensuring that the system is meeting the predetermined specifications and is compliant with Regulatory requirements. Validation activities required for validating a system depends on the GAMP5 software and hardware categorization, GxP Assessment, ERES Assessment and System Risk Assessment. The outcome of these assessments

will be included in the product specifications which will reduce rework and increase the robustness of the system by inoculating 'Quality by Design' with this risk-based approach.

Quality risk management starts with the identification of risks, evaluation of risk and control of risk by establishing proper controls that bring risk residue to acceptable limits. It also includes implementation of controls, communication and review of risks. It is a process that is used throughout the life cycle of the product starting from the planning phase to the retirement phase.

A practical risk-based approach to CSV consists of the following steps:

1. **Initial Risk Assessment and Impact Assessment to be Performed:**
   In this phase, the initial risk assessment is performed by analyzing process, business risk, user requirements, functional requirements and Regulatory requirements. This initial risk assessment and impact assessment helps to identify whether the system is GxP regulated. The level of effort and documentation of subsequent steps is determined by risk & system impact and relevant regulated ERES is also identified in this step.

2. **Identify the Functions of the System that may Impact Patient Safety, Product Quality and Data Integrity:**
   Functions identified and gathered during step-1 shall be assessed for their impact on patient safety, product quality and data integrity. The risk will be measured against the key critical quality attributes of the process and apply adequate risk management techniques based on risk priority.

3. **Functional Risk Assessment and Establishment of Controls:**
   dentified functions in step 2 are assessed by identifying possible hazards and how the potential harm arising from these hazards will be controlled by selecting tools like FMEA (Failure Mode Effective Analysis). In this step, a detailed assessment will be performed to further identify the severity of harm, the likelihood of occurrence and the probability of detection by which we can establish the risk priority ranking. Appropriate control measures are identified based on the assessment. Examples of control measures are modification to system design, modification to process design, addition of requirements, establishing rigorous testing and procedural controls. Elimination of risk by design is the best-preferred approach.

4. **Implementing and Verifying Established Controls:**
   The controls identified at step 2 and step 3 are implemented and verified to ensure that they have been successfully established. And all the controls are traced to the relevant risks that are previously identified. This verification activity will ensure whether the identified and established controls are effective in achieving the required risk reduction.

5. **Risk Review and Monitoring Controls:**
   The risks are reviewed during periodic reviews of the system, which will verify that the controls are still valid and if any deficiencies are found, corrective actions will be taken by following change management. The frequency of the periodic reviews depends on the criticality of the risk.

Software Development Life Cycle

SDLC (V-Model/Waterfall Model) represents a high-level view of the process followed for the development and deployment of the software products. SDLC comprises the following phases:

1. **Phase 1-Planning:**
   Below are the documents related to the planning phase:
   - Change Request Form
   - Project Management Plan
   - Impact, GxP, ERES and Risk Assessments
   - Validation Master Plan
   - Validation Master Plan

2. **Phase 2-Requirement Phase:**
   Below are the documents related to the requirement phase:
   - User Requirement Specifications
   - Functional Specifications
   - Requirement Traceability Matrix (RTM)
   - Quality Gate Review

3. **Phase 3-Design and Coding Phase:**
   Below are the documents related to the design and coding phase:
   - Design Document
   - Code Review
   - Updated Requirement Traceability Matrix(RTM)
   - Quality Gate Review

4. **Phase 4-Testing Phase:**
Below are the documents related to the testing phase:
   - Test Plan
   - IQ, OQ and PQ
   - Defect Tracker
   - UAT
   - Updated Requirement Traceability Matrix (RTM)
   - Test Summary Report
   - Quality Gate Review

5. **Phase 5-Release Phase:**
Below are the documents related to the release phase:
   - Validation Summary Report
   - Release Note
   - Validation Certificate

6. **Phase 6-Operational and Maintenance Phase:**
Below are the documents related to the operational and maintenance phase:
   - Periodic Reviews
   - Change Management
   - SOP
   - CAPA
   - Scheduled Maintenance Report.

7. **Phase 7-Decommissioning Phase:**
Below are the documents related to the operational and maintenance phase:
   - Decommissioning Plan
   - Decommissioning Report
   - Project/ Product Retirement

Note:
All the above-mentioned deliverables may vary from organization to organization depending on the type and criticality of the system.

Conclusion

Implementation of the risk-based approach to CSV will bring best practices, that offer good opportunities for increasing the levels of quality and Regulatory compliance while reducing the costs with effective use of resources and reduction of rework. The risk-based approach and SDLC process will establish evidence that the system meets its predetermined specifications, thereby complying with the Regulatory agencies.

REFERENCES

- ISPE GAMP 5 Guide: A Risk Based Approach to Compliant GxP Computerized Systems. International Society for Pharmaceutical Engineering (ISPE)
- ICH Harmonised Tripartite Guideline- Quality Risk Management-Q9
- Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S)
- Guidance for Industry-Part 11, Electronic Records; Electronic Signatures- Scope and Application

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Software as a Medical Device (SaMD)

Demystifying the EU MDR Regulations

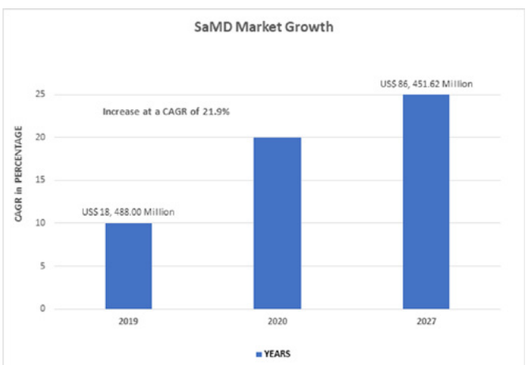
Software emerged as a revolutionary development and transformed the working ways of every industry, including life sciences.

Center of Excellence
Global Medical Device Regulatory Services

The integration of software into medical devices surfaced as, Software as a Medical Device/s (SaMDs) and has been a key game-changer for the medical industry. Currently, SaMDs are the new normal and sophisticated medical devices, altering the perceptions of medical functions. From simple wearable devices to complex invasive devices, SaMDs can monitor and diagnose medical conditions, suggest treatments and provide secure and reliable data management. SaMDs are of utmost importance in remote healthcare services for their accessibility, sophisticated design, and delivering accurate and expedite medical outcomes. However, the production of SaMDs are confined to country-specific laws, regulations, stringent standards and certification procedures. While there are many types of software for medical and non-medical purpose in healthcare, the Regulatory Authorities have provided clear-cut definitions and Regulatory frameworks to develop and establish SaMDs. The EU MDR (The European Medical Device Regulation) has put in place specific Regulatory structures to qualify, classify and clinically evaluate SaMD to improve patient safety and device effectiveness in real world performance. This article intends to provide a better understanding of the EU MDR Regulatory requirements for placing SaMD in the European countries.

1. SaMD Introduction

Software as a Medical Device (SaMD) is a result of evolving high-end technologies, which integrate software, medical devices and connectivity. Notably, these devices are addressed and abbreviated differently by various Regulatory bodies. Likewise, SaMD is a jargon used by the International Medical Device Regulators Forum (IMDRF) wherein, the European Commission's Medical Device Coordination Group (MDCG) recognizes these devices as Medical Device Software (MDSW). As these devices are beneficial in all the levels of medical functions ranging from monitoring health conditions to in-patient treatments, the healthcare sector is obliged to invest in medical software development. In addition, the SaMD market is expected to reach US$ 86,451.62 Million in 2027 from US$ 18,488.00 Million in 2019, with an estimated CAGR (Compound Annual Growth Rate) of 21.9%, during the years 2020 to 2027. Though there is a threat of data breach hindering the market growth, the increasing adoption of Internet of Things (IoT), connected devices in healthcare and advantages of SaMD are the driving growth factors. However, there are complexities and challenges with increasing integration of technology into medical devices in terms of patient safety, clinical care and device functionalities. Hence, balancing the safety concerns and benefits of medical innovations, the EU MDR has issued regulations to qualify, classify, and clinically evaluate SaMD in real world performance.



Software as a Medical Device (SaMD) Market Forecast to 2027

2. IMDRF and MDCG Definitions

The IMDRF defined SaMD as, "a software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device". These devices can determine the disease condition by monitoring, diagnosing, screening, preventing, and suggesting treatments. For example, let's take a software that aids clinicians and radiologists to identify and diagnose a cardiovascular condition by analyzing Magnetic Resonance Imaging (MRI) scans; a mobile application that takes input from a patient's food log and blood glucose meter to provide insulin recommendations for diabetes; a software that analyzes a patient's medical history and diagnostics data to determine the correct drug dosage and which gathers, retrieves or organizes the actual medical data; and a software that monitors a mole for a given period of time to assess the risk of melanoma. As these SaMDs are used to determine the disease condition, they are applicable to New Rule 11 of MDR for Medical Device Software (MDSW), exclusively for software, which is detailed in section 4.2. Software which do not have a medical purpose but are supplied as an accessory to a medical device or the software which drives or controls hardware of a medical device such as embedded software or firmware or micro-codes are not considered as SaMD. Software used to monitor working of a medical devices or the software used for workflow management, data saving and clinical communication do not qualify for a SaMD definition.

Besides defining the intended use, manufacturers should consider the following healthcare scenarios in which SaMD will be used:

- A critical condition
- A serious condition
- A non-serious condition

As per the European Commission's Medical Device Coordination Group (MDCG), Medical Device Software (MDSW) is a software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a "medical device" in the medical devices regulation (Article 2(1) of Regulation (EU) 2017/745 – MDR), regardless of whether the software is independent or driving or influencing the use of a device.

- Note 1: MDSW may be independent, by having its own intended medical purpose and thus meeting the definition of a medical device on its own (i.e. alone)
- Note 2: If the software drives or influences a (hardware) medical device and also has a medical purpose, then it is qualified as a MDSW
- Note 3: Software may be qualified as MDSW regardless of its location (e.g. operating in the cloud, on a computer, mobile phone, or as an additional functionality on a hardware medical device)
- Note 4: MDSW may be intended to be used by healthcare professionals or laypersons (e.g. patients or other users)

3. EU MDR Qualification Criteria

With various types of SaMDs available in the market, there is a dire need for stringent Regulatory guidelines and principles than can clarify on what types of software are qualified for the medical purpose. As specified by the EU MDR, a software must have a medical purpose on its own to qualify as a Medical Device Software (MDSW). The SaMD must fulfill the definition of a "medical device", "software", or "in vitro diagnostic medical device", according to the Article 2(1) of Regulation (EU) 2017/745 – MDR. When a software is not a MDSW but is intended by the manufacturer to be an accessory for a medical device or in vitro diagnostic medical device, they respectively fall under the scope of the MDR. The qualifying factors for SaMD include:

- Software that directly controls a medical device (hardware)
- Software that provides immediate decision-triggering information (e.g. blood glucose meter software)
- Software that provides support for healthcare professionals (e.g. ECG interpretation software)
- Software intended to process, analyze, create, or modify medical information when the software is governed by a medical intended purpose (e.g. searching image for findings that support a clinical hypothesis as to the diagnosis or evolution of therapy)
- Independent software, by having its intended medical purpose
- Software that runs on different operating systems in remote locations (e.g. operating in the cloud, on a computer, mobile phone, or as an additional functionality on a hardware medical device)

Besides, it is relevant to clarify that not all software used within the healthcare settings are qualified as medical devices. For example, 'simple search', referring to retrieval of information, does not qualify as a MDSW. Also, software intended for non-medical purposes, like, invoicing or staff planning are not qualified as MDSW and do not fall under the purview of MDR.

4. Classifications under EU MDR

4.1 Risk-based Classification

Considering the intended purpose of the device and their inherent risks, the EU MDR 2017/745 has 4 main categories for medical devices classification, such as, Class I (low risk), Class IIa (medium risk), Class IIb (medium/high risk), and Class III (high risk). The categorization goes from the products with low risk (Class I) to the products with highest risk (Class III).

4.2. New Rule 11 of MDR for Medical Device Software (MDSW)

All the implementing rules in Annex VIII of Regulation (EU) 2017/745 shall be considered to determine the classification of medical devices. Specially, the rule 3.3 of Annex VIII is applicable to software influencing the use of a device and an independent software. In addition, Recital 5 of the MDR and international guidance from IMDRF introduced a new classification rule 11, exclusively for software. This rule intends to address the risks related to the information provided by an active device, such as MDSW. In particular, rule 11 describes and categorizes the significance of information provided by the active device to healthcare decision (patient management) in combination with healthcare situation (patient condition).

Rule 11 states:

Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as Class IIa, except if such decisions have an impact that may cause:

- death or an irreversible deterioration of a person's state of health, in which case it is in Class III; or
- a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as Class IIb

Software intended to monitor physiological processes is classified as Class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as Class IIb. And, all other software products are classified as Class I.

State of healthcare situation or patient condition	Significance of information provided by the MDSW to a healthcare situation related to diagnosis/therapy*		
	High	Medium	Low
Critical Condition	Class III	Class IIb	Class IIa
Serious Condition	Class IIb	Class IIa	Class IIa
Non-serious Condition	Class IIa	Class IIa	Class IIa

**High significance when used to treat or diagnose a health condition, Medium significance when used to drive clinical management and Low significance when provides information for clinical management.*

5. EU MDR Clinical Evaluation

According to IMDRF guidance, clinical evaluation of a SaMD is defined as a set of ongoing activities conducted in the assessment and analysis of a SaMD's clinical safety, effectiveness and performance, as intended by the manufacturer in the SaMD's definition statement. Every SaMD must undergo the clinical evaluation process, involving:

5.1 Valid Clinical Association of a SaMD: The SaMD's output (concept, conclusion, measurements) is clinically accepted based on established scientific evidence, which determine its accurate correspondence with the healthcare situation and clinical conditions. Also known as scientific validity, valid clinical association is an indicator level of clinical acceptance and how much meaning and confidence can be assigned to the clinical significance of SaMD's output in the intended healthcare situation and clinical condition or physiological state.

5.2 Analytical Validation of a SaMD: The ability of a SaMD is measured to generate accurate, reliable and precise intended output from the input data. Analytical validation provides confirmed evidence that, the software is correctly constructed with reliable input data and generates output data with appropriate level of accuracy,

repeatability and reproducibility. It also demonstrates that, the software meets the specifications conformed to user needs and intended uses.

5.3 Clinical Validation of a SaMD: The SaMD is evaluated based on its ability to yield clinically meaningful output for the intended use as well as for the healthcare situation. Clinically meaningful signifies the positive impact of a SaMD on the health of an individual or population, like, meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to the function of the SaMD (e.g., diagnosis, treatment, prediction of risk, prediction of treatment response).

According to MDCG guidance, software that qualifies as a medical device is subject to the same general clinical evaluation (MDR) principles, such as:

- Establishing and maintaining a clinical evaluation (MDR) plan and criteria applied to generate the necessary clinical evidence based on the characteristics of the device
- Identification of the relevant data pertaining to performance and/or safety of the device and any remaining unaddressed issues or gaps in the data
- Appraisal of the relevant data in terms of quality and its contribution to the clinical evaluation (MDR)
- Analysis of the available data and its relevance with regard to demonstrating conformity with the relevant General Safety and Performance Requirements (GSPRs)
- Documenting the relevant data, their assessment and the clinical evidence derived therefrom, in the clinical evaluation (MDR)
- Updating the clinical evaluation (MDR) and its documentation throughout the life cycle of the MDSW concerned with data obtained from implementation of the manufacturer's Post Market Clinical Follow-up/Post Market Performance Follow-up (PMCF/PMPF) plan

There are three components to be taken into account when performing clinical evaluation for every MDSW. Though the components don't represent a distinct stepwise approach, they portray a methodological principle for the generation of clinical evidence. They include:

A. Valid Clinical Association of a MDSW should demonstrate that it corresponds to the clinical situation, condition, indication or parameter defined in the intended purpose of the MDSW. It is understood as the extent to which, the MDSW's output (e.g. concept, conclusion, calculations) based on the inputs and algorithms selected, is associated with the targeted physiological state or clinical condition. Evidence supporting valid clinical association can be generated through, literature research, professional guidelines, proof of concept studies, or manufacturer's own clinical investigations/clinical performance studies.

B. Technical Performance is demonstrating the validation of a MDSW's ability to generate the intended output accurately, reliably and precisely, from the input data. Evidence supporting this performance can be generated through verification and validation activities, e.g. unit-level, integration, and system testing or by generating new evidence through use of curated databases, curated registries, reference databases or use of previously collected patient data.

C. Clinical Performance is demonstrating the validation of a MDSW's ability to yield clinically relevant output in accordance with the intended purpose. The clinical relevance of a MDSW's output is a positive impact on the health of an individual expressed in terms of measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, prediction of risk, prediction of treatment response(s), or related to its function, such as, screening, monitoring, diagnosis or aid to diagnosis of patients, or on patient management or public health. Evidence supporting clinical performance can be generated by testing the MDSW under evaluation, or an equivalent device, in the target population and for the intended use.

6. EU MDR Certified Registrations

6.1 CE Markings and Conformity Assessments

To access the European market, it is mandatory to have a CE marking for all the software developed with intended medical purpose. With CE certification, the device is expected to comply with all the European Regulatory requirements regarding health, safety and environment. For all device classes, an Authorized Representative (EC REP) located in the EU and who is qualified to handle any Regulatory issues shall be appointed. The EC REP name and address should be placed on the device label and obtain a single registration number from EUDAMED (once available). CE marking can be obtained by the following steps:

Classification and Assessment of Medical Device – Based on the nature of the device, manufacturers can determine the set of regulations applicable to their device (Medical Device Regulation (MDR 2017/745). Classification is done as per the device risk profile followed by identification of requirements for the identified device class. The requirements for each of the device classes are listed below -

Class I (Self-Assessment)

- Implement a QMS (Article 10 (9), Annex IX (Chapter 1) and Annex XI Part A (6))
- Technical Documentation and QMS – Quality Management System (Annex II and III)
- Declaration of Conformity (Article 19 and Annex IV)

Class IIa (Notified Body Assessment)

- Annex IX – QMS
- Article 52 Para 6 – Assessment of Technical Documentation of a Representative Device for each Category
- Declaration of Conformity (Article 19 and Annex IV)

Class IIb (Notified Body Assessment)

- Annex IX – QMS or Annex X & XI – Type Examination and Production QMS
- Article 52 Para 4 – Assessment of Technical Documentation of a Representative Device of each Generic Device Group
- Declaration of Conformity (Article 19 and Annex IV)
- Annex II and III – Technical Documentation and QMS

Class III (Notified Body Assessment)

- Annex IX – QMS or Annex X & XI – Type Examination and Production QMS
- Annex II and III – Technical Documentation and QMS
- Article 52 Para 3 – Assessment of Technical Documentation
- Declaration of Conformity (Article 19 and Annex IV)

Establish a Quality Management System (QMS) – A compliant QMS is essential to ensure the product's design, manufacturing process and quality are safe and effective for best results. There is no QMS or technical file audit by the Notified Body, for Class I devices. The rest of device classes are audited by the Notified Body for QMS and technical file. Upon successful completion of the audit, an ISO 13485 certificate will be issued for the facility.

Creating a Technical Dossier – Manufacturers should compile a technical file enclosing the conformity requirements of the device (in risk classes I, IIa, IIb & III) as set out in the European regulations. For Class I devices, prepare a CE technical file according to MDR Article 10 and a Clinical Evaluation Report (CER) according to MDR Article 61. For the other device classes, prepare a CE technical file in accordance with MDR Article 10 and provide the device information and its intended use, testing reports, CER, risk management plan, Instruction for Use (IFU), labeling and more. The file should be inclusive of:

- Product Description and Specifications
- Manufacturing Information
- Risk Management File
- Design Verification and Validation Test Reports
- Clinical Evaluation
- Intended Use and Safety
- Labeling and Packaging
- Transportation and Storage Effects
- Post-Market Clinical Follow-up (PMCF) plan
- Post Market Surveillance (PMS) Plan

Audit by Notified Body – The device related QMS and documentation will be reviewed by a notified body to prove device conformity.

Conformity Declaration – For Class I Medical Devices, prepare a Declaration of Conformity in accordance with MDR Article 19 and Annex IV, which state the device compliance with applicable European requirements and affix the CE marking. For all other device classes, post to a successful audit, a CE marking certificate will be issued establishing the device compliance with European standards. Following, a Declaration of Conformity document is created, which legally declares that the device meets all of the essential requirements as laid out by the EU MDR and any other applicable Regulatory standards. Finally, the device can obtain a CE marking, after it meets all the compliant European regulations.

Post CE Mark Compliance - Register the device and its Unique Device Identifier (UDI) in the EUDAMED database (once available) and the UDI must be on the label. The technical file and CER must be kept up to date for Class I devices and for the other device classes, clinical evaluation, PMS (Post Market Surveillance), PMCF (Post-market Clinical Follow-up) activities must be performed to maintain certification. While ISO 13485 certification must be renewed every year, the CE marking certification is valid for a maximum of 5 years but are reviewed during annual surveillance audits. The Notified Bodies will conduct annual audits to ensure ongoing compliance with the MDR and failure to pass the audit will invalidate the device CE marking certificate.

7. EU MDR Quality Management System (QMS)

The development of medical device software is a big undertaking and requires effective management to bridge Regulatory gaps. Failing to meet the requirements will decelerate the time to market and raise liability concerns. SaMD manufacturing includes all of the following principles: *SaMD Quality Management Principles: Relationship Between Governance, Processes and Activities*

SaMD Quality Management Principles

SaMD Quality Management Principles: Relationship Between Governance, Processes and Activities

7.1 Leadership/Organizational Activities - The organization's management provides an overall governance structure and leadership for all SaMD lifecycle activities with adequate resources that assure the safety, effectiveness and performance of SaMD. They include, resources (people, tools, environment, etc.) and infrastructure management (equipment, information, communication networks, tools, the physical facility, etc.).

7.2 SaMD Lifecycle Processes – The SaMD lifecycle activities are supported by certain processes, which are essential to build and manage an organization's QMS. These processes are typically scaled to address the complexity and size of a SaMD product that needs to be created and are required to be considered throughout the SaMD lifecycle activities, regardless of specific approach/method used by the organization. The processes comprise:

- Product Planning
- Risk Management (a patient safety focused process)
- Document Control and Records
- Configuration Management and Control
- Measurement, Analysis and Improvement of Processes and Product
- Managing Outsourced Processes and Products

7.3 SaMD Lifecycle Activities – Organizations' manufacturing SaMD should identify the key lifecycle activities that scale the type of SaMD, the size of the organization and consider important elements required for assuring the safety, effectiveness and performance of SaMD. Alongside SaMD lifecycle processes, the SaMD lifecycle activities are inclusive of design, development, verification and validation, deployment, maintenance and decommissioning.

8. UDI Assignment to Medical Device Software (MDSW)

To clearly identify medical devices within the global supply chain, EU MDR 2017/745 has introduced the Unique Device Identification (UDI) system. As per EU regulations, the basic UDI-DI (Device Identifier), connects software with same intended purpose, risk class, essential design and manufacturing characteristics. When UDI-DI is changed in accordance with Annex VI Part C, Section 6.5 of the MDR, a new UDI-DI is required, whenever there is a modification that changes the original performance, the safety of the software or the interpretation of data. Such modifications include new or modified algorithms, database structures, operating platforms, architecture, user interfaces and new channels for interoperability. Such changes would be considered "significant." MDCG has proposed specific considerations on UDI rules and requirements for software. They include:

- In accordance with Annex VI, Part C of the EU MDR 2017/745, only software which is commercially available on its own, as well as software which constitutes a device in itself shall be subject to UDI requirements
- In accordance with Annex VI, Part C, point 6.5.4 of the MDR, minor software revisions require a new UDI-PI (Product Identifier) and not a new UDI-DI. Minor software revisions are generally associated with bug fixes, usability enhancements that are not for safety purposes, security patches or operating efficiency. Minor software revisions shall be identified by a defined manufacturer-specific form of identification
- UDI placement criteria for software are laid down in Annex VI, Part C, point 6.5.4 of the MDR

As the changes to a software could trigger a new basic UDI-DI, manufacturers should evaluate the possible impact of any changes to the function of software (software's qualification as medical device software, its classification, its intended purpose, essential design and manufacturing characteristics), as a part of their maintenance and post-market surveillance activities. Accordingly, any changes will be assessed in defining the need of a new UDI-DI.

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Conclusion

Revolutionary advancements in software are transforming the functionalities of healthcare and medical industries. Further, the convergence of software into medical devices created Software as a Medical Device/s (SaMDs), which interact with human body, diagnose health conditions and determine the appropriate treatment methods. The software-driven medical devices gained magnifying importance with their ability to be independent of hardware and process accurate information for end-users. SaMDs are constantly evolving, posing opportunities and challenges for device organizations and regulators. Hence, the Regulatory paradigms of SaMDs are piloted for better innovation, while ensuring the patient safety and clinical effectiveness. This article chalks out the key EU MDR Regulatory standards to accommodate continuous adaptation of SaMDs in the European market. The SaMD manufacturers can navigate through the EU MDR regulations right from the defining aspect, qualification criteria, classification, clinical evaluation, CE certification and QMS. For continued innovation and in interest of public health, the SaMD manufacturers should understand the proposed regulations and adopt a robust system supporting all the device and software functionalities with EU MDR Regulatory recommendations, to ensure high quality and compliant patient healthcare.

REFERENCES

1. http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf
2. https://www.globenewswire.com/news-release/2020/05/12/2031716/0/en/Insights-into-the-Worldwide-Software-as-a-Medical-Device-Industry-to-2027-Featuring-Velentium-Tietronix-Software-S3-Connected-Health-Among-Others-.html
3. https://ec.europa.eu/docsroom/documents/37581?locale=en
4. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745
5. https://ec.europa.eu/docsroom/documents/37581/attachments/1/translations/en/renditions/native
6. http://www.imdrf.org/docs/imdrf/final/consultations/imdrf-cons-samd-aqms-150326.pdf
7. http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170921-samd-n41-clinical-evaluation_1.pdf
8. http://www.imdrf.org/docs/imdrf/final/consultations/imdrf-cons-samd-ce.pdf
9. https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2018_5_software_en.pdf
10. https://ec.europa.eu/health/sites/health/files/md_topicsinterest/docs/md_mdcg_2019_11_guidance_en.pdf
11. https://ec.europa.eu/docsroom/documents/40323?locale=en

SPL and SPM Software & Ideal Features for Consideration

Structured Product Labeling (SPL) and Structure Product Monograph (SPM) are the mandatory document mark-up standards for the submission of label content, product and facility information and any subsequent changes to the existing label information in an electronic format.

SPL format defines the structure and content of label information as per the United States Food and Drug Administration (US FDA), whereas SPM is for Health Canada (HC). Across the industry, there are many types of drug registration, drug labeling and drug listing requirements which can be submitted through various SPL and SPM submission types. Complying with all of them requires a sophisticated and one-stop solution.

Need for an SPL/SPM Software

To submit SPL/SPM to the Health Authorities, applicants must have a thorough understanding of the submissions in XML format to avoid errors that may cause reworks viz. incomplete data, improper hyperlinking, section misalignment, etc. Hence, the need of the hour is to deploy a robust submission tool to create, validate, store and submit complex content structures aligning with SPL/SPM standard in the region-specific formats.

SPL/SPM Software - Ideal Features for Consideration

An SPL/SPM software must be equipped with:

- Automated process to reduce the burden of the end-user
- A tracking module to provide information on all the stages during the submissions and also to follow the review comments until the SPL format finalization/ approval
- A strong editor to work on multiple SPL formats that helps to create MS Word & PDF documents, Control Versions, Table borders, Audit Trails, etc.
- A comprehensive repository to efficiently maintain the SPL lifecycle
- An inbuilt validator to provide accurate files as per the FDA/HA's guidelines
- Feasibility to import the earlier submissions, which enables the user to handle all the Regulatory submissions in one repository

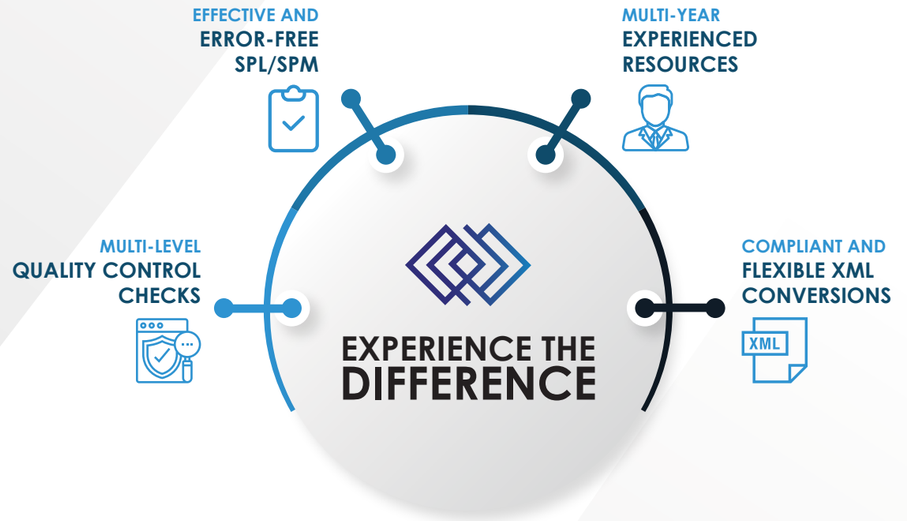
As manufacturers aiming at the US market-entry need to update their drug listing with the US FDA or submit blanket no certification SPL between October and December, Health Canada market-entrants must quickly adapt to SPM guidelines. In the process what should be the ideal approach? Integrate a one-stop-solution for SPL and SPM. Act wise and be compliant.

The Time Is Now To Adapt To Structured Product Monographs (SPM)

STREAMLINE AND AUTOMATE WITH

Freyr SPL/SPM

Freyr SPL/SPM is specialized in:



REQUEST A PRODUCT TOUR

Right Away!

Changes in Consumer Trends in Beauty and Personal Care During Global Pandemic

The global pandemic has had a profound impact on consumer lifestyles, influencing their behaviours and shifting general purchase priorities. Even the consumer habits and buying behaviour prevalent among beauty and personal care industry has changed quite a lot, creating relevant shift in the consumer trends.

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So, what is the current situation and what can be done to win this run? This draft throws a light on the changing scenario of the beauty and personal care industry and provides insights about the approaches to comply with it.

Introduction – Adjusting to a 'New Normal'

As the world is gradually moving out of lockdown, the consumers are adjusting to a 'new normal' and changing the way they live once again. They are still spending a lot of time at home, preparing themselves to face ongoing social distancing measures and trying to retain the sense of normalcy. Meanwhile, their expectations for the beauty industry and personal care products are changing constantly and creating many challenges apart from opportunities.

On one hand, as home living scenarios have increased, many products deem not to be indispensable anymore, like hair styling products or perfumes. Additionally, since traveling options are limited and the Northern Hampshire is slowly moving to the winter season, the demand for sunscreens and hair removal products has also dropped significantly. On the other hand, slow beauty and hair care products, and light makeup remain flat as consumers are trying to keep a day-to-day normalcy in the comfort of their own houses. At the same time, hair and beauty salons are struggling to retain their clients due to the increased post-lockdown home SPA and self-care routines as well as clients' safety concerns.

Post-lockdown Buying Trends

The 'new normal' has drastically impacted the shopping patterns of the consumers. The key drivers of consumer buying behaviour remain the same while focusing on value for money and buying convenience. However, post-lockdown, consumers started evaluating the aspects of personal safety. Even though many shops are being opened with restrictions, consumer are not willing to spend long hours at stores and they are looking for 'safer' options, such as appointment-based, or pick-up based shopping, while some are strictly restricted to online shopping.

The shopping experience has also changed with testers not being allowed anymore, and consumers being resistant to purchasing unfamiliar products. They are now seeking brands that offer single-dose testing, thus, focusing on more hygienic samples or strictly digital testing opportunities. Retailers offering sample sets, increased online assortment, contactless delivery and cash-less payment systems are predicted to attract new customers. To meet these evolving demands of consumers, brand owners should also consider virtual beauty consultations and targeted subscription services.

Constant Focus on Health and Well-Being

As a result of COVID-19, consumers are focusing more and more on maintaining their overall health of body, as well as mind. Due to this rising concern of consumers, there is a rise in demand for beauty products that not only intend to improve general body condition but also ensure consumers are relieved from stress and boosts the mood.

Prior to pandemic, product safety was directly related to ingredients and formulations. But now, the safety concerns of consumers are evolved and are more focused on natural, organic and 'clean' products. Additionally, consumers are looking for more hygienic products with longer shelf life and airless packaging. Brands that educate their customers more about their ingredients and product safety will be able to gain a much larger market share, than the others.

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New Sense of Awareness

Consumers are developing a new sense of awareness about the way they view themselves and their surroundings. They come to new realizations regarding their lifestyles, the environment, and social issues. As a result, people will choose brands in a more conscious way and will support retailers that share the same values. To face that, cosmetic companies should focus on giving back to the greater good demonstrating their drives and convictions, showing how they make a positive impact on a daily basis.

Sustainability will be of even greater importance as many consumers view the COVID-19 as a natural disaster, associating the global pandemic with concerns about climate change. In response, consumers will rate not only the ingredients and recyclable packaging in personal care products but also the entire supply chain, production, and environmental impact.

Authenticity Plays a Major Role

Prior to global pandemic, authenticity has been a key in the beauty industry. Consumers looked up to brands that were committed to rewarding loyal customers with exclusive promotions and deals as well as other benefits like virtual consultations or meet-ups. This method can also greatly benefit cosmetic brands in today's situation by showing commitment to their consumers during difficult times.

At the same time, during post-lockdown period consumers are looking for ways to support their local communities and give back to the greater good. Retailers that will help consumers with that by pairing purchases with supporting medical healthcare or frontline workers will stand out and benefit well into the future.

Conclusion

The 'new normal' will become a long-time reality for which beauty brands should adapt by repositioning, reinventing and innovating their products. New claims leaning towards holistic well-being (such as stress release, mood boosting and sleep improvement, etc.) will become more popular among people. Consumers will now be even more attracted to clean and safe products with natural and organic ingredients. They will seek online platforms not only to shop and connect with their brands, but also to educate themselves and instil confidence in their shopping choices. Furthermore, they will want to make an impact by giving back to their communities and supporting sustainable products. Beauty brands should keep all these in mind to remain attractive and sustainable in the consumer's mind in the long run.

REFERENCES

1. Mintel's Germany report: 'Impact Of COVID-19 On Beauty And Personal Care', May, 2020
2. McKinsey & Company: 'How COVID-19 is changing the world of beauty', May, 2020
3. Mintel's US report: 'The Impact Of COVID-19 On Household, Home Care And Personal Care', June, 2020
4. Mintel's Blog: 'How COVID-19 Accelerated The 2030 Global Beauty And Personal Care Trends', September 14th, 2020
5. NPD's Blog: 'Rediscovering Normalcy Through Beauty Routines', September 29th, 2020
6. Mintel's report: 'How The Beauty Industry Survives A Recession', June, 2020

FWS Freyr Webinar Series

WEBINARS THIS QUARTER (Upcoming)

In a view to make the industry understand the most recent updates of the Health Authorities and to ensure they follow the best practices for compliance, Freyr is going to conduct on-demand webinar sessions on following topics:

COSMETICS

Understanding AICIS Regulations for Cosmetics

May 27, 2021

FOOD AND FOOD SUPPLEMENTS

New Dietary Ingredient Notification (NDIN) Application - Food and Dietary Supplements in the USA

May 26, 2021

REGULATORY AFFAIRS

eCTD Ad-Promo Submissions – Compliance Best Practices

June 9, 2021

MEDICAL DEVICES

Demonstrating Performance of Diagnostic - Devices for IVDR Compliance

June 16, 2021

PHARMACEUTICALS

Drug Importation to India - A Regulatory Blueprint

June 17, 2021

PHARMACEUTICALS

A Guide to the Regulatory Landscape of Medicinal Products in Malaysia

June 23, 2021

Know More and Register Now

Prepare Your Organization for Remote Audits

It is well known that COVID-19 has pushed many organizations to drive their auditors and the compliance teams adopt the right technology to perform remote audits. While remote audit techniques are similar to those of traditional audits, they leverage electronic means to obtain audit evidence for evaluations.

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The way or the procedure for remote audits depends on the business function and the operational procedures. For example, for manufacturing processes or product storage, remote audits can be done with the help of live/surveillance video to gather the necessary audit evidence.

Conducting a Remote Audit

To adapt to the Remote Audits, organizations must have a thorough knowledge of how these audits are conducted. Below are some steps followed by an auditor/auditee for conducting an ideal Remote Audit:

- The auditee must dedicate one or two personnel to the audit over the designated period
- The auditor must request information from the auditee prior to the start of the remote audit, which includes procedures, quality manuals, complaints log, non-conformances log, CAPA log, deviation log, Master Validation Plan (MVP) and other information in PDF or another searchable format for off-site review. The auditor must ensure data privacy.
- If the auditee does not make the documents available for the auditors' review, then the documents and records must be shown via video conferencing tool.
- For video conferencing, both parties must agree on the technology to be used.
- The meeting invitations must be sent giving ample time for each party to plan conferencing.
- In the case of manufacturing processes and product storage, the auditor may request a virtual tour by the auditee.
- Audit plans and agenda must be scheduled.
- Closing meeting must be held via video conferencing tool.

Tips to Implement Remote Audit

If you are trying to implement remote audits for your organization for the first time, here are a few suggestions to support the transition:

- Define the scope, purpose, requirements, timing and method before the audit
- Security-enhanced technologies such as VPNs, password-protected documents, encrypted data and Public Key Infrastructure (PKI) must be adopted to mitigate the risk of network attacks.
- An onsite facilitator must be appointed to manage audit logistics and resolve any technology-related complexities.
- Build rules to engage between the organization and the compliance/audit team.
- Streamline the flow of communication by providing status updates between defined points of contact.
- Arrange audits in a way that the activities do not disturb the workflows.
- Regular check-in times must be scheduled with the auditors to assess the progress.

As the above-mentioned points are just a high-level focus points on remote audits, organizations must go much deeper to understand them; like the comprehensive 3-stage risk-based approach that the industry is following. For more information on remote audits and the compliant approach, consult a proven compliance partner. Be compliant all through.

Japan Revises Labeling Standards for Food Products

On July 16, 2020, Japan's Consumer Affairs Agency (CAA) revised the labeling standards for food products in the country. To do so, the CAA appointed a study group to discuss the current labeling system and make necessary changes in it. These changes aim to strengthen the labeling standards for food products in Japan, while streamlining their safe distribution.

Here is what the new labeling system of Japan focusses on.

Removal of Certain Terms

Amongst the revisions made by Japan's CAA, the most significant change is the removal of the terms "artificial" and "synthetic" from the labels of food products. These terms can no longer be used to indicate the sweetness, colorants, preservatives, fragrance, and flavouring of a food product. This means, "artificial sweetener" will be changed to "sweetener", "synthetic preservatives" will be revised as "preservatives", and so on. Although the manufacturers are still required to indicate all the food additives on the label of the product, the removal of these terms was deemed necessary to avoid any false impression or misleading information regarding the safety of the product.

Implementation Date: The new labeling standards came into force from the date of revision. However, the food product manufacturers are given a transitional period till March 31, 2022, to modify the labels of their products.

Classification of Organic Livestock Products

According to the revisions, organic livestock products are now classified as special raw materials, hence, they are subject to specialized labeling rules and must be underscored on the food product labels. The special raw materials also include the following:

- Food products with specific place of origin
- Organic products (agricultural, livestock, processed)
- Non-GMO (genetically modified) products
- Food products that have specific manufacturing places
- Specially cultivated agricultural products
- Specific variety named food products
- Branded products

With the above-mentioned revisions, it is clear that Japan is in the process of upgrading its labeling system to ensure consumers make an informed choice about safety. To make it practically viable, manufacturers must align their product data and procedures with the revised standards to ensure compliant market-entry. Are you game for food products unmatchable compliance in Japan? Consult. Stay safe. Stay informed.

Holding True: Food Product Claims and Regulations

Arundhati Kasbekar discusses the importance of food product claims and examines some of the regulations industry must adhere to across the globe.

How do consumers make an informed decision before buying a food product or a food supplement? They simply usually look for the claims mentioned on the label to confirm the nature and purpose of the product. Consequently, claims have become an important part of any food product packaging.

This article explores the definition of claims and its importance in the labelling of food products. The article also sheds light on the regulatory scenario of claims and the requirements of some of the major food product markets across the globe.

What is a Claim?

Claims can be simply defined statements, symbols or wording made on a product label; they can be advertising or any promotional material that gives detail about the product performance/its usage/indication/application/composition.

The claims on product labels, promotional material and advertising are a representation of the connection between consumption of a food/food supplement and its supporting health benefits in the most effective manner.

By 'claims consulting and substantiation,' we mean defining new claims, devising or recommending new claims, promotional claims, or advertising claims on new product developments (NPD) or existing products in new markets with complete guidance of the required supporting scientific data to validate the claims.

Food and Food Supplement Claims

In most countries, there are specific regulations and scientific standards available to make food labelling claims. These should be expressed accurately and are required to be substantiated scientifically according to the claim's supporting data. The scientific requirements and substantiation can differ based on various factors, such as the type of claim (eg, health claims, nutrient content claims, functional claims, non-additional claims or declarations, including sugar-free, gluten-free, etc) for the product of interest and country-specific requirements.

In some regions, in order to get a health or any other claim approved, you must apply to the respective health authority (HA). The HA then verifies the application and supporting documents in order to authorise the claim on the product label.

In a process known as claims substantiation – mentioned above – new claims/health claims must be identified, suggested or defined based on the formulation, type/list of ingredients, product classification, regulations and the number of studies/papers available in scientific literature to justify the claims. Health claim experts have in-depth knowledge of the possible market hurdles and can assist you with the preparation of the necessary scientific evidence and claim substantiation applications to Government agencies/HA.

Providing comprehensive data that supports your product's claims is vital and can prevent loss of consumer confidence, legal fees and tarnished brand reputation.

Claim Examples

The following are some examples of claims that can be made around nutrition and health.

Nutrition

1. **Low Fat:** the food has reduced levels of fat content
2. **Low Sugars:** the food is low in sugars. A product may read 'NMT' (no more than), specifying certain threshold levels.
3. **Sugar-free:** the product is sugarless
4. **With no Added Sugars:** a claim stating that sugars have not been added to a food, where it may not contain any added mono- or disaccharides, or any other food used for its sweetening properties. If sugars are naturally present in the food, the following indication should also appear on the label: 'contains naturally occurring sugars'.
5. **High fibre:** indicates that the food has high levels of fibre.

Health

1. Boosts the immune system
2. Anti-ageing
3. Powerful antioxidants
4. Supports skin texture
5. Fibre helps reduce cholesterol
6. Helps reduce weight
7. Helps reduce body fat.

Food and Food Supplement Claims and Regulations in Major Markets

USA

The Dietary Supplement Health and Education Act (DSHEA) 1994 defines and regulates dietary supplements in the US. Under the Act, supplements are effectively regulated by the Food and Drug Administration (FDA) for Good Manufacturing Practices (GMP) under 21 CFR Part 111.

The DSHEA requires that all claims related to dietary supplement labelling (including labels, website and other marketing or promotional materials at the point of sale) have scientific substantiation, and that the claims are truthful and not misleading. This means that a dietary supplement distributor or manufacturer must have, at the time the claim is made, competent and reliable scientific evidence to substantiate all claims in its possession.

As per the USFDA regulations, the food labelling and nutrition regulations among the claims that can be used on food and dietary supplement labels fall under three categories of claims that are defined by statute and/or the FDA regulations. These are: health claims, nutrient content claims and structure/function claims.

India

The Food Safety and Standards Authority of India (FSSAI) has laid down criteria for claims that food companies can make in their advertising and promotions, such as nutrition claims, non-addition claims (including non-addition of sugars and sodium salts), health claims, claims related to dietary guidelines or healthy diets, and conditional claims. In case an advertiser wants to make claims for which regulations have not been specified, they must seek approval from the authority with trusted scientific literature to substantiate the claims.

South Korea

Health Functional Food (HFF) is a food (product) manufactured (including processing) using functional ingredients that are nutritious and helpful for our body.

To enable distribution of HFF products in the market, each product is strictly controlled by the Government with preliminary reviews of its advertising and health claims on the labels. They are managed through a record tracking system, which demonstrates the product's quality and provides consumers with accurate information. Therefore, all the HFF products approved by the Government's system are required to have proper health claims in order to receive the official 'Health Functional Food' mark.

Japan

Dietary supplements are regulated as 'Food with Health Claims', under two categories: 1) Food with nutrient function claims (FNFC) for vitamins and minerals, 2) Food for specified health uses (FOSHU) for other functions.

Qualified dietary supplements approved by the Consumer Affairs Agency are allowed to be marketed as FOSHU, with a formal logo and claims on the product label indicating the product's dietary uses for promoting health. In addition, other forms of health food or functional food that meet FOSHU requirements can also be marketed as 'FOSHU', provided adequate evidence on products' effects and safety (clinical trials are usually required) is given. However, the amount of newly approved FOSHU has seen a sharp decline in recent years.

Indonesia

Health supplement claims are categorised as nutrition claims, health claims and glycaemic index claims. Claims without prior approval will be subjected to scientific evaluation.

Malaysia

Health supplement claims are classified as general, nutritional, functional and/or disease risk-reduction claims. To make a general or functional claim on vitamins and/or minerals for a health supplement product, the product must contain a minimum of 15 percent of the Codex Nutrient Reference Value (NRV) per daily dose of the vitamins and/or minerals, and other ingredients must be substantiated by supporting evidence. Disease risk-reduction claims must be substantiated with supporting evidence.

Conclusion

So, how does your company leverage regulatory requirements for claims? Follow the process of claims consulting, substantiation and assessment meticulously to devise the best route to your product's success. Bear in mind the following when doing so:

- Strategy to assess the regulations of claims (basis country-specific claims standards/ regulations)
- Identification of new/allowable or promotional claims that can be used on the label, advertising and promotional material, as per the regulatory requirement based on ingredient list/nutrients
- Identification of claims based on the product classification, ingredient type/levels, health function support it is intended for, and availability of supporting claims data/studies
- Protocol of clinical studies to substantiate claims made on supplement/nutrition labels and conducting scientific literature reviews and data searches in the preparation of petitions for Health Authority approvals is necessary
- General principles for claims and advertisement (market specific) with applicable regulations
- Product formulations to be evaluated to determine qualification of the proposed claims with the market/country-specific regulations on claims
- Review of these claims to ensure compliance with existing applicable regulations, including reviewing claims on advertising and promotional material
- Classification of claims; guidelines on use of certain words or phrases in claims, synonyms that can be used to define a claim in the specified regulations and number of claims or objectionable/prohibited claims, if any
- Understanding the process of claim applications of various health authorities.

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Health Canada New Validation Rules (Version 5.0)

For eCTD and non-eCTD Submissions

Health Canada is the Agency responsible for the wellbeing of the Canadians by ensuring high-quality health services and minimising the health risks. Regulatory submissions for Health Canada can be done in both electronic Common Technical Document (eCTD) and nonelectronic Common Technical Document (non-eCTD) formats. However, they need to comply with the validation rules provided by the health authority to avoid rejections and follow-ups. Health Canada keeps amending these validation rules to assist the sponsors for the successful dispatch of the submissions. The Agency will be using the recently updated version of validation rules (version 5.0) for eCTD and non-eCTD submissions effective from November 01, 2020. Upon submissions, the Agency will detect and notify the validation failures to the sponsors in a .zip format, which must be reviewed, corrected and resubmitted with the necessary modifications. Recent updates in the validation rules mainly focus on file characters, size, type, document properties, naming conversion, metadata and XML elements.

Validation Rules - Classification

Health Canada eCTD and non-eCTD format updated validation rules (version 5.0) are broadly classified as:

- General
- Portable Document Format (PDF) Analysis
- Referenced Files
- XML Analysis
- Regional
- ICH Backbone
- Study Tagging Files (STF)
- Regulatory Enrolment Process

Validation Criteria for Regulatory Submissions in the eCTD format

GENERAL

This section mainly discusses the files (documents) and folders in the sequence of the submission. In a sequence folder structure, there should not be any empty files and subfolders present. Also, the files should be opened without any security access permission for the viewer. The file size should not exceed 200 MB for PDF and 100 MB for XPT documents, respectively. The sequence of the submission that is validated should be the highest in the application folder. A proper sequence lifecycle should be seen in the application folder. While validating the current sequence, the previous sequence should be made available; otherwise, the validation will throw errors. Word documents should be in the readable format and no password is allowed while submitting the dossier.

PDF ANALYSIS

PDF documents should be in a readable format and should not be damaged. Bookmarks and hyperlinks should be active, relative and should have a magnification setting of 'Inherit Zoom.' There should not be any password-protected documents. Document properties such as PDF version, page layout, magnification, fast web view should match ICH eCTD criteria.

REFERENCED FILES

Referring to the other files (Hypertext Reference – HREF) within the application is allowed as per the ICH eCTD specification. The operational attribute of the files for the initial sequence should always be new.

REGIONAL

All the files should have only one file extension. The sequence number should be followed by subfolder M1 which in turn followed by subfolder 'CA'. All the documents

and leaf should have appropriate naming fulfilling the ICH eCTD criteria. The leaf title should not be left blank. The application number should start with the letter 'e' for all CA submissions. Replaced files should have identical content as referenced files. The cover letter should not exceed more than three (3) pages. Node extensions in module 1 backbone (ca-regional. xml) are not allowed, except in 1.2.6 - Authorization for Sharing Information, 1.2.7 - International Information and 1.6.1 - Comparative Bioavailability Information Also, the node extension title should not be left empty. No 'append' operation is allowed in Module 1.

ICH BACKBONE

Checksum type attribute should have MD5 value. Index and MD5 checksum files should exist. The utility folder should be present in M1. The number of leaves directly under a single node must not exceed 1000. The rule applies only to module 5 while using node extensions and also to leaves with operation attribute 'new'. Do not mention strength values in the dosage form attribute in the sections 2.3.P, 3.2.P, 3.2.A.1 or 3.2.A.2. Any numeric value found in these attribute values will be reported as an error. If the strength value was already present in the previous sequence, the rule will not report an error for the current sequence. Leaf elements in 3.2.R Regional Information heading must be provided using node extensions. PDF fi are not allowed as leaf elements directly under 3.2.R Regional Information heading.

STF

The value of the study-identifier/category/study-id/title element must not be empty. STF leaf element must reference another STF leaf upon append. Category information must be provided for certain STFs. Leaf references in the STFs should always target content files, not STFs. The STF study IDs should not be changed in the application life cycle. There should be only one file tag for each doc-content. If Study Tagging Files (STFs) are used in the current validating sequence being validated, the node *5.3.7* must not be used. The Case Report Forms must be referenced from the STFs. The previous sequences present in the same dossier will not be checked. Leaf elements present in module 4 (except those in subsection 4.3), with an operation attribute 'new,'can use either node extensions, STFs or may be placed directly under the TOC sections. Leaf elements, with an operation attribute 'new,' in subsections *5.3.1, 5.3.2, 5.3.3, 5.3.4, 5.3.5* & *5.3.7* must use only node extensions or STFs. Although both node extensions and STFs are acceptable for study reports, only one or the other approach must be used consistently throughout the lifecycle of a leaf. Also, in a specific sequence, all leaf elements must use the same approach.

Validation Criteria for Regulatory Submissions in the non-eCTD Format

GENERAL

All empty folders must be deleted before submitting the transaction to Health Canada. Check the size of each file before submitting, to ensure it does not exceed the maximum file size limit (200 MB). File extensions written in uppercase letters are not accepted and no manual change is allowed. The document should not have password protection and should be in a readable format.

PDF ANALYSIS

Before submitting to Health Canada, ensure PDF documents are not password protected. The acceptable PDF versions are 1.4, 1.5, 1.6, and 1.7 and ensure the PDF documents are created using acceptable PDF versions. All the bookmarks must have only one assigned action that should open the destination page. The settings should be verified in the bookmark properties. Ensure that the PDF document does not include attachments/portfolio documents. PDF documents exceeding 10 pages should have bookmarks except for literature references in sections 3.3, 4.3 & 5.4; and Health Canada application e-forms.

REFERENCED FILES

File path length character includes the file name, and the count starts at the application folder. The correct structure path for a non-eCTD transaction is x123456\m1.

Conclusion

Health Canada has updated the validation rules for Regulatory transactions submitted in the eCTD and non-eCTD formats. The purpose of the validation rules is to help sponsors in providing a valid electronic transaction to Health Canada and reduce errors and followups. Sponsors can use a commercially available tool to validate their Regulatory transactions in eCTD and non-eCTD formats, before filing them to Health Canada. Health Canada validates each Regulatory transaction and if the errors are detected, a Validation Report describing the errors will be sent to the sponsor. So, it is very important to file a submission to the Health Authority without any errors and warnings by complying with the ICH specifications and by validating the submissions which in turn results in approval of license to the product for marketing and human use.

SFDA Guidance: e-IFU Requirements for Medical Devices

Recently, the SFDA (Saudi Food and Drug Authority) has issued a guidance to clarify the e-IFU (electronic Information for Use) requirements for medical devices in Saudi Arabia. This guidance is issued in reference to the Essential Principles specified in, "Guidance on Requirements for Medical Device Listing and Marketing Authorization (MDS-G5)."

It is applicable for medical devices (including IVD medical devices) supplied to the KSA (Kingdom of Saudi Arabia) market, with IFU in electronic form and is intended for professional users. Medical devices and IVDs intended for layperson use and near-patient testing are excluded. As per the guidance, the users may be provided with the following IFU requirements in electronic format.

The e-IFU Requirements

Indication that IFU is supplied in electronic form

- The information provided with the device shall clearly indicate that, the IFU of the device is supplied in electronic form instead of paper form. The URL (Uniform Resource Locator) indicating the e-IFU web address should be provided to the users with clear navigation, where relevant
- The IFU display shall not impede the safe use of the medical devices fitted with a built-in system, visually displaying the IFU (in particular, the life-monitoring or life-supporting functions)

Risk Assessment: Medical device manufacturers willing to provide IFU in electronic form shall undertake a documented risk assessment, covering the following elements:

- Knowledge and experience of the intended users, in particular, regarding the use of the device, user needs and the hardware and software needed to display the IFU in electronic form
- Environmental characteristics of the device
- User's access to reasonably foreseeable electronic resources, needed at the time of use
- Performance of safeguards, to ensure the protection of electronic data and content from tampering
- Safety and back-up mechanisms in the event of a hardware or software fault, particularly, if the e-IFU is integrated within the device
- A provision for IFU in paper form, during foreseeable medical emergency situations
- The impact caused by the temporary unavailability of a specific website or the internet in general, or their access in the healthcare facility, as well as, the safety measures to overcome such situations
- Evaluation of the time period, while providing IFU in paper form, as per the user's request

e-IFU shall clearly state information about the target Regulatory jurisdiction and the date of release should be version controlled. For online IFU, where appropriate, the obsolete versions of the IFU shall remain accessible to the public. Also, the risk assessment shall be updated in view of the experience gained in the post-marketing phase.

Information in the e-IFU

- The e-IFU information shall include all the items specified in essential principles of, "Guidance on Requirements for Medical Device Listing and Marketing Authorization (MDS-G5)"
- Except implantable devices, for devices with a defined expiry date, the IFU shall be available for the users in electronic form for at least 2 years, after the end of the expiry date for the last produced device
- For devices (including implantable devices) without a defined expiry date, the IFU shall be available for the users in electronic form for a period of 15 years, after the last device has been manufactured

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Website: Any website containing e-IFU for a device shall comply with the following requirements:

- The IFU shall be provided in a commonly used format that can be read with freely available software and in such a way that, the server downtime and display errors are reduced as far as possible
- The IFU shall be protected against hardware and software intrusion
- All the e-IFU previous versions and their date of publication shall be available on the website
- The IFU should be readily accessible, without a need to create an online account or password
- The IFU approved for Saudi market should be readily identified as such

The e-IFU leads to better customer understanding, enhanced device safety and improved patient outcomes. To reap the complete benefits of e-IFU and avoid Regulatory pitfalls, medical device manufacturers must adhere to the addressed SFDA requirements. Consider approaching a local Regulatory labeling expert, to ensure device compliance. Stay informed. Stay compliant.

COFEPRIS Introduces New Electronic Appointment System for Medical Device Registrants

The Mexican Regulatory Authority, COFEPRIS (The Federal Commission for Protection against Sanitary Risk) has established a new electronic appointment system for medical device registrants for submitting applications or seeking in-person meetings with the Agency.

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This measure is a part of the digitization process and in compliance with the provisions of the Ministry of Health, to limit the number of visitors to the COFEPRIS facilities and reduce the risk of contagion by COVID-19.

As required by the Agency, all the users can utilize the new electronic appointment system by adhering to the following key criteria:

- The users must register in the new electronic system
- The users may request only one appointment per day
- The new electronic appointment system can be accessed with e-signature, or any other authentication mechanism determined by the Agency
- All the information on the procedures and specific services to be performed must be registered
- Users willing to cancel the scheduled appointment must inform the Agency at least 24 hours in advance
- All the fees related to appointments must be paid at least 48 hours ahead of the schedule

Alongside, the Comprehensive Service Center (CIS) facilities are incorporated with transparent acrylic protection covers at each window and a sanitary filter at the entrance. In addition, each executive must wear Personal Protective Equipment (PPE) and the applicants who arrive at the CIS facility must comply with the following provisions:

- A printed receipt of an appointment is a must
- As a mandate, users must put on face mask
- Access is exclusively given to users previously registered in the appointment system
- Users must present a valid official identification with photograph
- Users must show up 10 minutes before the time indicated in their appointment and failing to do so will lead to cancellation
- As stated in the appointment voucher, attention will be provided exclusively to the indicated person for the amount of procedures and services mentioned
- All procedures will be entered and processed in accordance with the applicable legal provisions
- Users can check the status of their request on the COFEPRIS portal

As the Mexican Regulatory body, COFEPRIS established a new electronic appointment system to reduce the risk of coronavirus exposure, the medical device stakeholders must ensure to comply with the Agency's regulations for all the necessary Regulatory operations and procedural best practices. Stay safe. Stay informed. Stay compliant.

Regulatory Considerations for Microneedling Products - Decode the US FDA Guidance

In a recent development, the US FDA has released a new guideline to assist the microneedling device manufacturers understand the product classification, applicable regulations, registration pathways and data requirements.

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What Are Microneedles?

Microneedles are an array of blunt or sharp micro-protrusion pins, tips or needles of varying lengths. These products may be used by a single user or multiple users, for either a single time or multiple times. The microneedles intended for multiple uses by multiple users may have additional needle cartridges, tips and cleaning solutions, either sold separately or along with the micro needles.

These products can be medical devices and are hence regulated by Center for Devices and Radiological Health (CDRH) or may be falling under combination product category, regulated by either Center for Drug Evaluation and Research (CDER) or Center for Biological Evaluation and Research (CBER) divisions of the US FDA. The devices intended for aesthetic use such as, facilitating skin exfoliation and improvement of the appearance of skin, treatment of scars, wrinkles and other skin conditions are considered as medical devices and other products such as, creams, ointments, gels, vitamin solutions, drugs, or blood products and combination products are regulated by CBER or CDER.

Acupuncture needles, hypodermic needles or other needles for injection, tattoo machine needles, needle probes that emit any type of energy (e.g., radio-frequency needles) or deliver any type of energy to a patient (e.g., LASER, ultrasound) and dermabrasion devices are not considered as Microneedling products. The dermabrasion devices are different from the Microneedling devices and are classified as Class I devices. Manual devices are regulated under 21 CFR 878.4800 and the motorized devices are regulated under CFR 878.4820 (motorized) where in both of the device types are exempted from 510(k) premarket notification process.

Various factors such as, the claims and statements, product design and technological characteristics such as, features that effect the penetration of microneedles into various layers of the skin including, needle length and arrangement, needle sharpness and degree of control, will determine whether the device is manual or motorized.

Microneedling devices for aesthetic use are classified as Class II devices under 21 CFR 878.4430 and are subject to 510(k) premarket notification and should comply with applicable special controls. The special controls include identification and testing of technical specifications and needle performance characteristics, such as, needle length, geometry, maximum safe needle penetration, depth and accuracy of needle penetration and puncture rate. The safety features of the device shall be demonstrated, including, fluid ingress protection for protection against cross-contamination.

The performance data must include electrical safety and Electromagnetic Compatibility (EMC) of all electrical components of the device. The biocompatibility of patient-contacting components of the device should be demonstrated. All the software components shall be verified, validated and hazard analysis must be performed. In case of the reusable devices, cleaning validation data and instructions for disinfection of the reusable components should be submitted. The data to support the claimed shelf life of the device such as, package integrity, device functionality and continued sterility throughout the claimed shelf life shall be demonstrated. All the patient contact parts of the device shall demonstrate sterility.

Labeling for these types of devices must include information on device components, technical description of device and device components (such as, needle length, needle

geometry, maximum penetration depth and puncture rate), suggested course of treatment, disposal instructions, reprocessing instructions for reusable components and shelf life. The device labeling for patients must include details on instructions for device operation, suggested course of treatment, probable device risks and benefits and post-operative care instructions.

Given many aspects of microneedles discussed, what we could showcase here are only a few from the recent guidance from the US FDA. For sure, manufacturers of Microneedles are required to understand all the aspects that are discussed in the document for a compliant US market-entry. Decode it with an expert. Stay informed. Stay compliant.

What Is SPOR?

The global pandemic has had a profound impact on consumer lifestyles, influencing their behaviours and shifting general purchase priorities. Even the consumer habits and buying behaviour prevalent among beauty and personal care industry has changed quite a lot, creating relevant shift in the consumer trends. The aim of IDMP is to facilitate the reliable exchange of medicinal product information in a robust and consistent manner.

The use of these standards is a regulatory requirement as they are mandated by the EU legislation (Commission Implementing Regulation (EU) No 520/2012 [articles 25 and 26])

While the most important need for IDMP is to enhance Pharmacovigilance, speed of response, electronic prescription of medicines in the EU, controlling the authenticity of medicines, identifying substances across regions, and addressing shortages stand as other essential objectives. IDMP enables faster identification and recalls, improves the communication between supply chain and Regulatory affairs, and facilitates process efficiencies in Regulatory activities.

What is SPOR?

The European Medicines Agency (EMA) is implementing the ISO IDMP standards for the identification of medicinal products in a phased programme, based on the four domains of master data in pharmaceutical regulatory processes: Substance, Product, Organization and Referential (SPOR) data.

EMA is delivering four SPOR data management services for the centralised management of master data that comply with the ISO IDMP standards. SPOR's objective is to deliver high-quality data management services for Substances, Products, Organizations, and Referentials.

The SPOR Data Management Services Include

- Substance Management Services (SMS)
- Product Management Services (PMS)
- Organizations Management Services (OMS)
- Referential Management Services (RMS)

Need for SPOR

Need for IDMP SPOR Emerged Due To...	Results of Missing Data Standardization...
Scattered data across organizations, applications, databases and the industry	Inconsistent data, reduced data quality and data duplication
Names used for organizations differ in various departments	Inefficiencies relating to correcting data and investigating data discrepancies
Different names for substances used across different regions in the Europe and globally	Manual intervention required to resolve data issues
Data often entered manually	Slower decision-making based on inaccurate information

SPOR Implementation

The European Medicines Agency (EMA) is aiming at implementing ISO IDMP standards in phases through four projects, i.e., **SPOR Data** Services. In addition, the European Commission, European Union Network Data Board (EUNDB) and the EU ISO IDMP Task Force (a.k.a. SPOR Task Force) recommended the phased approach

of implementing ISO IDMP. The first phase includes the implementation of **RMS** and **OMS**, which lay foundation for the subsequent implementation of **SMS** and **PMS**.

EMA will set up ISO IDMP compliant business services for the central management of data in all SPOR areas. These comprises data management services for:

- **Substance data:** Consistent data and definitions to distinctively identify the ingredients and materials that form a medicinal product
- **Product data:** Standardized data and descriptions to exclusively identify a medicinal product based on regulations available (e.g., marketing authorization, packaging, and medicinal product information, etc.)
- **Organization data:** It comprises data of name, location, address, etc. for MAH, sponsors, Regulatory authority, manufacturers, and more.
- **Referential data:** Lists of terms (controlled vocabularies) used to describe attributes of products, e.g., units of measurement, lists of dosage forms, route of administration, etc.

SPOR applies to both Human and Veterinary domains and aims to implement the Identification of Medicinal Products (IDMP) standards developed by the International Organization for Standardization (ISO). Once EMA implements the SPOR programme phases and exploits opportunities for integrating the SPOR services with other systems, SPOR's advantage will increase predominantly.

SPOR is Incepted to Prove Beneficiary to Organizations and Public. The Key Benefits Include

- Easier decision making with improved data integrity and reliability
- Enhanced data quality and clarity in data management procedure with data examined, assessed, and approved, as part of a new data operating model
- Effective data standardization with reduced data silos and enhanced interoperability across EU systems
- Operational efficiency and cost-savings with decreased data redundancy

The submission and maintenance of data on authorised human medicines is already mandatory since July 2012. This is based on a format called Extended EudraVigilance Product Report Message (xEVPRM), which will be replaced by the ISO IDMP compatible format. For implementing IDMP, the EMA has already published a roadmap to master data management in April 2015. The incorporation of SPOR data stored around multiple systems into a specific MDM solution will enable the establishment of high-quality, coherent, and consistent data for stakeholders. SPOR master data solution increases decision making of enterprises offering a crystal-clear recognition of the benefits linked to businesses.

SPOR's full benefits will get more visibility once implemented by EMA in phases and in ISO IDMP compatible formats.

ANVISA: New Registration Regime for Class II Medical Devices

Brazil's National Agency of Health Surveillance (ANVISA) published a new Resolution of the Collegiate Board of Directors (RDC No. 423/2020). The new resolution declared the elimination of the Cadastro registration pathway for Class II medical devices and IVDs and substituted the same with a notification registration pathway (Notificação).

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The main goal of this new resolution is to further concentrate on high-risk medical devices and IVDs.

The new notification registration pathway (Notificação) outlines the following rules and requirements applicable for Class II medical devices and IVDs:

- Unlike the Cadastro pathway, where the manufacturers are obliged to submit comprehensive technical dossiers, labeling materials and proposed Indications for Use (IFU) documents, Notificação does not require any submissions. However, manufacturers are expected to have all the documentation available and shall make them accessible upon request (in case of an inspection by the ANVISA).
- A re-validation is not required for Class II devices that are already registered with the ANVISA, except if the changes are requested. However, manufacturers must be compliant with Good Manufacturing Practice (GMP) requirements and any other applicable technical standards and regulations. The initial registration number could be used as a notification number and the additional notification is not required, except for the cases, when certain changes have been made to the devices.
- For entities responsible for the device changes, it should be sufficient to submit the appropriate notification containing the description of the changes. The sponsor should duly prepare and keep a record of any additional information and must provide it on request. Related notification form for the same could be downloaded from the official ANVISA`s website.
- The device's labeling information and IFU should meet the general requirements applicable for the appropriate type of device class, under the risk-based classification of medical devices. Labeling of a medical device under the notification procedure should contain the ANVISA's notification number, which should be in Portuguese and in the form of appropriate symbols.
- In case if the ANVISA identifies non-compliances or irregularities during the audit or inspection, the Agency is entitled to cancel the notification. If the change notification contains incorrect data, the same rule of cancellation will be applied. The notification can also be canceled upon the request submitted by the sponsors themselves, in case, if they no longer intend to market the medical device in Brazil.

Medical devices and IVD manufacturers aiming for a Brazilian market-entry are obliged to adapt to the ANIVSA's new Regulatory framework as mentioned above for streamlined device registration. What is your adaptation approach for the new notification pathway? Chalk it out with a regional Regulatory expert to forgo last-minute challenges. Stay informed. Stay compliant.

Infographic

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BREXIT

GB ARTICLE 95 LIST COMPLIANCE

GB Article 95 List

EU article 95 is now GB article 95 list after Brexit (from 1st Jan 2021)

2 Year Transition Period

Details will automatically be transferred to GB article 95 list and will remain in the list till 31st December 2022

Actions to Remain in the GB Article 95 List

1. Submission of data – Either resubmit the dossier (data required) or letter of access supporting your EU article 95 listing to HSE.
2. Establishment in UK: Company needs to establish itself in the UK within 2 yrs.

Submission Process

Applicant needs to fill application form and send it to biocidesapplications@hse.gov.uk. Applicant will receive a link through which right submission of attachments can be done using HSE Secure File Sharing Service.

Is your product in Article 95 List? Analyse Now!

https://csra.freyrsolutions.com

FREYR CONNECT

FDA Announces New Improvements to Electronic Medical Device Reporting (eMDR)

As you may know, the FDA (Food and Drug Administration) uses Medical Device Reporting (MDR) as one of the post-market surveillance tools, to monitor device performance, to detect potential device-related safety issues and to contribute to benefit-risk assessment of the devices.

In order to simplify the procedure of submitting medical devices adverse event reports, recently, the FDA and CDRH (Center for Devices and Radiological Health) have initiated electronic Medical Device Reporting (eMDR) and also published a guidance.

As per the guidance, based on the frequency of reporting, the FDA suggests two (2) potential pathways to submit the reports, such as:

- Low-volume reporting (few reports) via the eSubmitter software – a special tool developed by the CDRH
- High-volume reporting (numerous reports) using the XML files via the Health Level Seven (HL7) Individual Case Safety Report (ICSR) standard

Health Leven Seven (HL7)

HL7 is a non-profit volunteer organization, constituting of various industry representatives aiming for the development and advancement of clinical and administrative standards for healthcare. Duly accredited by the American National Standards Institute (ANSI), HL7 is one of the several Standards Development Organizations (SDOs) that develops messaging standards for the exchange, management and integration of data that supports the clinical patient care, management, delivery and evaluation of healthcare services. The ICSR is a special standard developed by the HL7 and is intended to be used for reporting adverse events. Currently, the ICSR could be used for drugs and medical devices and later its scope would be extended to veterinary products, food and dietary supplements and cosmetics.

Health Leven Seven (HL7) Version 3

The HL7 version 3 addresses the definition of the data to be exchanged, communication of certain errors to the application, timing of the interchange and also supports functions, such as, participant identification, security checks, exchange mechanism, availability checks, negotiations and most importantly, data exchange structuring. The HL7 version 3 is characterized by utilizing standard approaches with appropriate guidelines, to reduce miscommunication and aligning submissions with applicable standards in the healthcare industry, using the Extended Markup Language (XML).

FDA Electronic Submissions Gateway (ESG)

The FDA ESG is an Agency-wide entry point for all electronic submissions and eMDR uses the ESG to receive electronic MDRs. This gateway enables:

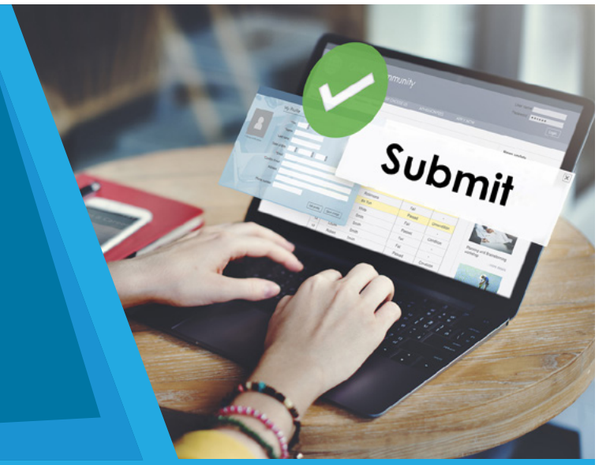
- Regulatory submissions
- Functions as a single point of entry for processing all electronic submissions, in compliance with secure messaging standards
- Serves as a conduit or highway, through which submissions reach the FDA
- Automatically routes submissions to the appropriate FDA Center or Office

According to the guidance, the electronic submission process through the ESG is as follows:

1. The ESG receives an inbound submission
2. The ESG sends a Receipt or MDN (Message Delivery Notification) or Acknowledgment 1 to the submitter, confirming the submission was successfully received by the ESG
3. The submission is automatically transferred to CDRH
4. Acknowledgment 2 is sent by the ESG to indicate the submission reached CDRH

5. CDRH validates and processes the submission and sends Acknowledgment 3, indicating the submission is successfully loaded into the Adverse Event database

On that note, the FDA states that the medical device manufacturers can utilize this approach to simplify and accelerate all the Regulatory procedures associated with medical devices adverse event reporting. This might be hassle-free but without proper knowledge on the adverse reporting for medical devices may cause potential setbacks for compliance. Opt for a proven Regulatory expert. Stay informed. Stay compliant.



EAEU Mandates Electronic Submissions

For new Market Authorizations and Follow-up Submissions

Aim for Compliant Transition Before the Deadline

New Market Authorizations
Dec 31, 2020

Follow-up Submissions
Dec 31, 2025

Leverage
Freyr SUBMIT PRO

Request A Demo

Face Shields Market-entry in Canada – Health Canada Standards and Authorization Pathways

Face shields have gained utmost significance as the primary protective equipment to curb the spread of the COVID-19.

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Global Medical Device Regulatory Services

Considered as a Personal Protective Equipment (PPE), face shield is made up of a transparent window or visor, that protects The face and associated mucous membranes (eyes, nose and mouth) against the potential exposure to infectious diseases. To guide manufacturers in these rapidly increasing market demands, Health Canada has devised several Regulatory standards and authorization pathways for importing or selling face shields.

In Canada, the PPE is considered as a medical device and is obliged to follow the standard requirements outlined in the Medical Devices Regulations. Based on their risk to health and safety, the medical devices are classified into 4 groups (Class I, II, III and IV) and the face shields are considered as Class I medical devices. For compliance, Health Canada recommends the face shield manufacturers to align with some or all of the following standards throughout the design and testing stages:

Health Canada Standards for Face Shields

- ANSI/ISEA Z.87.1 (2015) - American National Standard for Occupational and Educational Personal Eye and Face Protection Devices
- CSA Z94.3 (2020) - Eye and Face Protectors
- CSA Z94.3.1 (2016) - Guideline for Selection, Use, and Care of Eye and Face Protectors
- BS EN 166 (2002) - Personal Eye Protection and Specifications

To ensure the production of safe and effective face shields, minimum specifications must be incorporated during the design and verification stages. They include:

- Device should fit snugly to afford a good seal to the forehead area and to prevent slippage of the device
- Device should be made of optically clear, distortion-free, lightweight materials
- Device should be free of visible defects or flaws that would impede vision
- The device should provide adequate space between the user's face and the inner surface of the visor to allow the use of ancillary equipment
- Device should display anti-fog characteristics on inside and outside of shield, if available
- The device should provide user-contacting materials with adequate material biocompatibility
- The device need not be impact- or flame- resistant, if used for protection in hospital settings
- The device should withstand impact from sharp or fast projectiles
- The device must provide validated cleaning instructions for re-use

Regulatory Authorization

To authorize, sale or import face shields into the Canadian market, manufacturers should keenly review the following Regulatory pathways and select the appropriate authorization route for their product:

- Pathway 1: Interim order authorization to import and sell medical devices related to COVID-19
- Pathway 2: Expedited review and issuance of Medical Device Establishment Licences (MDEL) related to COVID-19
- Pathway 3: Exceptional importation and sale of certain non-compliant medical devices related to COVID-19

While Health Canada has devised the aforementioned regulations and registration pathways for face shields, manufacturers aiming for the Canadian market-entry are obliged to adhere to the required procedural activities. To forgo last-minute challenges, get in touch with regional Regulatory expert for streamlined market-entry. Stay informed. Stay compliant.

Who is a UKRP?

UKRP stands for United Kingdom Responsible Person. Medical Device manufacturers located outside the United Kingdom (UK) and without any local business offices, shall appoint a United Kingdom Responsible Person (UKRP), on their behalf, as a pre-requisite for device registration and launch of the device in the United Kingdom.

What is the Legal Basis for a UKRP?

Pre-requisites to appoint a UKRP, responsibilities of a UKRP and other related information is defined in the UK MDR 2002.

When should a Medical Device Manufacturer Appoint a UKRP?

Medical device manufacturers with already marketed devices in the UK should appoint a UK Responsible Person by 1st January 2021. The device manufacturers with an intention to place their device in the UK market, shall appoint a UKRP before the device registration. The UK Responsible Person shall register the devices with the MHRA.

What are the Responsibilities of a UKRP?

The UK Responsible Person is responsible for below activities:

- Shall act on foreign manufacturer's behalf and register the devices with the MHRA, before they are placed in the UK market
- Shall ensure that all the device technical documentation and applicable declaration of conformity documents are in place for the device in scope and that the conformity assessment has been completed by the device manufacturer
- Shall maintain copies of the original, amendment and supplements of technical documentation, the declaration of conformity and certificates. These documents should be readily available in case of the MHRA inspections.
- Shall be able to present the documents that ensure conformity of the device
- Shall inform the foreign manufacturer immediately about the suspected incidents, complaints and reports received from healthcare professionals, patients and users
- Shall cooperate with the MHRA for any corrective and preventive actions taken for mitigation or elimination of any identified risks posed by the devices
- Shall either maintain samples or have access to the devices, in order to provide to the MHRA, on request. If not, UKRP shall forward the MHRA request for sample or access
- Shall terminate the agreement with the device manufacturer in case of non-conformities with applicable regulations
- Shall keep the MHRA and relevant Notified Body informed, about the termination of agreement, if applicable

Who can Act as a UKRP?

Any third-party entity or an importer or distributor can act as an UK Responsible Person on foreign manufacturer's behalf. The appointed UK Representative shall register with the MHRA.

What are the Labeling Requirements in the Context of UKRP?

The name and address of the United Kingdom Representative shall be included on the label of a UKCA marked device, w.e.f. 1st,January 2021. For more information on UKCA marking of device or for end-to-end UKRP services, reach us at sales@freyrsolutions.com.

Case Study 1

Center of Excellence
Global Cosmetics Regulatory Services

Label Assessment for Skin and Eye Products in the USA and Canada

Client
One of the Leading and Fast-growing Personal Care Companies in Canada

Solution
Cosmetics

Industry
Cosmetics

Service Region
USA, Canada

Client Location
Canada

Therapeutic Area / Indication
Skin / Eye products

Health Authority
FDA, Health Canada

BENEFIT HIGHLIGHTS

- Freyr carried out the review and performed necessary changes for claims and label
- Delivered submission-ready documents
- Time and cost-effective service
- A detailed harmonized report

Business Imperatives

- The client is one of the leading and fast-growing personal care companies in Canada, and is specialized in developing and manufacturing Skin care/Eye products
- As the client wanted to launch their own products, it approached Freyr for label assessment with the draft copy of information on the product label for three of its cosmetic products

Challenges

- Most of the claims available on the label were unacceptable. All the claims had to be rephrased according to the target Health Authority requirements
- Few label claims were unacceptable and the rephrased claims which were acceptable were provided
- There were number of new changes after every round of feedback from the Clients

Freyr Solutions & Services

- Label assessment report, along with the INCI (International Nomenclature of Cosmetic Ingredients) list, was delivered to the client, and review and claims assessment was performed according to the USA and Canada Health Authority regulations for the given products
- Freyr informed the client about the required changes on the label according to country-specific cosmetic labeling guidelines

Client Benefits

- Freyr supported the client for the compliance check of the given products
- Freyr carried out the review and performed the necessary changes for claims and label
- Delivered submission-ready documents
- Time and cost-effective service
- A detailed harmonized report, including the location of placement of information on the label, was provided by Freyr which eased the designing of product artwork and helped prepare a single label

Case Study 2

Center of Excellence
Global Food and Food Supplements
Regulatory Services

Regulatory Compliance for Infant Formula in Malaysia and KSA Markets

Client
One of the Leading Brands of Infant Nutrition and Adult Nutritional Supplements in France

Solution/CoE
Food & Dietary Supplements

Industry
Infant Nutrition and Adult Nutritional Supplements

Service Region
Malaysia and KSA (Kingdom of Saudi Arabia)

Client Location
France

Therapeutic Area / Indication
Regulatory Compliance for Infant Formulas

Health Authority
NPRA & SFDS

Product
Infant Nutrition and Adult Nutritional Supplements

BENEFIT HIGHLIGHTS

- Transparent approach – Holding kickoff calls or weekly meetings based on client's availability
- Offering Regulatory Intelligence Support for Malaysia and KSA markets
- Answering Ad-hoc queries of the client for Infant Nutrition for various other markets viz, India, Vietnam and Indonesia
- Quick TAT by Freyr experts/ SMEs

Business Imperatives

- Leading manufacturer and supplier of nutritional supplements (Infant and Adult) in France required Regulatory compliance and product approval support for their Infant formulas

Challenges

- The project included product compliance including label assessment, claims assessment and formula review, translation support including guidance on documentation and challenges for the market-entry

Freyr Solutions & Services

- Freyr provided end-to-end support of product classification guidance, product compliance including label claims, ingredient analysis, guiding on product approval documentation
- Freyr team provided support on Product compliance overall for both the markets, promptly as per agreed timelines

Client Benefits

- Transparent approach – holding kickoff calls or weekly meetings based on client's availability
- Offering Regulatory Intelligence support for Malaysia and KSA markets
- Answering ad-hoc queries of the client for infant nutrition for various other markets viz, India, Vietnam and Indonesia
- Quick TAT by Freyr experts/ SMEs

LEAD THE WAY

With **Srikanth Vuppala**

Hi Srikanth, thank you for taking your time off for this Leadership CONNECT.

Thank you too for having me.

First things first. We are grateful to have experienced yours and your team's polite and lively conversations on the floor. Though most of us miss them now, in remote conditions, we could still experience the same in our online conversations too. How do you guys pull these conversations so elegantly and cheerfully?

The situation that we are in now is new for everyone, including us. The only good thing about this is that we get to manage this amazing team of resources who are working from different locations.

Thus, we are aware of the kind of engagement we have to do. Keeping that in mind, we did our research about companies that are already working from home and tried to understand the challenges, especially in terms of interaction. I believe that there should be a connect between the people working from home, because it is easy for people working from office to just step into any work station and have a quick chat and leave. But, in our current situation, every conversation is taking place over a call. Therefore, to amplify the connection, we requested employees to connect over video conference rather than audio ones. As HR, we understand the importance of in-person communications and that is what we tried to pull-off with video conferences. Earlier, we used to have such video conferences only with our clients, but now with the new normal, we are doing this even with our colleagues.

So, we understand the intensity of the situation. Which is why, after a month of rolling out the work-from-home policy, the HR team reached out to all the 750 employees of Freyr to understand the challenges they are facing with respect to connectivity, their teams and manager, etc. . Few of them even came forward to share their concerns and we tried our best to manage those issues. I feel that the only person who will be aware of all these issues is the HR, and I feel glad to say that we successfully managed to resolve all these issues and provide them the comfort to help them come over these concerns.

Being an HR, my only request to my team is not to lose their patience, as all of us are new to this situation, and this is something that we all have to adapt to while maintaining a proper connect.

From the updates of previous Town Halls, we could learn that Freyr has exponentially added new blood to the teams, when almost every other company was thinking in other terms. Virtually how did this onboarding happen so smoothly? Would you like to share any procedural challenges in the way, if any?

Virtual on-boarding is definitely not engaging because you are not able to gauge the first impression of the candidate. I believe that on-boarding helps us to give the candidate and new-joiners an experience about the company. So, while on-boarding virtually, we ensured to give the new-joiners the same experience by engaging them through storytelling. We ditched the traditional on-boarding PowerPoint presentations during the virtual inductions and adopted story-telling pattern, and that helped us to give more information to the candidates about our company. We also experimented with the video-based modules to increase our engagement during the on-boarding process. We tried to make the process very simple by reducing the documentation work and sharing everything online. We successfully created an engaging virtual culture which was easily accepted by the candidates. Going forward, I believe virtual on-boarding is going to be the new thing. We also managed to help the candidates connect with their managers and colleagues, via calls and introductory sessions, and gave them a warm welcome not only on behalf of the HR team but entire Freyr.

We did face our share of challenges through this process. For example, we struggled for a few initial sessions because there were a lot of network issues, as the candidates were from different cities with different network qualities. To overcome this, we shared a proper checklist with the candidates, including the network bandwidth requirement, to ensure seamless induction right at the onset. We feel it is the smarter, faster and more effective way to carry out inductions.

We fondly believe that core functionality of HR is not just overlooking the staffing, employee relations and other compensatory factors, but also is about ensuring the continuous employee engagement. In this new normal of work from home, hasn't it been difficult doing that? Or is it easier now?

Everyone is busy with their own schedule, but at the end of the day they all need some diversion from their work. Social isolation has put people in a bubble from which they need to break out every now and then. So, we came up with a few engagement activities. We asked all the managers to conduct virtual CONNECTS, like a coffee over video calls. We even rolled out a few fun activities, such as one-minute games and painting competitions. It is just like what we used to do in our Freyr office, but only this time it was online. We also suggested to include the employees' family members in these informal calls in order to increase the connect between the teams. I feel that regular communication between the teams increases the overall engagement which is what we are looking for. We have also done a few work-life balance activities and asked the managers to communicate with their team and encourage their team members to try to maintain that balance. Additionally, we reached out to our employees to ensure that they are well connected and taken their feedback for improvement. If I have to sum it all up in one sentence, I'd say that we've tried to engage our employees not only by conducting some fun activities, but also by pushing the next-level leadership to engage in their own ways.

Not many of us know that Srikanth was also a successful leader for Sales, as a function. In comparison to a typical business-oriented person and a core HRM leader, who would you personally

choose to be? And why?

I am a people's manager. Companies have appreciated me as someone who is good with managing people. Although I had an HR background at the time of joining Freyr, I took the opportunity to handle sales operations, as I was good with people management. Now, when I say people, they can be either internal stakeholders (i.e., employees) or external stakeholders (i.e., clients). The only thing is that when I was in sales, my only focus was on the external stakeholders, but now I see our employees as my internal stakeholders. So, as a HR, I act as an advocate between the employees and the management to maintain a perfect balance between both. That's my key role. In sales, my job was to understand the requirements of the clients and then push our services and products accordingly. Now, I am doing the same thing for my internal stakeholders, which are our employees. But, if given a choice between sales and HR, I'd choose HR.

"I am a people's manager. When I say people, they can be either internal stakeholders (i.e., employees) or external stakeholders (i.e., clients)."

Being a Human Resource persona in a rapidly growing organization, what do you think the best practice to handle some of the odd and interesting situations pertaining to employees? Could you please share any such experiences?

Handling people with incomplete knowledge about any particular issue is the most challenging part of being an HR. My approach with such people is to make them sit and understand all the aspects of the issue and then resolve it. Let's say that an employee has some issue with the policies of the company. Now as a HR, it is my responsibility to help them understand the vision of Freyr and what is that we can do as a company and what are our processes. That's my way of managing. In addition to this, a lot of people have issues regarding their compensation and designation, but mostly I try to make them understand and give them some clarity about the particular change in compensation or designation. That's something which is challenging. There definitely are a few tricky employees, but giving them accurate and complete information is the best HR practice. Apart from such employees, there are a few who are extremely stressed due to their personal as well as professional issues, and handling such people is what I find the most interesting. I like to help them with some counselling to ensure that they overcome the issues and stay healthy mentally.

The world is changing constantly. And like any other function, HR is also being automated. Considering this, what according to you would change the most in HR?

I'm looking forward to the digital culture in HR. And to stay at par, while adopting the proactive approach. Although, it might take time, but we have definitely started working towards the digital shift in the right direction.

It changes the way people can analyze and manage the business. As we all are aware that delivery insights like pattern analysis cant be seen with the naked eye. Overall it will help HR to provide data driven advice and solutions.

Rapid Fire:

Super Strength – Managing people

Client Testimonials

Thank you so much Freyr for all the hard work and dedication you guys have shown to this submission. We appreciate your dedication to this project, especially to work on a national holiday. On behalf of all the RA members involved, please accept our gratitude. Thank you again.

Sr. Regulatory Operations Specialist
A Japanese Pharma Group That Develops Innovative Specialty Drugs

Thank you so much for the good news on successful product registrations! We appreciate Freyr's work and effort for this project!

RA Assistant Manager
A global enterprise to provide comprehensive care for people's lives and lifestyles

I am glad to read it is done. Thank you Freyr and your team for the assistance."

Operations and Finance Personnel
A beauty care company

Freyr's work was very professional. We could find the same from the first CPSRs Freyr did for us last year. We are happy to consider giving 35 more products for CPSR preparation.

Director
Australia-based Professional Salon Product Manufacturer

I really appreciate Freyr's hard work to get a final product classification report done for one of our hand sanitizers in Japan.

CEO
A Japan-based High Definition Cosmetics and Skincare Products Provider

"We love working with Freyr and have been very impressed with their team. We plan on introducing our own branded products (or other white label products) in Indonesia with them in the future.

Partner
A Professional Corporation

Thank you Freyr team for the prompt response and assistance. I cannot thank you enough for getting this resolved so quickly. Appreciate your efforts.

Regulatory Affairs Specialist
US Based Leading Skincare Products Manufacturer

I know how you spent great effort to complete the notification. Thank you very much and we really appreciate your kind help for the solution/result-oriented work. Thanks again.

International Regulatory Affairs Specialist
A Market Leader in Infection Prevention Solutions

Freyr's approach was kind and careful in this project and here I would like to give my best regards to the entire team of Freyr. Thanks again for the cooperation and we could expect another chance in the future.

President
A Healthcare Activation Leader in Providing Strategic Solution for The Rx/ OTC, Health Supplement, Processing Foods, Cosmetics and Medical Networking Business

Performance is way beyond our expectations prior to the project initiation. Thanks for your kind support again.

President
A Healthcare Activation Leader in Providing Strategic Solution for The Rx/ OTC, Health Supplement, Processing Foods, Cosmetics and Medical Networking Business

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

About Freyr

Freyr is a leading, niche, end-to-end global Regulatory solutions and services company supporting large, mid, and small global organizations across different life sciences verticals - Pharmaceuticals | Generics | Medical Devices | Biotechnology | Biosimilars | Consumer Healthcare | Cosmetics | Food and Food Supplements | 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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