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LEAD STORY

NEXTGen Regulatory Solutions
The Future of Regulatory,
Delivered Today!

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What's INSIDE?

CONTENT

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FREYR CONNECT

FOREWORD

Dear Readers,

Greetings!

We trust that you all are staying safe.

It feels good to connect with you all once again with the latest Issue of our Newsletter – Freyr CONNECT, Volume 9.

Amid the multiple waves of COVID-19 and unlocking phases towards the new normalcy, there seems dependency on automation and next-generation technologies for the global industries. From manufacturing to global market entry, every aspect of the Life Sciences industry is being automated to streamline the processes, if not to ensure safety. Life sciences, especially the Regulatory aspect of it, is not an exception as we analyze the market trends.

With an emphasis on automation, we start this Issue with a lead story on the Next Gen Regulatory solutions, which covers automation and its benefits in Regulatory processes using AI and ML. It provides insights about Freyr AiM (a next-gen center of excellence from Freyr) and Freyr.NEXT.

This Issue also has a line-up of some of our external publications 'Patents and Exclusivity', 'Bio-summary tables of ANDA submissions', and an exclusive perspective on a Comprehensive Ingredients Database like Freyr iREADY along with other Regulatory views and best practices for compliance.

To sum it up, we are hopeful that this Issue will give you a good understanding of ever-changing life sciences regulations in a better way and leads you towards compliance.

Happy Reading!

Suren Dheenadayalan

CEO

Lead Story

NEXT-GEN REGULATORY SOLUTIONS

The Future of Regulatory, Delivered Today!

The Life Sciences industry is built on innovation in its constant search for new drugs, devices, and cures. Today, technology has become ubiquitous in driving scientific innovation in discovering and marketing new treatments and building, integrating, and managing platforms that support scientific innovation.

One of the most important reasons for this advancement is the ability of Artificial Intelligence (AI) and Machine Learning (ML) applications to tackle everyday procedural challenges and logical issues that compliance officers face.

AI proficiently manages a vast quantity of information with speed and precision, which has helped with renovating Regulatory compliance. It is safe to say that the technology can also help manufacturers simplify comprehension of compliance obligations and take appropriate actions soon. The continued usage of AI in the Regulatory landscape can reduce manual labor for executing the procedures.

In a life sciences organization, software applications that integrate with AI enhance the efficiency of many functions in the Regulatory compliance procedures. Although the probable aids of technological innovations in AI and ML are limitless, present applications of AI in compliance schemes have already demonstrated at least three benefits for Regulatory compliance. They include dropping incorrect positives, lowering the price, and correcting for human error.

During drug discovery, it is observed that AI has enormous capability and influence on the assessment of challenging data sets to conduct drug development research. AI has significantly helped identify new (plausible) drug development routes. Digital wellbeing expertise and AI have further transformed clinical trials operations. Apart from the Regulatory aspect, AI is also useful for the commercial side of the life sciences business, i.e., to perform sales and marketing more efficiently.

Automation Using AI/ML

Robotics is a form of AI. Robotics is a form of AI. Its adoption in the life sciences research space has significantly reduced human intervention and improved the precision of research protocols. There is a significant rise in the pharmaceutical industry for using robots to automate activities in various processes. The ROI on Robotics and its AI technology is a profitable investment. The flexibility, speed, efficiency, and efficacy of the evaluation and/or research methodologies have a superior accuracy level given robotics.

Automation of processes is gaining popularity among smaller organizations, as it uses minimum space, increases production speed, is less (manual) labor-intensive, has a systematic output, has higher quality results, and is cost-efficient. These benefits are pivotal for implementing AI/ML and Automation in the life sciences industries for the growth of the businesses.

Cloud Solutions

The ongoing global pandemic has accelerated technology adaption in the healthcare industry compared to the previous years. It has led to the healthcare industries adopting cloud solutions – a technology that received skepticism.

Improved computing methods have made their way into clinics, hospitals, and pharmaceutical companies. The convenience of ML/AI with cloud services has significantly improved the accuracy of managing a tremendous amount of patient data.

AI algorithms refine the process of managing massive amounts of data, making it significantly faster and cost-effective to sift through information, identify requirements, data patterns, and draw reasonable conclusions from research data collected. Several pharmaceutical organizations are inculcating AI for several reasons, one of the critical ones being AI for drug discovery.

Regulatory Space Challenges and Resolutions

Current Challenge	Freyr's Solutions
The process for **tracking, updating, and managing** change control for accurate and real-time Regulatory requirements, intelligence, and precedence is **highly de-centralized**, manual, cumbersome, and inefficient.	Compiling the Regulatory Requirements data collection, curation, and Consumption Manual; from Semi-automated to Automated Evolution.
The ability to locate accurate, real-time Regulatory requirements, intelligence, precedence, and operational, Regulatory data is de-centralized, manual, indirect, and imprecise.	Regulatory Intelligence Standardized parameterization and information categorization

There is an **inability** to **effectively access & assess** precedence and Regulatory operational data to re-use existing artifacts, work products to improve efficiency.	Regulatory Intelligence Standardized parameterization and information categorization.
There is an **inability** to identify Regulatory requirements **common across countries** to effectively align submission content resulting in duplicative effort for same/similar submission packages.	Provide answers to Regulatory strategy questions for global new product approvals and product maintenance. Global Multi-lingual approach with translation capabilities for submissions.
Consumption of Regulatory Data, whether by individuals or by systems, is needed at varying levels of detail/granularity, thereby hindering the ability to increase efficiencies by standardizing and automating Regulatory outputs: Regulatory Strategy, Submission / Filing Plan, National Dossier Structure, Authoring Content, and Submissions.	Proactive to Predictive Risk Management for better decision making through Regulatory Intelligence Standardized Parameterization and Information Categorization.

Importance of AI in Regulatory Operations

Regulatory technology, commonly referred to as RegTech, is a rapidly expanding area of digital technology. Its agenda is to simplify Regulatory compliance and introduce Automation.

Across the globe, Regulatory bodies face the obstacle of scrutinizing methods and procedures within their industries. Often, companies end up experiencing substantial investments to align with the regulations, thus, increasing their compliance expenses. By introducing Big Data and AI, both organizations and officials can ensure streamlined Regulatory compliance.

Benefits of AI

AI and Big Data in Regulatory Compliance

Companies can influence AI and Big Data as a component of their Regulatory technology plan to ensure compliance in today's information-centric world. Businesses can streamline their end-to-end processes by introducing AI and Big Data to make their enterprise entity compatible.

Simplification of the Compliance Process

Often, companies fall short of fulfilling various requirements simply because they rely on tedious manual tasks. The Regulatory compliance process mainly involves information gathering through different sources, verifying the information, and then presenting it to regulators. Without Automation, this whole process proves to be cumbersome, costly, and labor-intensive. However, using Big Data and AI can significantly decrease the required funds and timeline while diminishing mistakes.

Tracking Regulatory Changes

Regulatory guidelines change now and then due to several market forces. If an organization fails to align with the new regulations, it can risk its reputation and lead to financial penalties or even legal action. AI and Big Data products can help companies stay compliant by keeping them up to date with the latest Regulatory changes. AI and Big Data tools use native linguistic processing and deep learning to understand compliance requirements and notify companies.

Improving Decision-Making

Companies can ensure smart Regulatory compliance processes by using AI and Big Data. Perhaps, an essential value that AI and Big Data extend to companies

is empowering them to comprehend and foresee the complicated risk and data management patterns. AI and Big Data can be the backbones of Regulatory Agencies.

AI Makes Regulatory Compliance Efficient

Technologies like Deep Learning and Machine Learning also facilitate Regulatory organizations to monitor units. Instead of executing periodic audits, which are often troublesome and time-consuming, companies can easily monitor their compliance limitations. The acceptance of AI and Big Data can streamline the compliance process.

Digital Revolution – Freyr Digital

At Freyr, we use the power of Artificial Intelligence/ Machine Learning (AI/ML), Automation, and cloud to build the digital platforms critical for continuing innovation in the life science domains. Freyr's Digital transformation is the key component in streamlining Regulatory Operations. Freyr Digital is a next generation regulatory software solution based on Global Regulatory requirements management. We deliver simple, smart, disruptive, and incremental digital innovations for Regulatory, Safety & Clinical operational processes.

These tools help automate and enhance the everyday Regulatory decisions in strategy, submission planning, preparation, and dossier creation using AI/ML.

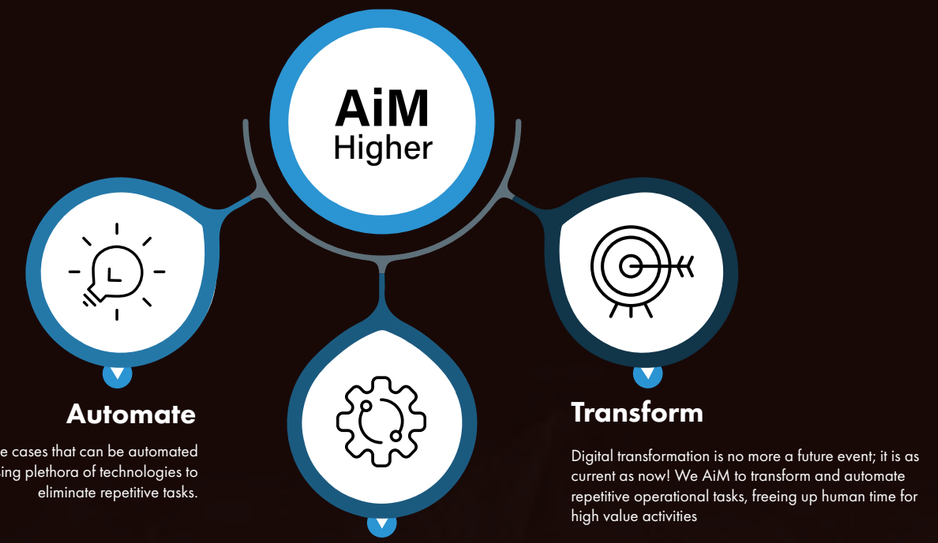


Fig.1: Freyr.NEXT technology

Freyr NEXT: Envisioning Future

Investing in the right technology raises the potential to unlock business possibilities by driving innovation. Freyr. NEXT is a technological revolution intended for Regulator transformation by accelerating progress at every step.

Freyr.NEXT provides a comprehensive solution package by streamlining automation work processes using AI and deep learning algorithms and creating small digital components like bots, MS Excel, and Word scripts. Putting the pieces to generate a Freyr.NEXT backed customized Regulatory processes ecosystem.

Freyr.NEXT is a suite of tools developed to resolve the time lag by using AI to manage and review large amounts of data.

Freyr.NEXT began with a need for quantifiable Regulatory process development and for streamlining of processes for internal use. Today it is evolving as per our customers' demands, because of its wide-spread popularity and ease of use.

Freyr has developed many resources to pick solutions depending upon the current operational process challenges and software solutions our clients face.

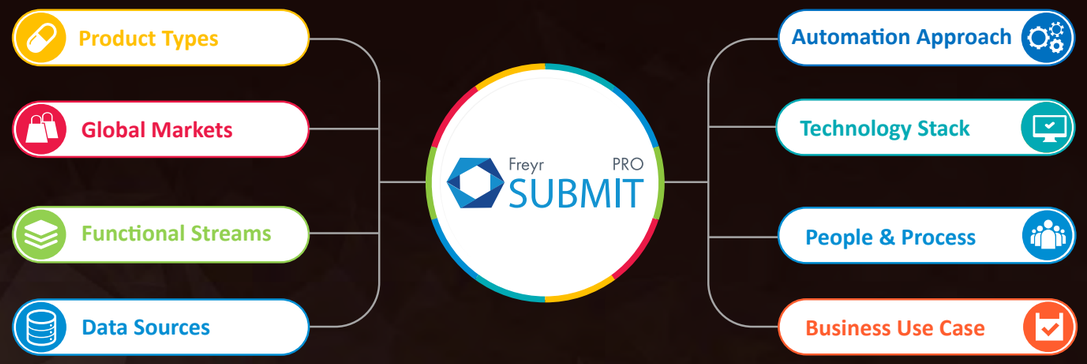


Fig.2: Freyr.NEXT Regulatory resources

Example: Freyr Impact - a Regulatory Intelligence software, part of the larger Freyr.NEXT suite, which enables comprehensive data collection, validation, population, and dissemination. The Freyr Impact includes decision enablers driven by progressive technologies, supported by manual/automated and hybrid data management approaches.

Fig.3: Freyr.NEXT Regulatory solutions suite

Predominantly created for process improvement internally and for providing business solutions to our clients, Freyr NEXT's increasing popularity has led Freyr to expand the technological suite's presence to provide customized Automation services.

Freyr strives to provide solutions that solve Regulatory operational problems and keep adapting and growing along with the ever-changing landscape of requirements. Freyr.NEXT is our initiative to bring an ecosystem of resources in one place to resolve challenges and make progress in all aspects of the Regulatory space.

In a nutshell, the combination of AI and technology can shape the Regulatory industry and bring advancement in compliance procedures across the globe. For digital transformation, companies are advised to keep track of ever-evolving regulations and go ahead with the procedures compliantly. Stay safe. Stay compliant.

Center of Excellence
Regulatory Affairs

PATENTS AND EXCLUSIVITY

A US Perspective

Drug patents and drug exclusivity. How are they different from each other? Why should the applicants/sponsors be fully aware of the Regulatory patent protection and exclusivities? The draft covers a comprehensive perspective on drug patents and exclusivities in relation to the United States.

When a pharmaceutical company first develops a new drug or any device to be used for the treatment of a disease, it is initially marketed under a brand name by which clinicians can recommend or prescribe the drug or any device for use by patients. The drug or device is covered under patent protection, which means that only the pharmaceutical company that holds the patent is allowed to manufacture, market the drug and eventually profit from it.

The United States Patent and Trademark Office (USPTO) will have the right to issue a patent to a discoverer or inventor to "eliminate others from manufacturing, utilising, offering for sale, or marketing/selling the innovation to over the United States or importing the discovery into the United States" for a constrained time, in exchange for public exposure of the discovery, when the patent is granted.

Generally, the term of a new patent is twenty (20) years from the date on which the application for the patent was filed with the USPTO. For any new patent, a company may submit an application from the USPTO anywhere with the development lifeline of a drug and can cover a wide range of claims. However, so many other factors can affect the time period of a patent.

The original New Drug Applications (NDAs) and supplements can be submitted on the FDA Form 3542a, prior to approval, along with patent information and if it is upon post-approval, the patent information should be submitted on the FDA Form 3542. After the approval of an NDA, if the patent has been issued, the applicant has thirty (30) days to file the patent to have it counted/deemed as a timely filed patent. Beyond the thirty (30) day period, the patents may be submitted, but the patent is not counted or considered a timely filed patent. If the generic application is submitted prior to the patent, an Abbreviated New Drug Application (ANDA) holder is not required to make a certification to an untimely filed patent. Patents protect the approved drug substance, drug product, or approved methods of use for the manufacturing or marketing of drugs. New Drug Application sponsors are required to submit for listing patents that protect their approved drug substance, drug product, or approved methods of use. For submission of patent information, the applicant must use the FDA provided form 3542a before approval or Form 3542 within 30 days of approval or issuance of patent (for later issuing patents). If there are no patents to list, that must be declared via a Form 3542/3542a submission.

For every patent in orange book, an ANDA applicant must certify:

- Patent has expired **(Paragraph II Certification)**
- Generic manufacturer will stay off market until patent expires **(Paragraph III Certification)**
- Generic manufacturer believes that the listed patent is either invalid or would not be infringed by the proposed generic product **(Paragraph IV Certification)** [if patent information has not been filed: **Paragraph I Certification**].

Inventors can search the USPTO's patent database to see if a patent has already been filed or granted, that is similar to your patent. Patents may be searched in the USPTO patent full text and image Database (Pat FT). The full texts of the patents issued from 1976 to the present and the PDF images of the patents from 1790 to the present are housed by the USPTO.

Exclusivity

Exclusivity is originated to promote a balance between new drug innovation and generic drug competition. It is a period when an innovator drug is protected from generic drug competition. There are different types of exclusivities for different circumstances.

Types of Marketing Exclusivity in Drug Development

Unlike a patent, marketing exclusivity is generally acquired early in drug development, runs considerably longer and is based upon intellectual property rights, rather than evidence of safety and effectiveness. When the constitutional or statutory requirements are met for a drug, the FDA would issue the approval and also the marketing exclusivity, where the exclusivity is a period of time during which no other applications can be accepted and/or approved for the same active ingredient. This means that, other manufacturers that may wish to develop alternative formulations or generic versions of the drug will not be able to have their products approved during the exclusivity period. The type of exclusivity would decide the length of the exclusivity period. Importantly, the exclusivity period is not added to patent life, so sponsors will need to be mindful of both durations and plan, accordingly.

The exclusivity duration: There are a few types of marketing exclusivity, and all of them vary in duration and the statutory requirements that must be met. Some are based on the product classification, others on the indication being treated on the intended patient population.

The Types of Exclusivity, Include:

- **Orphan Drug Exclusivity (ODE):** This type of exclusivity is seven (7) years and is granted to drugs designated and approved to treat a rare disease or condition affecting fewer than 200,000 or more than 200,000 and no hope of recovering costs in the United States.
- **Biologic Exclusivity:** For Biologics License Applications (BLAs), Under section 351(k)(7)(A) of the Public Health Service Act, the duration of the exclusivity is twelve (12) years. The USFDA will not accept biosimilar filings (under its 351 (K) pathway) until five (5) years after the original biologic is licensed.

» **New Chemical Entity (NCE) Exclusivity:** In most cases, a brandname drug with a new active moiety has a five-year exclusivity. During this five-year exclusivity period, no other company can submit an Abbreviated New Drug Application (ANDA) to the FDA seeking approval of a drug product containing the NCE.

» **Generating Antibiotic Incentives Now (GAIN) Exclusivity:** GAIN is a new law that addresses the antibacterial drug resistance by encouraging the pharmaceutical research, development and approval of new type of antibacterial and antifungal drugs. The drug products have been granted or designated by the FDA as "Qualified Infectious Disease Product" (QIDPs) and have the additional five (5) years of exclusivity.

» **New Clinical Investigation Exclusivity:** A brand industry's new brand-name drug with an active ingredient that has been approved before may be awarded a three-year exclusivity in certain circumstances, such as, if a new way of delivering the active ingredient is proposed (for example, a tablet rather than a liquid) or a different disease or condition the drug can treat is identified. To get this approval, the drug company must conduct new clinical studies in humans.

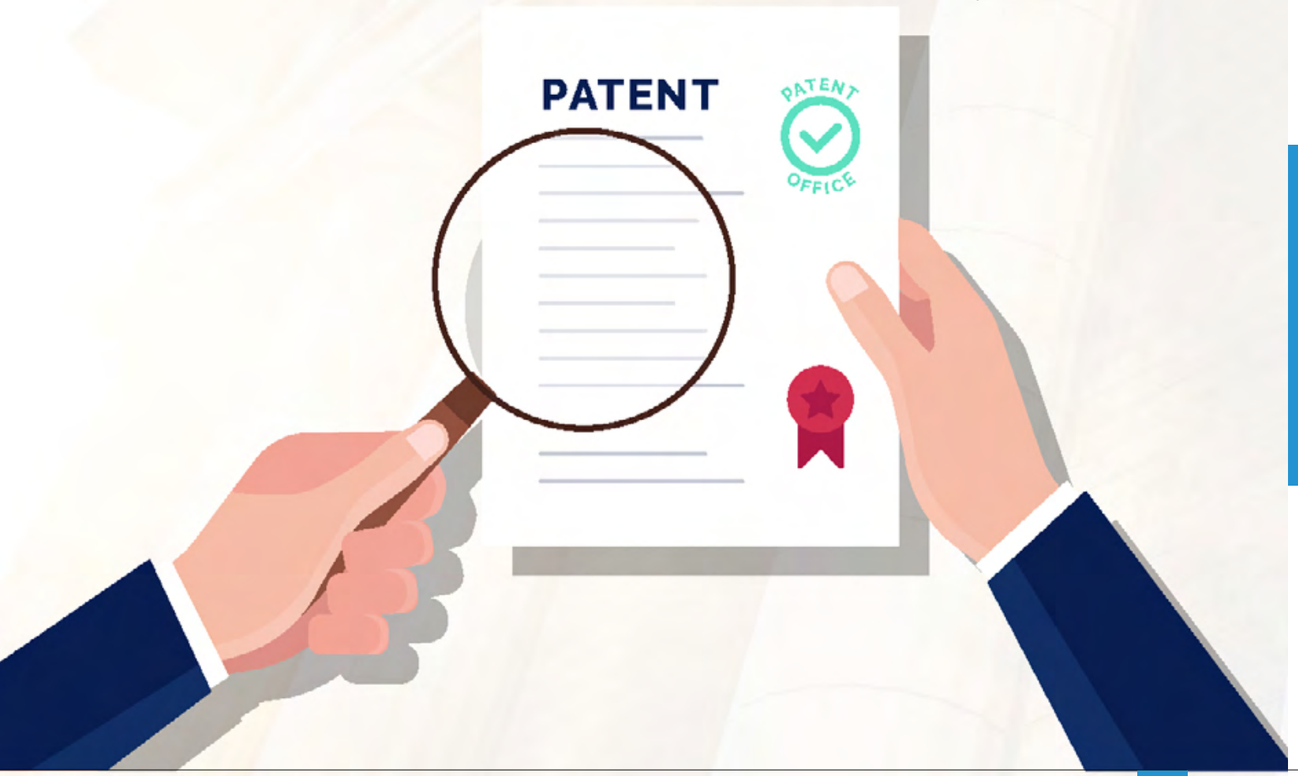
» **Paediatric Exclusivity (PED):** A patent protection for a new drug applicant for which the sponsor has done paediatric studies (in response to a written request from the FDA) may be eligible for a six-month exclusivity, which is added on to any other exclusivities or patents for that drug (six (6) months added to existing Patents/ Exclusivity). This exclusivity is an effective tool for drug developers, delaying the FDA ANDA and 505(b) (2) approvals six (6) months after the patent expiration.

» **Patent Challenge (PC):** This exclusivity is for Abbreviated New Drug Applications (ANDAs) only and the exclusivity period is 180 days.

» **Competitive Generic Therapy (CGT) or Generic Drug Exclusivity (GDE):** This exclusivity is for 180 days and is applicable for ANDAs only.

» **Qualified Infectious Disease Product (QDIP) Exclusivity:** This exclusivity is for five (5) years and it can be added to any existing exclusivity.

An Exclusivity Board has been established by the Center for Drug Evaluation and Research (CDER) to give oversight and recommendations about exclusivity determinations made by the Center. The CDER exclusivity board manages the granting of exclusivity determinations, that means whether and what type of exclusivity will be granted. The CDER board will not review or provide any recommendations with respect to exclusivity determinations. The five (5) year New Chemical Entity (NCE), three (3) year new clinical trial exclusivity and biological product exclusivity will be focused by the CDER board.



Difference Between Drug Patents and Drug Exclusivity

Regardless of the drug product approval status, the patents can be issued or expired at any time – before, during or after the FDA approval process. If the drug product meets the statutory requirements of the FDAs, the drug product will be approved with an attachment of an exclusivity. Further, few drug products have both patent and exclusivity protection while others have just one or none.

The patents will expire in 20 years from the date of filing, but the exclusivity is granted upon the basis of the drug product. For instance, the New Chemical Entity (NCE) gets five (5) years of exclusivity, while orphan drugs get seven (7) years of exclusivity.

According to the FDA, the other major difference between patent and exclusivity is patents can be issued or expired at any time irrespective of the drug approval status,, while the exclusivity is granted upon approval.

The expired patent or exclusivity drug products may not be available, or it is removed from the Orange Book. Patents and Exclusivity protection may or may not run concurrently and may not run the same aspects of the drug product. Exclusivity was developed to promote a balance between new drug innovation and greater public access to drugs that result from generic drug competition.

In some countries, like India and Brazil, they have compulsory licenses, which basically allow local companies to produce and locally market drugs that have not reached a point in time when generic competition is legally allowed.

Conclusion

The applicants/sponsors should fully be aware of the Regulatory patent protection and exclusivities. These exclusivities are developed to encourage the innovation in pharmaceutical research and development of new, safe and cost-effective treatment. While taking the advantage of Regulatory exclusiveness of the target country, it can help the sponsor realise a return on investment by utilising the Regulatory exclusivities. In the way of product identification or broadening of the line of products or market extension, one needs to evaluate patent as well as Regulatory exclusivities of the target country to have profit-making products, while serving the patient population.

This article was first published by: PHARMA FOCUS ASIA®

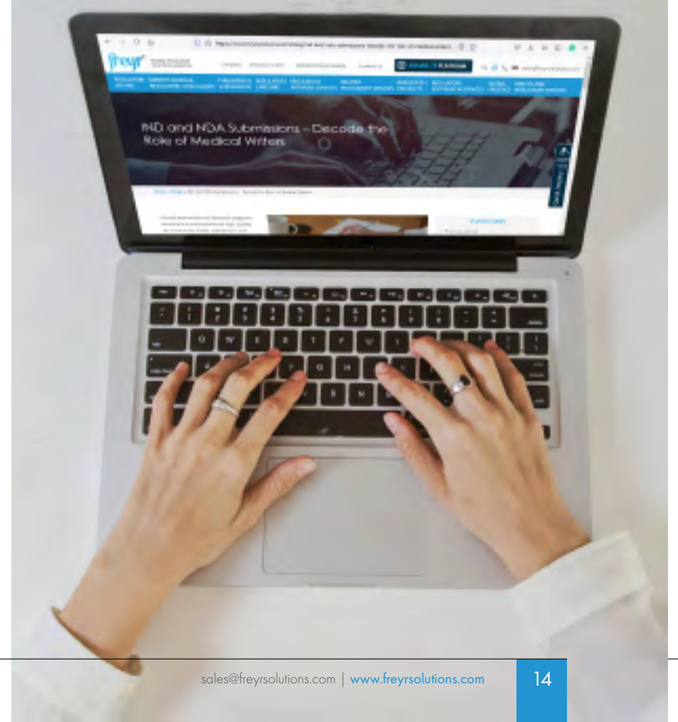
Center of Excellence
Regulatory Medical Writing

IND and NDA SUBMISSIONS

Decode the Role of Medical Writers

Clinical and nonclinical research programs demand the development of high-quality documents for timely submissions and approval of the drug product from Regulatory authorities. Medical writing plays a crucial role in drafting all the necessary documents right from drug development through submission and approval. When filing Investigational New Drug (IND)/ New Drug Applications (NDA) to the USFDA, medical writers are obliged to develop high-quality documents by collating all nonclinical, clinical and scientific data in a standard, comprehensive, and logical manner for Agency's review.

In such scenarios, drafting all the data accurately in agreement with the scientific requirements and as per the eCTD (Electronic Common Technical Document) specifications are challenging. Documents failing to meet the permitted eCTD structure may need last-minute changes facing timeline risks, and in worst conditions may lead to technical rejections by the Agency.



FREYR CONNECT

The Role of Medical Writers in IND/NDA Submissions

As with any eCTD submission, IND/NDA submissions also have five different modules, which span across:

Module 1: Region-Specific Administrative Information (not technically part of the CTD)

Module 2: Manufacturing, Nonclinical, and Clinical Overviews and Summaries

Module 3: Detailed Manufacturing Information

Module 4: Nonclinical Study Reports

Module 5: Clinical Study Reports

Of the five (5) eCTD modules, medical writers should be well-versed with the breadth and depths of the following in an IND/NDA submission:

eCTD Module 2.4 - Nonclinical Overview (Pharmacology, Pharmacokinetics and Toxicology)

eCTD Module 2.5 - Clinical Overview (Clinical Pharmacology, Efficacy, and Safety)

eCTD Module 2.6 - Nonclinical written and tabulated summaries (Pharmacology, Pharmacokinetics and Toxicology)

eCTD Module 2.7 - Clinical summaries (Summary of Clinical Efficacy and Summary of Clinical Safety)

eCTD Module 4 - Nonclinical study reports (Pharmacology, Pharmacokinetics, Toxicology, etc.)

eCTD Module 5 - Clinical study reports (Bioavailability and Bioequivalence, Clinical Efficacy, and Clinical Safety)

Modules 2, 4, and 5 require inclusive, efficient, and accurate reflection of the information within a defined framework. The amount and volume of information would, at times, be very complex, huge; and challenges the whole IND/NDA submission process. The information should be consistent and comprehensive for review and approval by the Agency. It requires clear-cut analysis and meticulous documentation capabilities.

The accuracy of scientific information plays a key role in the submission process. If medical writing is not contracted to professionals, Sponsors may tend to spend a lot of time writing, compiling, technical review, etc. Though product knowledge is crucial for medical writing, it alone may not suffice for requirements. The medical writers should be well-versed with region-specific Regulatory guidelines. In addition, the medical writers should possess specialized skill set for gap analysis, in-depth scientific understanding, capability to handle complex data and multiple stakeholders. In such scenarios, the best option for sponsors going for IND/NDA submissions is to opt for a proven Regulatory medical writing service provider.

Center of Excellence
Chemicals Safety and Regulatory Affairs

Market Entry of CHEMICALS IN THE APAC COUNTRIES

- *Regulatory Pathways*

The rapidly growing population and rising industrialization in food, agriculture, cosmetics, and many other manufacturing sectors drive the demand for chemicals in the APAC region. It is witnessed that chemical manufacturers are shifting their manufacturing base to the APAC region due to the stringent regulations in the US and Europe. Also, the growing profit margins and inexpensive labor cost are a few more compelling factors for manufacturers to operate from the APAC, a low-cost location.

Let us go through the registration, notification, manufacture and importation of Chemicals in a few emerging markets in the APAC region:

SOUTH KOREA

Chemical Regulations in South Korea are managed by various Ministries such as the Ministry of Environment, Ministry of Employment and Labor, Ministry of Health and Welfare, Ministry of Agriculture, etc., under numerous laws based on the uses and hazard properties of chemical substances. All the Authorities aim to protect human health and the environment from the toxicity of chemicals. The table below summarizes various Ministries and the Laws involved in the Regulation of chemicals in South Korea.

Products	Laws	Authorities
Industrial Chemicals	K-REACH Chemical Control Act (CCA) Consumer Chemical Products and Biocides Safety Act Occupational Safety and Health Act (OSHA)	Ministry of Environment Ministry of Employment and Labor
Cosmetics	Cosmetics Law	Ministry of Health and Welfare
Food Additives	Food Sanitation Law	Ministry of Agriculture
Pesticides	Agrochemicals Control Act	Ministry of Agriculture

Registration, Evaluation, Authorisation, and Restriction of Chemicals (K-REACH) for industrial Chemicals is monitored by the Ministry of Environment. The K-REACH amended Act was published in March 2018 and came into force on Jan 01, 2019. Any company with an intent to import or manufacture a new chemical substance or an existing chemical substance must register under K-REACH. The requirement for registration is as follows:

» Manufacturers must register all the new substances before manufacture or import. Any manufactured or imported substance below 100kg/y must require notification and does not need to go through hazard evaluation.

» One must register all existing substances manufactured or imported greater than or equal to 1 ton per year within given grace periods. Also, to benefit from these grace periods, manufacturers or importers must notify the following information to the Ministry of Environment (MoE) in advance ("pre notification"):

- Information of the Company
- Name of the Substance
- The volume of the Substance
- Classification of the Substance
- Information on the Use of the Substance

Based on the amended K-REACH, one must register new substances before manufacture or import, and the existing substances manufacturing greater than or equal to 1 ton per year must be registered within the deadlines (or grace periods) listed below:

» For the first 510 existing chemical substances manufactured or imported 1 ton per year - **July 01, 2018**

» For existing chemical substances greater than or equal to 1000 tonnes per year and CMR substances greater than or equal to 1 ton per year - **Dec 31, 2021**

» For existing chemical substances manufactured or imported 1-100 tonnes per year **- Dec 31, 2030**

In addition, any foreign manufacturer, who wishes to export chemical substances into Korea, must appoint a Korea-based representative for registrations and pre-notification submissions.

AUSTRALIA

The chemicals industry is one of Australia's largest manufacturing sectors and a key enabler of almost every value chain. In Australia, chemicals are regulated under both territory/state and national laws. There are four (4) leading Regulatory authorities for chemicals, and each Authority focuses on a particular type of use:

- Australian Industrial Chemicals Introduction Scheme (AICIS)
- Australian Pesticides and Veterinary Medicines Authority
- Therapeutic Goods Administration
- Food Standards Australia and New Zealand

AICIS regulates introducing and importing industrial chemicals (including polymers) such as cosmetics and personal care products, paints, cleaning products, inks, adhesives, solvents, manufacturing, construction, and mining applications. For manufacturing (introduce) or importing industrial chemicals into Australia, one must follow the following steps:

Step 1: Know If Your Business Needs Registration

Manufacturers, who wish to import or introduce industrial chemicals, must fall under the following categories to register their business:

- Manufacture industrial chemicals in Australia
- Import finished/packaged products that release industrial chemicals – e.g., labeled cosmetic products (such as soap, shampoo, lotion), glues, pens, paint, engine oil, etc.
- Import or produce industrial chemicals that release chemicals into Australia
- Import industrial chemicals and reformulate in Australia

Step 2: Register Your Business

Determine the Registration level that applies to your business. Sign up with AICIS to register your business and pay the registration fee. There is no need to register the chemicals separately.

Step 3: Categorize the Chemicals

Kindly make a list of all the ingredients in your product and categorize them according to the inventory. Check whether all the ingredients fall under the defined regulations. It is necessary to keep the correct records of the ingredients to ensure the introduction is authorized under the 'listed' category. There is no need to share any information about the product or the chemicals before importing.

Step 4: Submit the Annual Declaration

At the end of the registration year (1 September – 31 August), submit the annual declaration about all the chemicals imported or manufactured during the past registration year.

JAPAN

The Chemical industry is the second-largest manufacturing industry in Japan. With increasing production and use, the Chemical Regulatory Authorities of Japan aim to reduce exposure to hazardous chemicals and protect the workers' health. One of the aspects of sound chemical management is the establishment and implementation of legal frameworks. Therefore, chemical companies that intend to manufacture/import a new chemical substance must notify the same to the following three (3) ministries at least three (3) months before the manufacture or importation:

- Ministry of Economy, Trade and Industry (METI)
- Ministry of Labor, and Welfare (MHLW)
- Ministry of the Environment (MOE)

Also, companies must submit two (02) different types of notifications under the following:

- Chemical Substances Control Law (CSCL)- To prevent the environmental pollution
- Industrial Safety and Health Law (ISHL) - To secure the health and safety of workers

Both CSCL and ISHL require that the new substance be notified before its production and importation. Each has its notification system and a list of existing substances.

New Substance Notification Under Japan CSCL

Chemical Substances Control Law (CSCL) was enacted in 1973 to prevent environmental pollution by chemical substances that poses a risk to human health or the environment. The latest amendment was made in 2009 and implemented on Apr 01, 2011.

The National Institute of Technology and Evaluation (NITE) is the main body that evaluates new substance notifications under Japan CSCL. A new substance is defined as any chemical substance other than the following substances:

- A substance on the list of Existing and New Chemical Substances (ENCS)
- Class I or II specified chemical substance
- Priority assessment of chemical substances
- Monitoring chemical substances

The ENCS consists of two (2) parts:

- Existing chemical substances placed on the Japanese market before 1973 (around 20,600 substances)
- New chemical substances notified under the CSCL, determined to be "safe" and published on government Gazette (around 8,000 substances)

There are four (4) types of notifications under CSCL:

- **Standard Notification:** To manufacture or import >1 ton/year
- **Low Volume Notification:** To manufacture or import non-biodegradable and not bio-accumulative substance <=10 ton/year
- **Small Amount Confirmation:** To manufacture or import <=1 ton/year
- **Other Prior Confirmation:** For substances used in a closed system and polymer of low concern

New substances notified with a standard notification will be added to the ENCS five (5) years after its notification. New substances that go through the confirmation process will not be added to the ENCS.

New Substance Notification Under ISHL

Industrial Safety and Health Law (ISHL) was first established in 1972 for the health and safety of workers in workplaces. ISHL requires manufacturers or importers to notify a new substance to the Ministry of Labor and Welfare (MHLW) before its production and importation. Any substance that is not on the ISHL list will be subject to new substance notification under ISHL.

ISHL list also consists of two (2) parts:

- Existing chemical substances under CSCL before 1973- around 20,600 substances
- New substances notified under ISHL and published on government Gazette

There are two (2) types of notification under ISHL:

- **Standard Notification:** To manufacture or import >1 ton/year
- **Small Volume Notification:** To manufacture or import <=1 ton/year

In a nutshell, as safety is considered to be a major key point in the chemical industry, manufacturers must thoroughly understand, register, categorize and submit the required documentation of their products as per the defined processes mentioned above. Therefore, the manufactures/importers must decode the registration process and align with them. In such cases, approaching a regional Regulatory expert is highly beneficial.

freyr REPORTS

LEVERAGING REGULATORY INTELLIGENCE (RI)

In Lifesciences Industry The Need of the Hour

Sustaining the ever-evolving global Regulatory space of the Life Sciences industry is strenuous. Therefore, manufacturers must keep abreast with the latest Regulatory information to ensure compliance across all the business functions, such as clinical development, release, and marketing scrutiny of medicines.

However, considering the dearth of information from various sources, evaluating the right information, and analyzing what is required for submissions has become cumbersome. This is why focusing and concluding the right choices in favor of the manufacturer's Regulatory strategy within a limited time makes all the difference. And, one of the most fruitful ways of obtaining the information is to opt for Regulatory Intelligence.

Regulatory Intelligence (RI) is a way of administering data and information from several available resources to devise a compliant Regulatory strategy. RI also means micro-scoping the details and segregating the significant outcome of defining consequences, prospects and building the necessary block of business requirements and choices. How can one showcase these details? Through various types of RI reports such as:

FREYR CONNECT

01 **Structured RI Reports**
Produced using predefined templates. The concerned company can decide the template (Table of Content).

02 **Regulatory Insights**
This report is based on pre-decided topics. The topics can range from labeling, CMC, Regulations to specific departments. The report is presented with a summary (Synopsis), associated literature documents as attachments. These insights can be qualified under many predefined categories.

03 **Regulatory Events Tracking**
Global Regulatory live and virtual events that impart Health authority and industry-based intelligence are tracked. It supports Regulatory learning and development.

04 **Regulatory News Tracking**
Relevant global Regulatory News can be tracked and distributed to subscribers.

05 **Regulatory Guidance Tracking**
Health Authorities and other industry directives, guidance, regulations, and recommendations can be tracked through the lifecycle of guidance from draft state to implementation and withdrawal (if any).

What are the Components of RI?

The components of Regulatory Intelligence are defined by outlining the possibility (e.g., GxP, quality), sponsors, and transmission networks. It requires the knowledge of the company agenda and its products, the sequences, enhancement, and quantification. The primary focus of any RI is on the quality of in-house Regulatory intelligence functionalities, which cannot be compromised at any cost since this holds the responsibility of guaranteeing recognition and research to update the life sciences landscape.

Having said that, Regulatory Intelligence is far more than just data mining. Marginally, it might be responsible for a few assessments, shareholder identification, ranking, and trends in the Regulatory world, and estimation. Sometimes Regulatory strategy and reactions from the Health Authorities might also influence the same. Life Sciences enterprises worldwide expect robust Regulatory assistance to decide on crucial choices, like intensifying their product portfolio or promoting their products across various geographies. Meanwhile, they face key challenges while deciphering local database requirements, new regulations, component and evaluation, labeling and packaging obligations, import regulations, local GxP requirements, etc. In these circumstances, there is an indisputable requirement to guarantee that firms are informed of current geo-specific regulations and any future guidelines to be announced. When this becomes vital, companies require reliable Regulatory Intelligence (RI), which can focus on all the challenges correctly.

Hence, companies looking for Regulatory Intelligence are advised to reach out to a Regulatory Expert with a global network. Additionally, companies can also lookout for a Regulatory Intelligence Software that can instantly help them track Regulatory information from various sources in real-time.

Center of Excellence
Regulatory Affairs

WHAT DOES BREXIT MEAN FOR THE EU AND THE UK

Regulatory Submissions?

The withdrawal of the United Kingdom from the European Union had many concerns. One of them being Regulatory Submissions. To smoothen the submissions process, the EU and the UK have set up a clear set of rules. Many of them are related to the existing and new Marketing Authorization Applications (MAAs) for CAPs, DCP and MRP, Batch testing, QP Certification, etc. Let us have a look at what Brexit means for the EU and the UK Regulatory Submissions. Here is a clear-cut Brexit impact summary that a consulting firm has recently published.

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EU	UK
New Marketing Authorization Applications for Centrally Authorized Products (CAPs)	
» MAH must be present in the EU	» MAH must apply for a separate authorization
New Marketing Authorizations for Mutual Recognition Procedure (MRP)/Decentralized Procedure (DCP)	
» The same process applies to the EU	» MAH must have a separate application
Existing Marketing Authorizations	
» MAH must be located in the EU/EEA » CAPs must have an MAH in the EU » UK (Co-)rapporteurs must be assigned to other EU/EEA member states » In case of MRP/DCP, RMS/CMS cannot be in the UK. If UK is the RMS, it must be transferred to RMS in the EU	» MAH must be located in the UK by the end of 2022 » CAPs are automatically granted authorization for one (01) year to share the baseline data with MHRA » Contact is needed in the UK from Feb 1, 2021
Batch Testing and QP Certification	
» Batch testing must be within the EU/EEA or with a Mutual Recognition Agreement (MRA) country. » QP certification must be within the EU/EEA. From Jan 1, 2022, products exported to Northern Ireland must have re-testing and QP certification in Northern Ireland.	» Batch testing must be within the EU/EEA/MRA country. » QP certification is not if certified by a QP in the EU/EEA » Wholesalers importing from EU/EEA must name an RP on WDA by Jan 1, 2023.
Batch Testing for Products Manufactured in the EU/EEA	
» Batch testing must be performed within the EU/EEA	» No additional batch testing is required for imports until Jan 1, 2023
Batch Testing for Products Manufactured in a Third Country with No MRA with the EU	
» Batch testing must be performed within the EU/EEA	» Batch testing must be performed within the EU/EEA or the UK » No additional batch testing is required for imports until Jan 1, 2023
Access to Eudravigilance	
» EU can continue reporting to Eudravigilance	» The UK will no longer have access to Eudravigilance. with UK's new systems, ADRs must be reported to the MHRA
GMP and GDP	
» EU's GMP and GDP guidance applies	» The UK will follow EU's GDP and GMP guidance until Jan 1, 2023

With many changes expected to be developed in the UK and the EU post-Brexit, it is essential to keep a tab on the upcoming Regulations. You can also reach out to a partner with high-level Regulatory and operational expertise to navigate the changes in the Regulatory landscape. Stay informed. Stay updated.

Center of Excellence
Regulatory Affairs

UNDERSTANDING BIO-SUMMARY TABLES for ANDA Submissions

Bio-summary tables a mandatory requirement for Clinical Summaries submitted to the USFDA as a part of ANDA. These tables provide a standard format for data representation consistent with the FDA recommendations. This paper emphasizes the importance of Bio-summary tables, which are reviewed for a new generic drug product by Division of Bioequivalence (DBE).

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Bio-summary tables, also known as "Division of Bioequivalence (DBE Tables)", are one of the main prerequisites for Module 2.7, submitted to the United States Food and Drug Administration (US FDA), as a part of the eCTD dossier. The FDA mandates the submission of these tables as PDF format and in MS Word document format in the appropriate eCTD/CTD locations (Module 2.7).

The main purpose of these summary tables is to provide a standard format for data to be in an Abbreviated New Drug Application (ANDA) in a concise format consistent with the current recommendations. The FDA provides specific instructions to fill in these tables. There are different types of summary tables based on the type of formulation and characteristics of the ANDA application.

The different types of summary tables for which individual instructions are provided by the FDA include the following:

- Bioequivalence Summary Tables for In-Vitro Feeding Tube Testing
- Comparative Clinical Endpoint Bioequivalence Study Summary Tables
- Model Bioequivalence Data Summary Tables
- Topical Dermatologic Corticosteroids In-Vivo Bioequivalence Study Summary Tables and SAS Transport Formatted Tables for Dataset Submission
- In-Vitro Binding Bioequivalence Study Summary Tables and SAS Transport Formatted Tables for Dataset Submission
- Summary Tables for the Listing and Characterisation of Impurities and Justification of Limits in Drug Substance and Drug Products (consistent with the recommendations delineated in the Guidance for Industry ANDAs: Impurities in Drug Substances and ANDAs: Impurities in Drug Products)
- Model Bioequivalence Data Summary Tables: A detailed content and format information resource for generic drug applicants submitting ANDAs to the FDA
- Bioequivalence Summary Tables for Aqueous Nasal Spray Products
- BCS-Based Study Summary and Formulation Tables
- Pharmacy Bulk Package Sterility Assurance Table
- Irritation/Sensitisation/Adhesion Study Summary Tables
- Bioequivalence Summary Tables for Pressurised Metered Dose Inhaler Products

MODULE 2.7.1
2.7.1.1 Background and Overview
Table 1: Submission Summary
Table 4: Bioanalytical Method Validation
Table 6: Formulation Data
Table 10: Study Information
Table 11: Product Information
2.7.1.2 Summary of Results of Individual Studies
Table 5: Summary of In Vitro Dissolution Studies
(Comparative in Vitro Dissolution Data, Certificate of Analysis (CoA) for Test and Reference products should be included along with potency, assay, content uniformity, date of manufacture and the lot number)
Table 9: Reanalysis of Study Samples
Table 12: Dropout Information
Table 13: Protocol Deviations
Table 14: Summary of Standard Curve and QC Data for Bioequivalence Sample Analysis
2.7.1.3 Comparison and Analysis of Results Across Studies
Table 2: Summary of Bioavailablity Studies
Table 3: Statistical Summary of the Comparative Bioavailability Data
Table 16: Composition of Meal Used in Fed Bioequivalence Study
(A statement of compliance to the FDA standard meal should be provided, if the standard meal is as per the CDER guidance for food effect bioavailability and fed BE studies. In case of any alternative meal used, the summary table needs to be provided, which mentions the food item(S), amount (g), energy(kcal), Protein(kcal), fat (kcal) and carbohydrates (kcal),
2.7.1.4 Appendix
Table 15: SOP's Dealing with Bioanalytical Repeats of Study Samples
Module 2.7.4 (Summary of Clinical Safety)
2.7.4.1.3 Demographic and other Characteristics of Study Population
Table 7: Demographic Profile of Subjects Completing the BE Study
2.7.4.2.1.1 Common Adverse Event
Table 8: Incidence of Adverse Event in Individual Studies

Bioequivalence Summary Tables

The absence a of significant difference between test and reference with regards to rate and extent at which the drug is available at the site of action when administered at the same molar dose and under similar conditions is termed as Bioequivalence (BE). Hence, reports providing data from BE studies conducted to compare the rate and extent of drug absorption in-vivo for a generic and corresponding reference product, are one of the critical components of ANDA submissions. The therapeutic equivalence of an active moiety as per the Regulatory standards depends on the determination of pharmaceutical equivalence along with establishing BE. A separate division [Division of Bioequivalence (DBE)] is designated in the Office of Generic Drugs (OGD), which is involved in the review of BE studies of new ANDA applications.

For ANDA BE submissions that contain the results of in-vivo studies, the four major study report components are as follows: in-vitro dissolution testing, bioanalytical methodology, clinical study reports and statistical analysis.

There are a total 16 BE summary tables for a typical product, which focus on the above information in a concise manner for DBE review. They are:

» **Table 1:** Submission Summary

» **Table 2:** Summary of Bioavailability Studies

» **Table 3:** Statistical Summary of the Comparative Bioavailability Data

» **Table 4:** Bioanalytical Method Validation

» **Table 5:** Summary of In-Vitro Dissolution Studies

» **Table 6:** Formulation Data

» **Table 7:** Demographic Profile of Subjects Completing the Bioequivalence Study

» **Table 8:** Incidence of Adverse Events in Individual Studies

» **Table 9:** Reanalysis of Study Samples

» **Table 10:** Study Information

» **Table 11:** Product Information

» **Table 12:** Dropout Information

» **Table 13:** Protocol Deviations

» **Table 14:** Summary of Standard Curve and QC Data for Bioequivalence Sample Analysis

» **Table 15:** SOP's Dealing with Bioanalytical Repeats of Study Samples

» **Table 16:** Composition of Meal Used in Fed Bioequivalence Study

Formatting points to be followed while filling the information in the above summary tables1:

- Margins for the paper should be "1" for the top and bottom and "1.25" for the left and right sides
- All text should be in Times New Roman, with font size 10
- Default Table Style should be used while creating the tables in Microsoft® Word (Select Menu Table-Table Auto Format-Table Normal)
- "Portrait" orientation should be followed for Table 1, Table 4, Table 7, Table 8 and Tables 10-16
- "Landscape" orientation should be followed for Table 2, Table 3, Table 5, Table 6, Table 9.

As per the checklist provided by the FDA for an ANDA application, the above tables are to be placed in Module 2.7 in the following sequence.

Importance of Bio-summary Tables from Refuse to Review (RTR) Perspective

As per the RTR guidance from the FDA, it is mentioned that the FDA will RTR an ANDA, if the Study Information (Table 10) BE table is incomplete. The Study Information BE table compiles important information about study type and site locations and should be placed in Module 2.7 of the ANDA (along with the other BE summary tables).

The other minor deficiencies with respect to module 2.7 and summary tables that may trigger a RTR are as follows:

» Failure to provide separate PDF and Word documents of Summary tables

» Missing summary data tables in module 2.7

» Failure to provide the certificate of analysis for each strength of the RLD

» Failure to provide the exact location of the long-term storage stability (LTSS) study reports and data (Table 10), along with working hyperlinks to the respective information

Major Deficiencies, include:

» Inadequate dissolution studies, lacking

» Minimum of 12 units

» Use of the FDA-recommended test media

» ½ tablet dissolution for modifiedrelease products with functional score marks

» General deficiencies of in-vitro dissolution (Table 5)

» Not conducted on 12 units

» Not conducted on all strengths (test vs. RLD)

» Not conducted in all test media

Conclusion

In summary, this information regarding the Bio-summary tables will help understand the standard format for data to be submitted to the Office of Generic Drugs in accordance with the current recommendations of the FDA for ANDAs. The pharmaceutical industry can take steps toward eliminating recurring problems related to summary tables by following the format and content of these tables and hence can submit the acceptable, complete, and well-organised BE submission to ANDAs without any RTRs.

This article was first published by: PHARMA FOCUS ASIA®

Announcement

Center of Excellence
Regulatory Medical Writing

Freyr Completed

1500+

PDE Reports in **Three (3) Years**

Freyr is pleased to announce the feat of completing 1500+ Permissible Daily Exposure (PDE) reports. The feat has been achieved within three (3) years of the implementation of the European Medicines Agency's (EMA's) 'Guideline on setting health-based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities (EMA/CHMP/CVMP/SWP/169430/2012) across the globe for all the Health Authorities (HAs).

Here is the Press Release

FREYR CONNECT

Center of Excellence
Global Food and Food Supplements
Regulatory Services

FOOD FACILITY REGISTRATION With the USFDA

Decode What, Where, Who, When and How

To streamline the food facility registration for manufacturers in the United States (US), the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Act) (Pub. L. 107-188) has added section 415 to the Federal Food, Drug, and Cosmetic Act (FD&C Act). Under the Section 415 of the FD&C Act (21 U.S.C. 350d), domestic and foreign facilities in the US that manufacture, process, pack, or hold food for human or animal consumption are required to register with the US Food and Drug Administration (FDA). The revised Guidance for Industry "Small Entity Compliance Guidance (SECG)" issued by the FDA intends to help small entities comply with the food facility registration regulations outlined in the 21 CFR. Section 415 of the FD&C Act, as amended by the FDA Food Safety Modernization Act (FSMA) also requires food facilities to register with the FDA to renew such registrations every other year. The section also provides the FDA with the authority to suspend the registration of a food facility in certain circumstances. The initial registration with the FDA is required once and must be renewed every other year between October 1 and December 31 of each even-numbered year. However, before applying for food facility registration to the FDA, manufacturers must first understand its Regulatory requirements to ensure end-to-end compliance. Let's take a look at a step-by-step guide better understanding of the FDA's food facility registration in the US.

What is a Food Facility Registration?

In the US, food facility registration requires domestic and foreign facilities that manufacture, process, pack, or hold food, as defined in 21 CFR 1.227, for human or animal consumption to register with the FDA.

Which Facilities are Required to Apply for Food Facility Registration?

Domestic and foreign food manufacturers/processors, packers, and storage operations that handle food for consumption in the US. For purposes of registration, "food" is defined in 21 CFR 1.227.

When Should a Facility be Registered?

Before a facility begins to manufacture, process, pack, or hold food for consumption in the US, it must be registered with the FDA.

Who Can Register a Food Facility?

The owner, operator, or agent in charge of a facility, or an individual authorized by one of them, can register that facility.

Foreign facilities must designate a US Agent who lives or maintains a place of business in the US and is physically present in the US, for purposes of communication between the facility and FDA. The US agent also may be authorized to register the facility.

How to Register a Food Facility with the FDA?

Registration can be done either online or by mail or fax.

What Kind of Information is Required for Registration?

- Facility name, full address, phone number
- Facility's Unique Facility Identifier (UFI) recognized as acceptable by the FDA
- Preferred mailing address, if different from that of the facility
- Parent company name, address and phone number (if applicable)
- Email address for the contact person of the facility or, in the case of a foreign facility, the name, address, phone number, and email address of the US Agent for the facility
- An emergency contact phone number and email address (for domestic facilities, the email address is required only if this is different from the contact person)
- Name, full address and phone number of the owner, operator, or agent in charge. Additionally, the email address of the owner, operator, or agent in charge is required, unless the FDA has granted a waiver under 21 CFR 1.245
- All trade names that the facility uses
- Applicable food product categories, as listed on the registration form
- The type of activity conducted at the facility for each food product category identified
- Assurance that the FDA will be permitted to inspect the facility at times and in the manner permitted by the FD&C Act
- Certification that the information submitted is true and accurate and that the person submitting it is authorized to do so

How is the Registration Confirmed?

The FDA confirms the registration either electronically (online registration) or by mail (paper) and assigns a registration number.

As mentioned before, for manufacturing/processing, packing, or holding food for consumption in the US requires registration of the facility with the FDA. However, FAILING TO REGISTER FACILITY, RENEWING REGISTRATION, UPDATING REQUIRED ELEMENTS or CANCELING REGISTRATION in accordance with the applicable regulations may create unwanted consequences. In addition to this, if a foreign facility is required to register but fails to do so, food from that facility that is offered for import into the US is subject to being held at the port of entry or a secure facility until the foreign facility is registered. Therefore, manufacturers must understand the requirements of the Food Facility Registration to avoid last-minute challenges and delays. Devise the best of Regulatory methodologies and strategies. Stay informed. Stay compliant.

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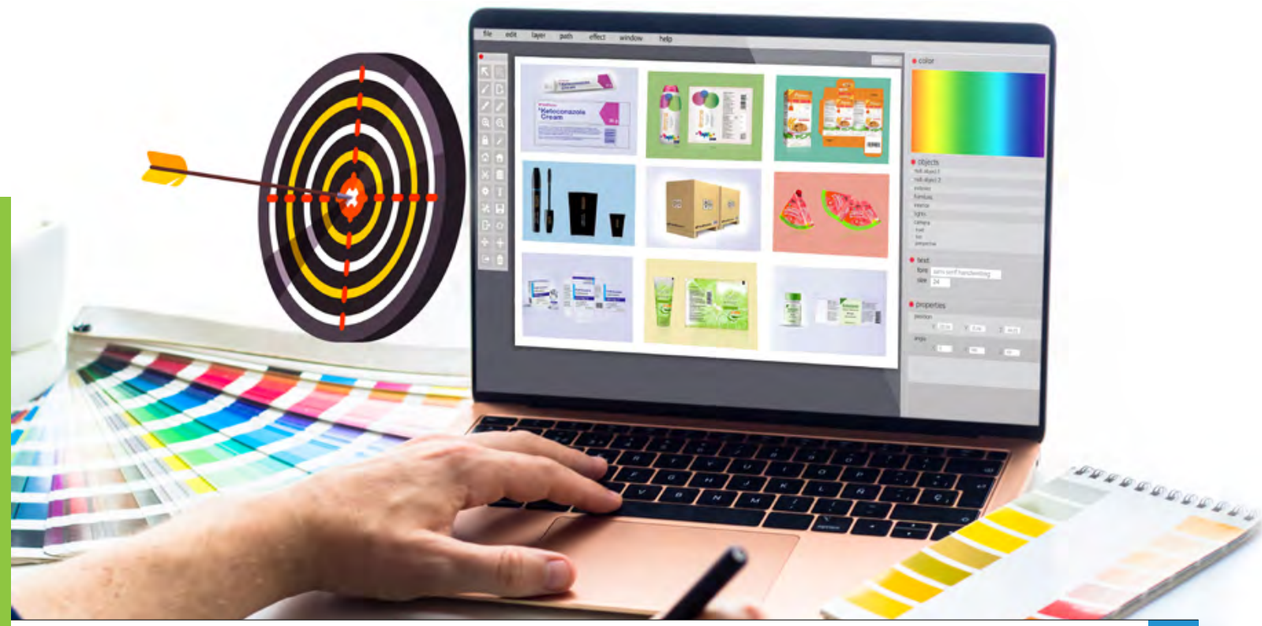
FREYR REGULATORY ARTWORK SERVICES

LEGACY ARTWORK MANAGEMENT System & Challenges

Supply Chain, Packaging, and Artwork Management System - In Life Sciences, any delay or mishap in the latter two segments will affect the former, which results in the product not reaching the markets on time and thus leading to heavy cost burden on the companies. As a crucial step towards smooth functioning of the supply chain, packaging must not only be done at the right time and right place, but also in regulated standards concerning artwork which should project the safety information in a compliant way.

The company's Artwork Management System plays a key role in curtailing the delay in packaging. The system must be in line with the latest technological advancements to keep up with growing Regulatory standards. If companies continue utilizing legacy systems, they may face procedural, functional, and time-bound challenges.

What are they? Here we go...



- Lack of Procedural Standards
- Lack of Centralization in Processes
- Existing Manual Artwork Creation Processes
- No Version-controlled Digital Assets Management
- Electronic Record Keeping of Artworks
- High Costs in Artwork Creation
- Weak Workflows
- Lack of Traceability of Artworks and Approval Processes
- No Timely Notifications and Reminders
- Reworks or Loops in Artworks that May Affect the Delivery Timelines
- Risk of Being Non-compliant
- Not Being Audit Ready
- Missing Process Step(s) related to Electronic Proofreading
- Difficulties in Product Life Cycle Management
- Difficulties in Artwork Coordination with all Stakeholders viz., external partners, i.e., CMOs, printers, PLD partners, artwork vendors, etc.

To steer clear of these challenges, organizations must stay updated and supply their products according to market demands and on time. With ever-growing challenges, companies have to keep working on finding solutions and be competitive in the market. But sometimes, it becomes elusive to get the right approach towards a solution, or you lack the needed resource for finding it.

In such a scenario, to ensure companies align with the new standards as they evolve and be compliant, it requires a comprehensive approach. It should include intelligence-driven gap analysis followed by Regulatory strategy to expedite the procedures in a cost-effective way right from artwork creation to aligning with packaging standards. If you have a process limitation arising from existing Artwork Pack Management System, Freyr can prove to be a strategic partner in laying out the right path ahead.

Would you like to evaluate your existing systems with that of the Freyr solution? Contact us at sales@freyrsolutions.com

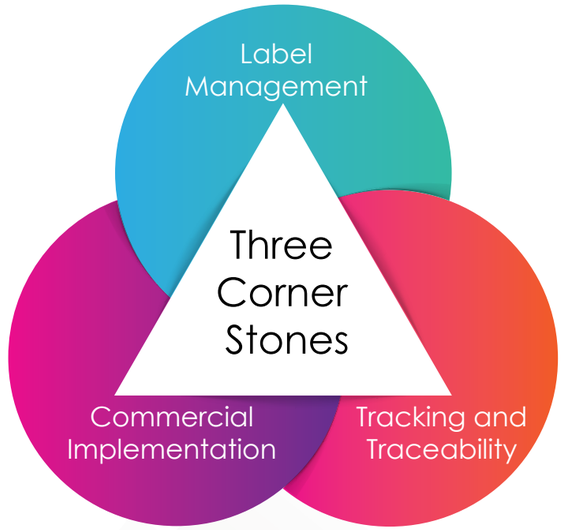
A One-stop Labeling Solution

For Comprehensive and Real-time Content to Carton Traceability

Change is inevitable. If it is in relation to the drug safety data, it should be informed across the channels in real-time for the best of compliance practices and patient safety. To enable organizations keep track of such safety data and label changes in real-time, we bring you:

Freyr LABEL360

As a comprehensive labeling solution, Freyr LABEL 360 is equipped to address all the cornerstones of a label life cycle right from content to carton such as:



Evaluate the Real-time Traceability

Request a Demo

Phone: +1 908 483 7958 | Email: sales@freyrsolutions.com

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Global Medical Device
Regulatory Services

DESIGN HISTORY FILE (DHF) COMPILATION

For Medical Devices

As part of the Safe Medical Device Act in 1990, the FDA mandated the Design History File (DHF), which contains all the development documentation of a medical device/product/diagnostic, which is generated by the design control process. Preparing a DHF as per the Regulatory requirements and withstanding the Regulatory Agencies' scrutiny is a crucial challenge for all the medical devices manufacturers and developers.

However, as long as the respective Regulatory demands are met while preparing the DHF, the documentation processes are seldom scrutinized for efficiency improvements. The best way to get through this is to establish and maintain a DHF that demonstrates the design developed following a particular Regulatory Agency's approved design plan and the requirements. But, how should we go about compiling a DHF? What should it contain, and what are the common pitfalls to avoid? Let's look into them.

Common Challenges: While trying to put together a DHF, organizations often face the below-mentioned challenges.

Paper Formats: Not surprisingly, paper is the common format of a DHF for many companies. Due to voluminous paper files all over, finding the appropriate content for a DHF, missing information or incomplete paperwork may occur as hurdles. And, most importantly, one may come across missing signatures or incomplete vital sections, which hinder the approvals. Kindly note that DHFs must be accurate and updated.

Disorganized Filing: Misfiled and mislead documents cause a big challenge, and it can happen when filing structures are spread across multiple platforms and the naming conventions are not consistent throughout the process. When documents are disorganized, companies find it hard to gather the apt information during audits and inspections, which leads to product recalls.

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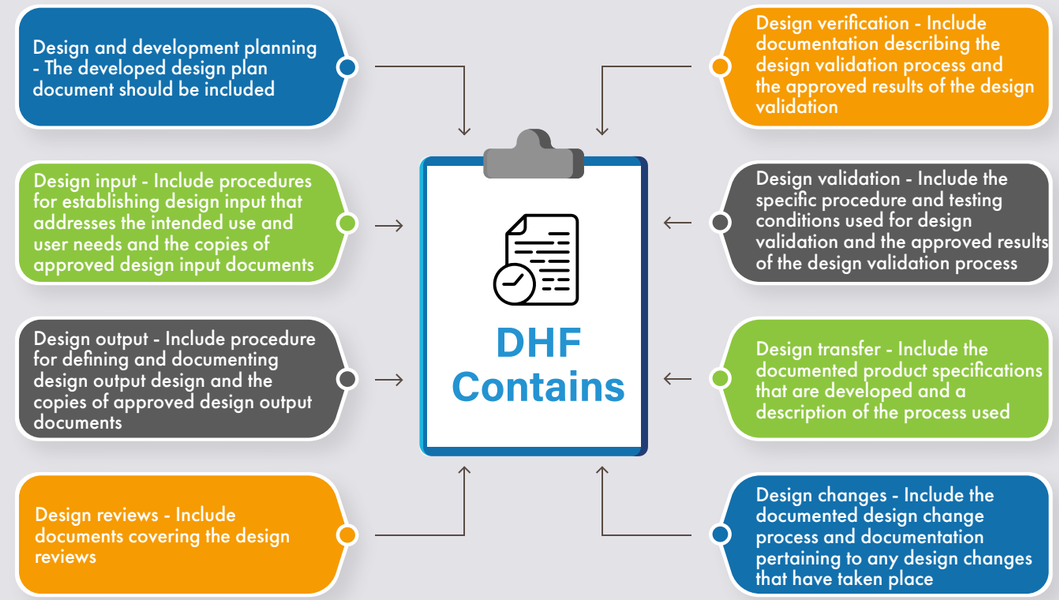
Overloading DHF: In the name of safety and efficacy, companies often tend to add everything possible to the DHF, like cost studies or competitor analysis, which are not necessary. These aspects don't relate to safety and efficacy and neither they meet the end-user's needs. On a real note, a DHF should fit within a project file and must have information on design control activities.

What Should a DHF Contain?

A DHF is inclusive of all the documentation, which is created during the product development phase of a medical device. As a thumb rule, DHFs must be accurate and consistently updated, even beyond the development phase and should contain detailed design and development plans, specifying the design tasks and deliverables for the device. Below listed are the important steps of the design control process and the list of documents that should be included in each step.



On an end note, it is all about keeping the DHFs consistently updated and compiling them as per the Regulatory requirements. Though organizing the DHF together takes a considerable effort than anticipated, the above-mentioned points can give you a better perspective on the compliant DHF process. Avoid Regulatory Authorities warnings and ensure your DHF is organized, accessible and updated. Consult a proven Regulatory expert. Stay informed. Stay compliant.

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Freyr iREADY

The Need for

COMPREHENSIVE COSMETICS INGREDIENTS DATABASE

As we all know, each country has its own set of cosmetic regulations that manufacturers must follow. Many countries have banned several ingredients, while some substances are restricted to a maximum concentration, which makes it difficult for the product manufacturers to market in different countries. During the product formulation, manufacturers must be sure that the substances used in the product formulation are permitted in the targeted country.

At the same time, the Regulatory Authorities are providing stringent guidelines for the use of cosmetic ingredients such as preservatives, colorants, etc., to ensure consumer safety. Here is a quick video to help you understand such Regulatory hurdles.

Lack of knowledge on these distinct and ever-changing cosmetic regulations may slow down product development and market expansion, and sometimes make it difficult for manufacturers to track and keep abreast with them regularly. This may result in non-compliance, missed product launches, product recalls, etc. To avoid such difficulties, it is necessary to adopt a technology-driven Regulatory platform that tracks all the global Regulatory data of ingredients.

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Ideal Features of a Technology-driven Regulatory Platform for Cosmetics Ingredients:

1. It must consist of different categories of ingredients such as approved, restricted or prohibited across global markets.
2. The industry standards for all the ingredients must be provided by Name, Country, Function, INCI and CAS Number.
3. Apart from active ingredients, information on allergens, impurities and residual solvents must be provided, along with the toxicity levels.
4. It should be able to create and assess product formulae and formulations for Regulatory compliance.
5. It should provide acceptability levels of the ingredient use and combinations across global markets.
6. The ingredient platform must be aligned with the latest Regulatory developments and scientific opinions from Health Authorities.

With the above features integrated, an ingredient database shall address your cosmetic product's market-entry challenges by providing accurate information within no time. Start analyzing your ingredient's Regulatory compatibility across the global markets. Initiate it with Freyr iREADY - a comprehensive cosmetics ingredients database.

Center of Excellence
Global Cosmetics Regulatory Services

EUROPEAN GREEN DEAL AND ITS IMPACT

On the Cosmetics Industry

Are you sure that your cosmetic products or their ingredients are safe for the environment? It's alarming to hear climatic challenges faced by the world. Maintaining climatic health is one of the major concerns for every individual, and many revolutionary changes have been adopted across various parts of the world to slow down the effects of climate change. To align with the same, Europe as a continent has initiated the European Green Deal. The proposal is supposed to directly generate a new growth strategy and transform the EU into an eco-friendly and a competitive economy. As per this new proposal, there would be no net emission of greenhouse gases by 2050. The main intention of the European Green Deal is to make the European economy sustainable by focusing on climate neutrality by 2050. The EU cosmetic industry welcomes the Green Deal and its goals but also recognizes the challenges related to the expected outcome.

The initiative directly impacts cosmetic ingredients and packaging. Now, the new approach of companies would be investing in cosmetic raw materials and packaging, which are safe for consumers and sustainable for the environment by design and their lifecycle. Implementation of new environment-friendly activities would be essential. The industry is expecting a holistic assessment based on scientific evidence of the environmental impact caused by cosmetic and personal care products, which are essential for any human being.

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Innovation is certain and the cosmetics industry will continuously deliver products that are safe, compliant and effective. The cosmetics industry itself is very dynamic and it plays a big role while we think about environmental initiatives. Shifting to low or zero greenhouse gas emissions requires radical change throughout all sectors. And it's expected that the cosmetic industry as a whole should be perceived as a great contributor towards the green goal. Well, many of the regulations have subsided as the European Green Deal. It is still under an initial phase, but the Regulatory change in the cosmetics or consumer industry as a whole is about to happen. To know more about the European Green Deal and other Regulatory updates and support get in touch with our experts at Freyr

Center of Excellence
Global Food and Food Supplements Regulatory Services

NUTRITIONAL LABEL UPDATES

For Food and Food Supplements by the US FDA

One of the most recent amendments applied in the year 2020 for the labeling compliance of food and drinks is the update of the Nutritional Facts Panel by the United States Food and Drug Administration. It is solely based on scientific information, new nutrition research, and various other inputs from the public. The amendment has been made by taking certain factors into consideration, most important of which was the ease for a consumer to choose better food and make informed food choices leading to a long and healthy life.

How are these aspects different from the previous labels? Let's have a look at what exactly needs to be updated.

FREYR CONNECT

1 Enlargement of the Serving Size:

The information related to servings, i.e., servings per container and the serving size information will have to be printed in large and in bold format from now onwards. Since, the FDA clearly states that serving size is not a recommendation of how much to eat, although, this change was inspired on having a better understanding of the consumer's eating and drinking patterns.

2 Enlargement of the Calories Font:

For customers to find the number of calories in a much easier way, the FDA now mandates to use larger and bold font while mentioning calories on food and drinks. Calorie requirement varies with respect to sex, age, height, weight, and physical activity level. While one should be aware of the number of calories that are to be consumed in a day, the FDA wants the consumers of America to be aware of the calories they are consuming in the packaged food.

3 Prominent Description of High and Low Percentage of Daily Value:

As per the FDA, the percent Daily Value (%DV) shows how much a nutrient in a serving of food contributes to a total daily diet. A new guidance has been provided which defines what constitutes lower and higher daily values. These are:

- 5% DV or less of a nutrient per serving is considered low
- 20% DV or more of a nutrient per serving is considered high

Also, the footnote at the bottom of the label has also been updated to better explain %DV.

4 Updated Nutrients List:

FDA has made significant additions and deletions in this section.

To talk about deletion, two (02) things have been removed from the nutrients list:

- **Calories from fat** have been removed as research shows the type of fat consumed is more important than the amount.
- **Vitamin A and C** are no longer a mandate on the label since deficiencies of these vitamins are rare in today's world. Hence, these nutrients can be included on a voluntary basis but are not compulsory to be updated on the label as per the guidelines of the FDA.

Additions to the nutritional facts panel include:

Added sugars have been added to the label because consuming high quantity of added sugars can make it hard to meet nutrient needs while staying within calorie limits. Added sugars include sugars that are added during the processing of foods (such as sucrose or dextrose), foods packaged as sweeteners (such as table sugar), sugars from syrups and honey, and sugars from concentrated fruit or vegetable juices.

Vitamin D and potassium are now required to be listed on the label because Americans do not always get the recommended amounts. Diets higher in vitamin D and potassium can reduce the risk of osteoporosis and high blood pressure, respectively.

Original Label

Nutrition Facts
Serving Size 2/3 cup (55g)
Servings Per Container 8

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

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

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

New Label

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

Amount per serving	
Calories	**230**
	% Daily Value*
Total Fat 8g	10%
Saturated Fat 1g	5%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 160mg	7%
Total Carbohydrate 37g	13%
Dietary Fiber 4g	14%
Total Sugars 12g	
Includes 10g Added Sugars	20%
Protein 3g	
Vitamin D 2mcg	10%
Calcium 260mg	20%
Iron 8mg	45%
Potassium 235mg	6%

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

1. The serving size now appears in larger, bold font and some serving sizes have been updated.
2. Calories are now displayed in larger, bolder font.
3. Daily Values have been updated.
4. Added sugars, vitamin D, and potassium are now listed. Manufacturers must declare the amount in addition to percent Daily Value for vitamins and minerals.

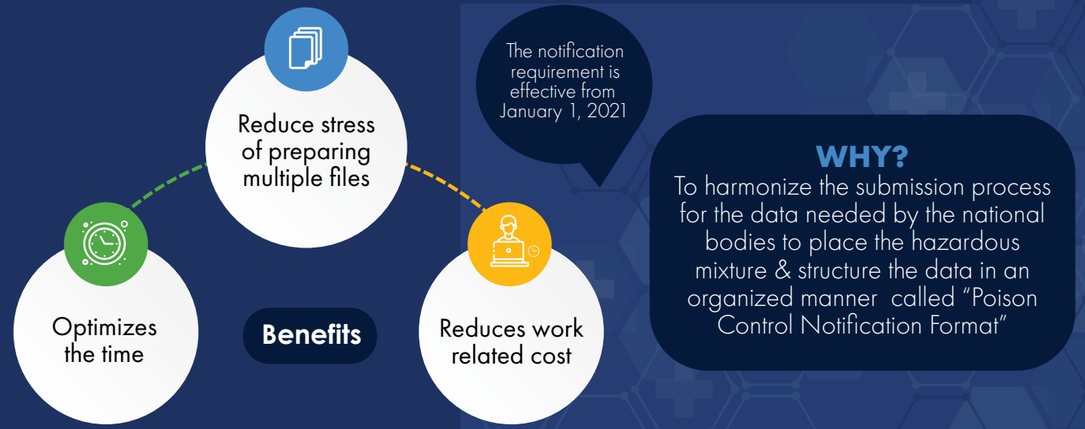
Reference: https://www.fda.gov/media/135197/download

It has happened for the very first time in a span of 20 years that the FDA has updated the nutrition facts label for all packaged food products. While existing manufacturers have time until July 2021 to comply with the updated regulations, the new manufacturers and distributors are already taking care of the label compliance in this regard. As per the FDA, manufacturers with $10 million or more in annual sales were required to update their labels by January 1, 2020; manufacturers with less than $10 million in annual food sales were required to update their labels by January 1, 2021. Have you made your food product's label aligning with the amendment? Evaluate now. Consult an expert.

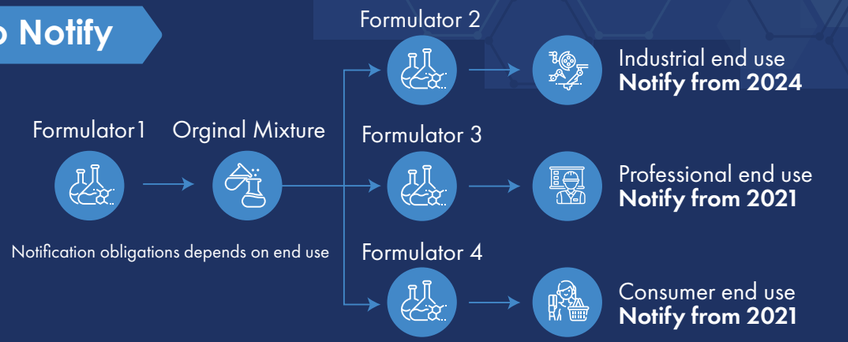
Infographic

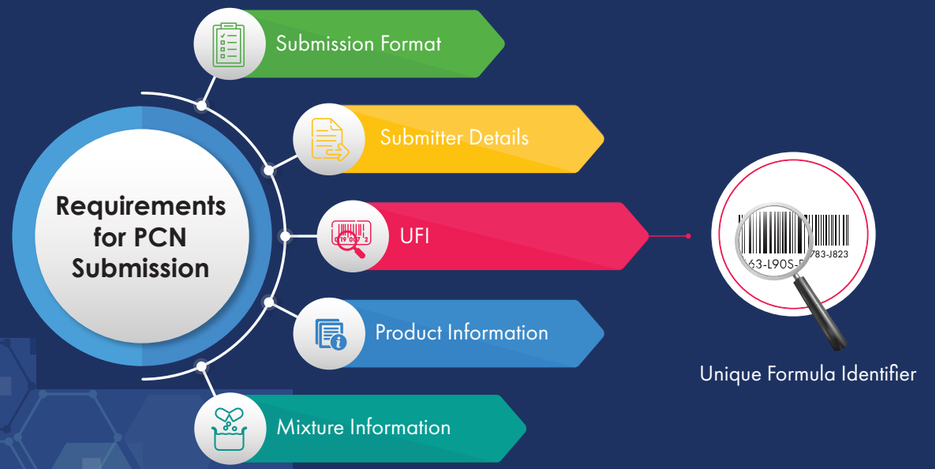
Center of Excellence
Chemicals Safety and Regulatory Affairs

POISON CENTRE NOTIFICATION



When to Notify





For more details, Visit: https://csra.freyrsolutions.com

Center of Excellence
Chemicals Safety and Regulatory Affairs

GB BPR TRANSITION PERIOD
And Deadlines

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

Here are a few updates on the GB BPR

Table 1

Authorization	Authorization Holder must be Established in	Deadlines
Great Britain	UK (Great Britain or NI)	January 01, 2022
Northern Ireland	NI/EU/EEA/Switzerland	January 01, 2021
EU/EEA	NI/EU/EEA/Switzerland	January 01, 2021

Ref: https://www.youtube.com/watch?v=BIremnIINIs&feature=youtu.be

» Ongoing active substance approvals and product authorizations will remain valid in GB and Northern Ireland (NI) until their expiry dates. (subject to establishment requirements)

» NI continues to follow the EU

» The EU and the UK negotiations have no impact on the biocides

Establishment Rules:

» GB BPR requires authorization holders to be established in the UK (including NI)

» EU BPR requires authorization holders to be established in the EU/EEA. An NI authorization holder must be established in the EU/EEA/NI

Consequences of Establishment Rules:

» To change the authorization, applicants must submit an 'Admin change' application available in the Health and Safety Executive (HSE) website.

» One (01) year transition period will be provided for products that are already authorized in the GB market.

» Timelines will be provided by the HSE for resubmissions in GB.

» Authorization for new products will be provided based on the applications.

» For market-entry in both GB and NI, – two (02) sets of certificates are issued with both the addresses mentioned on the product label.

Transitional Arrangements:

» Ongoing active substances and product applications must be resubmitted to the HSE by:
- March 31, 2021, where the UK stands as the lead
- June 29, 2021, where the UK is not the lead

» A new application form from the HSE website must be used

» Highlight and justify the data gaps

» No automatic non-approval decisions

Routes to the UK Market for Products:

For GB:

» Apply to the HSE as per the GB BPR or

» Apply to the HSE via unfettered access (once the product is authorized in NI)

For NI:

» Apply to the HSE as per the EU BPR (national or MR) or

» Apply to the ECHA for a Union Authorization under the EU BPR

Submissions or Resubmissions of Applications and Dossiers to GB:

» Download the relevant application from the HSE website

» Fill in the form and submit to the HSE via eMail

» An upload link with a validity of five (05) days will be sent, where you must upload the files specific to the application

Hence, authorization holders must be established as per Table 1 and be aware of the deadlines issued by the HSE. Adhering to the Regulatory deadlines is quite complex and requires clear-cut knowledge of the regional Regulatory frameworks. Consult an expert for compliance. Stay informed. Stay updated.

DO YOU KNOW?

The Clock is Ticking!
Start Aligning with the **EU IVDR Requirements and Stay Compliant**

Compliance Deadline - May 26, 2022

The UK MHRA Compliance Countdown
Has Started for the Manufacturers of

- Class IIB Non-Implantable Medical Devices
- Class IIA Medical Devices
- IVD List B Products
- Self-Test IVDs

Article 45 of the CLP Regulation Describes the Notification Obligations to Place Hazardous Chemical Mixtures in the EU

- For mixtures classified as hazardous for **consumer use and professional use** products - deadline ended on January 01, 2021. Comply with the new harmonized PCN format.
- Mixtures intended for **industrial use** must comply from **January 01, 2024.**
- Mixtures that are already placed in the market and notified under the national legislation must comply from **January 01, 2025.**

Align with the Mandatory Deadlines Now! **CONSULT**

FREYR CONNECT

Center of Excellence
Chemicals Safety and Regulatory Affairs

RISK ASSESSMENT OF CHEMICALS in the US and Canada

With a dramatic increase in chemicals in recent years, many new compounds and mixtures are entering the global markets. These compounds might be harmful to humans and the environment as the toxicological properties are not previously studied. Therefore, a Risk Assessment of Chemicals is performed to understand the nature, level of toxicity, and potential adverse effects on human health and the environment. In developed countries, it is the foundation of Regulatory decisions for manufacturing and importing chemicals such as industrial chemicals, pharmaceuticals, cosmetics, food additives, and pesticides.

Let us understand the developed countries (such as the USA and Canada) Risk Assessment methodologies.

The USA

Amended by the Frank R. Lautenberg Chemical Safety for the 21 st Century Act, Toxic Substances Control Act (TSCA) requires the United States Environmental Protection Agency (EPA) to evaluate the safety of existing chemicals. How can manufacturers evaluate safety? Here is a stage wise approach that EPA follows for the chemical risk evaluation process:

Prioritization | Risk evaluation | Risk management

The following graphic provides an overview of the stages for chemical safety

Prioritization

Prioritization is the first step in EPA's process for evaluating the safety of existing chemicals. It is a risk-based screening process for assigning chemical substances as either high-priority substances or low-priority substances. TSCA requires the EPA to give specific preferences such as hazard exposure, persistence, and bioaccumulation to prioritize chemicals on the 2014 TSCA Work Plan. If high-priority substances are found, then the EPA will initiate a TSCA risk evaluation of the substance.

Low-priority substances are taken out of scope for further assessment at this time. It provides public notice of the chemical substances' hazard and/or exposure potential that is anticipated to be low or non-existent. It also provides insight into chemical substances that do not need additional evaluation and risk management.

Risk Evaluation

Risk evaluation is the second step in the EPA's process for evaluating the safety of existing chemicals. If the EPA designates a chemical as a high-priority substance, the chemical moves immediately to the risk evaluation phase. The EPA determines whether the chemical presents an unreasonable risk to human health or the environment in this phase. TSCA prohibits the EPA from considering non-risk factors (such as costs, benefits) during risk evaluation. This includes risks to subpopulations such as children and workers, who may be at more significant risks than the general population. The risk evaluation process has the following components:

» a scope document with information on the risk evaluation

» hazard and exposure assessments and risk characterization

» a risk determination affirming whether a chemical substance presents an unreasonable risk to health or the environment

Risk Management

Risk management is the third step in EPA's existing chemicals process. If the EPA determines the chemical presence is at unreasonable risk to health or the environment, the chemical will be immediately moved to the risk management action. During this process, the EPA has numerous options for Regulatory restrictions to reduce risk, including requirements regarding the use of chemicals in the products, labeling requirements, use restrictions, phase-outs, or bans on the use of the chemical in products.

Hence, companies who wish to manufacture or market their chemical-based products in the US must carefully follow the risk assessment process.

Canada

Risk Assessment of Chemical Substances in Canada is performed under the purview of Canada's Ministry of Health and the Ministry of the Environment. The risks posed by chemical substances are determined by the scientific evaluations or risk assessments conducted under the Canadian Environmental Protection Act, 1999 (CEPA 1999). It helps to determine whether risks are resulting from the nature of the substance or the extent of exposure of the substance to the Canadians or the environment. Also, it identifies whether or not a risk management measure is needed.

Under section 64 - Part 5 of CEPA 1999, any substance that enters/may enter the environment in a quantity/concentration is considered toxic under the following conditions:

» The substances have/may have an immediate/long-term harmful effect on the biological diversity or the environment.

» The substances constitute/may constitute a threat to the environment on which life depends.

» The substances constitute/may constitute a risk to human life or health.

If a substance is confirmed to be toxic or capable of becoming toxic, the risk assessment is considered to prevent or control the identified risks.

Risk Assessment for Existing Substances

Collection of the information on each substance/substance group is the first step in the risk assessment process. The information must comprise chemical properties, manufactured/imported quantity, concentrations in the environment, and the nature of exposure. Expert and stakeholder engagement is crucial throughout the process. The assessment reports must undergo external peer review and/or consultation involving experts, and the draft screening assessments are subject to a 60-day public comment period. While all the comments are considered, the conclusion of screening assessments will be provided by Health Canada and Environment & Climate Change Canada.

Risk Assessment for New Substances

All new substances must undergo an ecological and human health risk assessment before manufacturing/importing into Canada. The process begins with a pre-manufacture/pre-import notification of the substance. It means - any person intending to import or manufacture a new substance in Canada must submit a package containing all the information prescribed in the New Substances Notification Regulations. In general, the risk assessments of new substances and existing substances are conducted similarly.

In a nutshell, risk management is a global Regulatory requirement. Hence, the companies must mitigate risks and ensure maximum safety and effectiveness. If you are looking for a compliant and effective risk management system, reach out to a local expert team of Regulatory consultants.

Center of Excellence
Publishing & Submissions

HOW TO USE DMF CONTENT TO SUPPORT Your Application To The FDA

A drug master file (DMF) is a voluntary Regulatory application submitted to the US FDA at the discretion of the DMF holder to assist its customers. A DMF is used to provide confidential detailed information about facilities, processes, or articles used in manufacturing, processing, packaging, and storing one or more active pharmaceutical ingredients (APIs) and/or human drugs in the absence of relevant information about the drug substance, drug product, and/or container closure. A DMF is not an alternate Regulatory submission for an IND, an NDA, an ANDA, another DMF, an export application, or amendments and supplements to any of the mentioned, but can be used to support these applications.

Other countries/regions have their own versions (for example, Europe's active substance master file procedure and Japan's voluntary master file system), but this article explains DMF content requirements and how the application is prepared as a dossier and submitted to the US FDA In India, the FDA's process is generally used, unless you are a foreign manufacturer.

Each DMF submission should constitute:

» Transmittal letters - includes the type of the submission, name, address, and signature of the applicant or holder in the case of an original submission. For amendments, the DMF number, type, and updates to the original submission should be submitted.

» Administrative information contains the statement of commitment, name and address of the DMF holder or applicant and the manufacturing/processing facility, and updated sections in the case of amendments.

» Information in the DMF must be in English.

FREYR CONNECT

There are five types of DMFs

» **Type I DMF (phased out since July 2000):** Manufacturing site, facilities, operating procedures, and personnel. It is generally recommended for an applicant outside the United States to aid the FDA in carrying out manufacturing site inspections. Unless the applicant is not registered or inspected properly, this type of DMF need not describe the domestic facilities. In addition, standard procedures of the equipment and process should be clearly mentioned.

» **Type II DMF: Dr**ug substance (APIs), drug substance intermediates and material used in their preparation, or drug product. A Type II DMF also covers dosage form for the drugs manufactured under contract for another company that would file an ANDA.

» **Type III DMF: Pa**ckaging materials, from bottles and caps to PVC resin used in their manufacture, must be covered in a Type III DMF or other FDA document such as an NDA.

» **Type IV DMF: Ex**cipient, colorant, flavor, essence, or material used in their preparation. Excipients are inactive chemical substances used in the preparation of a tablet.

» **Type V DMF: Th**e FDA accepted reference information that is not included in the other types of DMFs.

The most common type of DMF is Type II, followed by Type III.

What Else To File Along With Your DMF Submission?

Type II, III, and IV DMFs should include:

» A company commitment stating that its facilities will be operated in accordance with environmental laws.

» Information related to the stability data, study design, and interpretation.

» A letter of authorization permitting the FDA to reference the DMF before the review of DMF information in favor of an application. This letter should include the applicant's name and address, date, DMF number, products reference section, and page numbers.

The DMF holder should also send a copy of the same to the affected applicant, sponsor, or other DMF holder who is authorized to incorporate by reference the specific information contained in the DMF.

All DMF submissions since May 5, 2018, other than Type III DMFs, are being done using an electronic Common Technical Document (CTD) (eCTD). eCTD is a standard format used for submitting applications, amendments, supplements, and reports to the FDA through the Electronic Submissions Gateway (ESG) by choosing "CDER" as the center and "eCTD" as the format. For Type III DMFs, this requirement has been effective since May 5, 2020. The eCTD submissions should be in the FDA's accepted forms and must include electronic signatures to enable automated processing of the submission.

How The FDA Evaluates Your DMF Submission?

A DMF goes through two stages of evaluation before it is submitted for review. First, the FDA assesses the content of DMF and whether its requirements are met. Once the FDA determines that the eDMF is acceptable, it will then undergo an administrative review as discussed above. The applicant will be informed if the DMF is not acceptable due to technical reasons. The holder must then satisfactorily respond to any deficiencies for the DMF to proceed to an administrative review, which will be conducted by the DMF staff in the Office of Pharmaceutical Quality (OPQ). If the DMF passes through the administrative review and is found to be acceptable, OPQ sends an acknowledgement letter, at which point the DMF is available for review of its technical content. At the same time, OPQ sends an Administrative Filing Issues (AFI) letter if the DMF is not accepted due to lack of administrative information. The holder must respond adequately for the DMF to be available for review of the technical content. The time frame for this could be from two to three weeks. DMF data and information availability to the public is ascertained under 21 CFR Part 20, 21 CFR 314.420(e), and 21 CFR 314.430. A DMF number will be provided only on receipt of complete and adequate administrative information of the holder or applicant.

How To Tackle The Annual Report?

The status of a DMF is "active" when it is acceptable by the FDA from an administrative point of view and "inactive" when it has been closed either by the holder or by the FDA. The DMF holder should provide an annual report to the FDA on the anniversary date of the original submission. In the meantime, if there are no updates, then the holder should provide the DMF content as current in the annual report. Failure to update the DMF can cause delays in the FDA's review of the pending NDA, IND, ANDA, or any amendment or supplement to such application; hence, the FDA can initiate procedures for closure of the DMF.

Conclusion

The drug master file is filed in support of various applications while launching drugs in the given market. The DMF provides information on Chemistry, Manufacturing and Controls (CMCs) on drug substance, drug product, and intermediates used in their preparations. A DMF helps the holder company shorten the IND, NDA, ANDA, or export application process by reducing the total number of review cycles and increasing the chances of approval in the first cycle. Also, the DMF supports Regulatory requirements for a drug to help prove its quality, safety, and efficacy.

This article was first published by: OUTSOURCED PHARMA

Webinars

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 the following topics:

01 **India's New Cosmetic Rules 2020 Decoding the Regulatory Framework**

Know More

Regulatory Perspective of Complementary Medicines in Australia 02

Center of Excellence
Global Cosmetics Regulatory Services

ANIMAL-DERIVED INGREDIENTS IN COSMETICS & Regulatory Requirements

The use of animal-derived constituents was pioneered at the beginning of the 18th century and slowly gained pace soon after advancing science and technology. Earlier, the application of animal-derived constituents was constrained to a few products such as leather products, colorants, cosmetics, etc. However, the scope of animal-derived constituents has also been extended to homecare, healthcare product formulations, and modern medicine. For example, common medicines contain lactose, gelatine, and magnesium stearate derived from animals.

Until the recent past, the regulations governing the animal-derived constituents were in the infancy stage. Groundbreaking development concerning the regulations can be attributed to two (02) significant dimensions. One, owing to the health risk emanated from the animal-derived constituents, and the other from religious and secular concerns. Studies show that animal-derived materials not only harbor but also support the growth of pathogens. Contaminated drug ingredients can cause potential health risks that may affect various patient populations, including immune-compromised patients and healthy people of all ages.

Halal Compliance

The term "Halal" is used to designate food that is permissible according to Islamic law. Halal is principally concerned with meat products. Thus, products containing pork (e.g. pork gelatin) and other animal-derived constituents are considered not Halal. However, alcohol is also not permitted, making it not Halal. Halal is mostly recognized for its food application, but it also applies to cosmetics, pharmaceuticals, and even business practices. For cosmetics, some products such as lipsticks and alcohol-based perfumes are particularly concerned for Halal-seeking consumers. Halal compliance is necessary while exporting to the Gulf Cooperation Council (GCC), Malaysia, Indonesia, and the Middle East. It also has significance all over the world. One of the significant challenges faced by cosmetic manufacturers is the practice of different Halal standards for different countries – some of the ingredients that may be Halal in some countries are either "not permitted" or "questionable" in others. GCC countries, which include the UAE, Saudi Arabia, Oman, Qatar, Bahrain, Kuwait, and Yemen, have harmonized their Halal standards. The significance of obtaining Halal Certification has intensified more than ever with the increasing demand for Halal products across the globe.

Kosher Certification

'Kosher' is used to describe food that complies with strict dietary standards of the traditional Jewish law. In 2017, the global market for kosher food was estimated to be $24 billion. It is projected to grow at a CAGR of 11.6% from 2017 to 2025, reaching nearly $60 billion by 2025. Kosher Certification Agency is the organization that grants a hechsher to beverages, ingredients, packaged foods, and certain materials, as well as food-service providers and facilities in which kosher food is prepared or served. Kosher also applies to non-food products such as cleaning products, food containers, water softeners, packaging, and cosmetics. To obtain Kosher certification, each ingredient, food additive, and processing aid used in its production must also be Kosher certified/approved. There are annual Kosher certificates that are valid for a year from the date issued. Kosher-certified products are of particular importance to the Jewish population, and many companies consider Kosher certification while exporting to countries like Israel, the USA, and the UK.

BSE/TSE Certificate

TSE/BSE free certification is one of the essential Regulatory requirements for animal-derived ingredients. Transmissible Spongiform Encephalopathy (TSE) is a family of diseases occurring in men and animals and is characterized by the degeneration of brain tissue, giving a sponge-like appearance that leads to fatality. These include conditions like Bovine Spongiform Encephalopathy (BSE), also known as mad cow disease, Scrapie in sheep, and Creutzfeldt-Jakob disease (CJD) in humans. The nature of the infectious agent that causes these diseases are unknown. However, as per the most accepted theory, Prion, a modified form of a normal cell protein, is considered an agent for this disease.

TSE/BSE certification is required for the ingredients derived from animals and could potentially be contaminated with TSE. TSE/BSE compliance certificate ensures that the animal-derived ingredients are free from the TSE/BSE and carry low risk. The EU regulation (EC) No 999/2001 covers the specification and requirements related to the TSE.

Majorly used animal-derived ingredients in cosmetics include Alanine, Lactic Acid, Honey, Beeswax, Cod Liver Oil, Cystine, Gelatin, Glycerin, Hyaluronic Acid, Keratin, Linoleic Acid, Musk, Polysorbates, Silk, Retinol, etc. However, in recent times, efforts are being taken to replace them with suitable alternatives.

Center of Excellence
Global Pharmaceutical Regulatory Services

COMPLEMENTARY MEDICINE APPROVAL In Australia

Have we ever realized various processes to consummate the sustainability of the products we manufacture? Won't it be cumbersome to understand the depth of different market regulations for Food products? Manufactures/Suppliers will have to realize that the Australian Regulatory requirements are pretty different from other countries for food products, otherwise referred to as complementary medicines by the Therapeutic Goods Administration (TGA). In Australia, the Food/Dietary Supplements also can be defined as products, which have nutritional ingredients such as herbs, vitamins, etc., and are often regulated by Therapeutic Goods Administration, and are referred to as Complementary Medicine.

What are Complementary Medicines?

According to the TGA, **Complementary Medicine** means a therapeutic good consisting wholly or principally of one or more designated active ingredients, each of which has an established identity and traditional use.

The salient points to consider are as follows:

1. Complementary Medicines are regulated as medicines under the Therapeutic Goods Act (1989)
2. These are generally available for use in self-medication by consumers
3. A majority of complementary medicines are indicated for the relief of symptoms of minor, self-limiting conditions. Many are indicated for maintaining health and well-being, or the promotion or enhancement of health.

FREYR CONNECT

To apply for complementary medicine in the in Australia, a particular entity (manufacturer or distributor) is contemplated through various basic procedures for product approval. It involves checking if the active ingredient has been registered in the 26BB legislative list of the TGA. Also, it is mandatory to hold the evidence for any therapeutic claims of the products along with the quality check of the finished product and the safety data of the ingredients of the finished product.

There are two (02) primary pathways for complementary medicines to be registered with the TGA:

1 The Listing (L-process)

The listing process consists of ingredients that are of low risk, where the indications should only be specific for use in listed medicine and the import of the product should not be restricted. Generally, for the Listing process, the manufacturer/distributor should get the online GMP clearance for the manufacturing site before submitting the product details and health benefit claims. The listing process generally takes two (02) weeks of time if the manufacturers' GMP certificate is approved by the TGA.

2 Registration (R-process)

On the other hand, the Registration process is applicable if the complementary medicine consists of a novel ingredient, which is not in the TGA-approved ingredient database. The product should contain therapeutic benefit claims which are not under the TGA-approved list. Almost six to twelve (06-12) months' minimum timeline is considered depending upon the complexity of the product. The dossier to be submitted in the registration process must be in CTD format containing information about the manufacturing process and site, quality control and clinical evidence to substantiate the claimed therapeutic / health benefits.

To market a food / dietary supplement in Australia, the manufacturer must have a local presence, with a minimum requirement of insurance policy to cover the liability of 20 Million people and a pharmacovigilance test, before selling/ marketing the finished product in Australia. Alerts on specific products are made due to the involvement of the Regulatory bodies to create a safe and compliant environment so that the stakeholders maintaining the quantum of responsibility align with the future of the world.

Keeping abreast with the various Regulatory Health Authorities can sometimes be challenging. To get more Regulatory updates and assistance contact Freyr.

Freyr What Is..?

WHAT IS B-GMP?

B-GMP stands for Brazilian Good Manufacturing Practices, the standards set by the National Agency of Health Surveillance (ANVISA), the Health Agency regulating the medical devices in Brazil. All medical device manufacturers marketing their devices in Brazil shall comply with the resolutions RDC 16/2013, the BGMP regulations.

Do All Devices Require a B-GMP Certificate?

As per the resolution RDC 15/2014, medical devices and in-vitro diagnostic devices falling under Class III and IV should comply with the B-GMP regulations and shall possess the Brazilian Good Manufacturing Practice (B-GMP) certificate for approval and commercialization of devices in Brazil. Class I and Class II devices are exempted from the B-GMP certification, but they must comply with the medical device GMP requirements set by the Brazilian Agency.

The Normative Instruction 8/2013 requires that the manufacturers ensure that the stakeholders (such as importers and distributors) comply with the medical device GMP requirements that are relevant to them. In case of an Original Equipment Manufacturer (OEM) or contract manufacturing business models, the Resolution RDC 183/2017 requires that the legal and contract manufacturers of final products or SaMDs and the site that releases the final product are required to have B-GMP certificates.

How Can One Obtain a B-GMP Certificate?

The Resolution RDC 183/2017 provides administrative procedure to grant ANVISA GMP certificate to device manufacturers, to be used for device registration. ANVISA may issue the medical device GMP certification (B-GMP Certificate) under any of the below situations, only after a thorough assessment of submitted documents:

- Manufacturer presents a valid audit report issued under the ANVISA recognized programs such as Medical Device Single Audit Program (MDSAP)
- Manufacturer presents a valid B-GMP audit report issued by the IMDRF member country or the auditing authorities accredited by these member countries
- Manufacturer presents a valid audit report issued by the ANVISA recognized third party auditing organizations
- Manufacturer submits inspection reports issued by the Health Authorities of other countries under certain agreements
- ANVISA performs a detailed risk analysis to assess the need for an on-site inspection before granting the B-GMP. The risk analysis is based on device risk, indication of use, device technology and complexity of the manufacturing process

Prior to the release of Resolution RDC 183/2017, the ANVISA suggests all foreign manufacturers to undergo on-site inspection for issuing a B-GMP certificate.

How Can One Leverage MDSAP Certification?

As a member of MDSAP, ANVISA grants B-GMP certificates after analyzing the audit reports issued by Auditing Organizations that are accredited under the MDSAP program. The reports should comply with the Brazilian regulations - RDC 16/2013. MDSAP should provide a surveillance report in special circumstances. ANVISA does not issue any Brazilian GMP certification to the manufacturing sites with Grade 4 and 5 Non – conformities. However, the sites with grades 1-3 non-conformity have to provide a detailed action plan to obtain the B-GMP certificate.

Given below are the statistics of B-GMP certificates issued by leveraging the MDSAP certificates issued through MDSAP program and those issued after an on-site inspection by the ANVISA.

Certificates issued by MDSAP on audits	On-site Inspections conducted by ANVISA
38 Certificates Issued in 2017 (4.7%)	238 Inspection (2017)
107 Certificates Issued in 2018 (19.3%)	110 Inspections (2018)
321 Certificates Issued in 2019 (48.7%)	84 Inspections (2019)

It is inferred from the above statistics that the ANVISA is relying on MDSAP program for issuing the MDSAP certification.

What is the Application Process for a B-GMP Certificate?

The process for obtaining a B-GMP certificate is detailed below -

- Request has to be made by Brazilian Registration Holder (BRH) for B-GMP certification. Manufacturer presents a valid B-GMP audit report issued by the IMDRF member country or the auditing authorities accredited by these member countries
- BRH can submit the certificates issued by the MDSAP or audit reports issued by the third-party authorized organizations

» ANVISA evaluates the reports issued by the MDSAP and other organizations, after the assessment the Agency issues a B-GMP certificate. BRH can submit the certificates issued by the MDSAP or audit reports issued by the third-party authorized organizations

» The obtained B-GMP certificate is submitted to the ANVISA along with the device dossier file for device registration

» Once the registration is completed, approved medical devices are legally commercialized in the Brazilian market

What are the Documents to be Submitted for B-GMP Certification?

The Brazilian Registration Holder (BRH) shall submit a request for B-GMP certificate on the manufacturer's behalf. The request should include-

» A Duly filled B-GMP certification request form. The form is available on the ANVISA's official website and requires the manufacturer to include device and manufacturing site information

» Proof of payment of B-GMP certification

» Quality manual

» List of devices produced at the manufacturing site in scope and the indication of devices intended to be exported into the Brazilian market

» Manufacturing process flow chart

» Manufacturing site layout

» INMETRO Certificate in case of electromedical devices

» Marketing information of the devices in scope – the countries to which the devices are exported and the evidence of registration in these countries

» List of all inspections in the past three (03) years along with the details of non-conformities or Regulatory actions

» Copy of the most recent audit report from the respective country's Health Agency.

» Copy of the most recent audit report issued by the IMDRF country or the auditing organization accredited by these countries or the third party auditing organizations recognized by the ANVISA

What is the Validity of a B-GMP Certificate?

The B-GMP certificate, issued by ANVISA, after a detailed scrutiny, is valid for two (02) years and it shall be renewed once in every two (02) years. Each Brazil GMP certificate is specific to a BRH-manufacturer. A manufacturer appointing a new BRH for a different product shall obtain another B-GMP certificate, to be requested by a new BRH.

Therefore, to market the medical devices in the Brazilian market, manufacturers must be aware of the here above mentioned B-GMP certification process set by the ANVISA. Are you looking for a BGMP certification for your medical device? Seek a Regulatory expert's assistance right now.

The Customer: Switzerland-based, Leading Medical Nutritional Company

Project Details: Product Compliance Services in the USA

The Customer: Sweden-based, Leading Chemicals Company

Project Details: Biocidal Product Registration in Albania, Bosnia & Herzegovina, Kosovo, Montenegro and Macedonia.

The Customer: UK-based, Multinational Consumer Goods Manufacturing Company

Project Details: Biocidal Products Registrations in Greece, Cyprus, Czech Republic, Slovakia, Hungary, Romania & Poland Herzegovina, Kosovo, Montenegro and Macedonia.

The Customer: UK-based, Multinational Pharmaceuticals Company

Project Details: Ad-Promo Material Regulatory Review

The Customer: UK-based, Multinational Consumer Goods Company

Project Details: Regulatory Formulation Assessment

The Customer: Germany-based, Multinational Pharmaceutical and Life Sciences Company

Project Details: Labeling and Artwork Services

The Customer: Germany-based, Innovative Medical Technology Company

Project Details: Products Classification, Manufacturing Site Registration, Product Registration in Oman, Bahrain, UAE & Kuwait and LR Services

The Customer: Australia-based, Global Cosmetics Company

Project Details: Product Compliance Check for Indonesia Market

The Customer: UK-based, Oncology Therapeutics Company

Project Details: RI and Development of Reports & Positioning Paper

The Customer: US-based, Global Male Grooming and Hygiene Products Company/US-based, Leading Cosmetics Company

Project Details: End-to-End Registration Support in Singapore

The Customer: UK-based, Leading Dietary Supplements Company

Project Details: Label Assessment Service for Singapore

The Customer: US-based, Global Generic Pharmaceuticals Company

Project Details: End-to-End ANDA Services

The Customer: Switzerland-based, World's Leading Consumer Goods Company

Project Details: Formulation Review

The Customer: UK-based, Leading Virtual Ward Healthcare Company

Project Details: Gap Assessment As Per the UK MDR

The Customer: Germany-based, Pharmaceuticals Distributing Company

Project Details: MA Transfer, LR Support and Cancellation of MAH

The Customer: UK-based, Leading Medical Device Distributing Company

Project Details: CE Accreditation and Gap Analysis

The Customer: NewZealand-based, Leading Natural Oral Care Products Company

Project Details: Regulatory Support in the EU

The Customer: Canada-based, Leading Biotechnology Company

Project Details: Regulatory Support For Product Launch in Mexico

The Customer: US-based, Leading Personal Care Products Company

Project Details: Regulatory Support For Product Launch in the UK and the EU

The Customer: Canada-based, Leading Hair Care Products Company

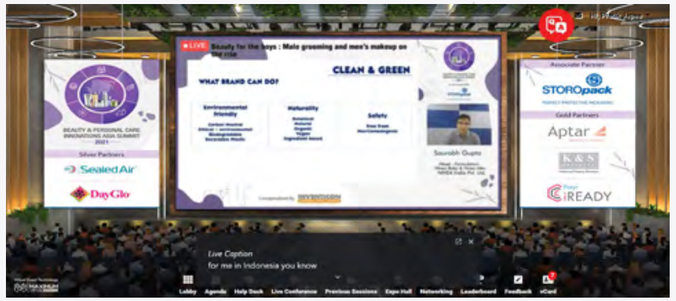
Project Details: Regulatory Support For Product Launch in the EU & the UK

Industry Events 2021

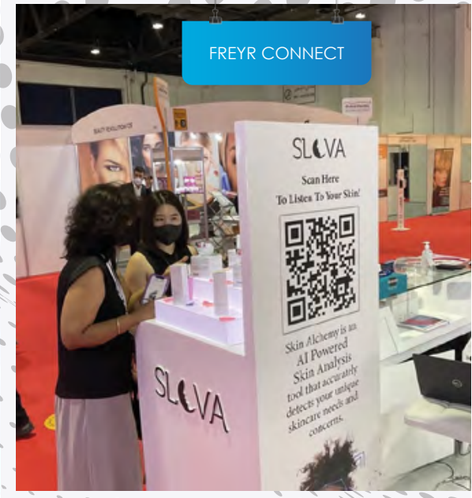
This quarter, we had a great experience and opportunity to exhibit our next-generation digital assessments platform – Freyr iREADY at Dubai Derma and at Beauty and Personal Care Innovations Summit 2021.

It was informative and exciting journey all through the events. Below provided are a few tete-a-tete moments from the event that we cherish forever.

B&PCI Summit



Dubai Derma



Case Study 1

Center of Excellence
Global Medical Device Regulatory Services

REMOTE INTERNAL AUDIT OF QMS SYSTEMS FOR 21 CFR 820 AND ISO 13485:2016 COMPLIANCE

Client
Global leader of myopia management technologies

Solution
Remote Desktop Internal Audit of QMS systems for 21 CFR 820 and ISO 13485:2016 compliance

Manufacturing site
Florida, USA

Geography
USA

Therapeutic Area / Indication
Myopia

BENEFIT HIGHLIGHTS

- Streamlined process with submission ready documents
- On-time delivery of the reports
- Cost advantage

FREYR CONNECT

Business Imperatives

- The client is a US based leading Medical Device manufacturer of advanced technologies used in ophthalmology
- The device in scope is indicated for management of myopia
- The internal audit of QMS systems for it's manufacturing site in Florida is due as per the organization's Quality Management Systems
- Client wanted to outsource the auditing activities to an external service provider

Challenges

- Due to current global scenario of COVID-19 pandemic, the audits had to be conducted remotely
- A strategy had to be formulated for internal audit preparation, remote auditing and audit reporting as per the defined regulations in scope

Freyr Solutions & Services

- Audit of Client's QMS systems for 21 CFR 820 regulations and ISO 13485:2016 Compliance - Audit requirements as per the EU MDR
- Networking platform to facilitate remote desktop audit
- Freyr supported the client through a three stepped approach for carrying out remote internal QMS audits

Audit Preparation: Framing of audit schedule and submission of document checklist to client for desktop review and internal audit preparation

Remote Audit: 5-day Remote audit of client QMS Systems as per the defined regulations in scope

Audit Reporting: Submission of Audit report along with the suggested remediation plan

Client Benefits

- Regulatory support by a strategic phase wise approach for carrying out internal QMS audits
- Successful preparation, conduction and reporting of remote internal QMS audits with compliant regulations
- Certified auditors for carrying out the required services
- Audit findings and remediation plans for observations around the audits

Center of Excellence

Pharmacovigilance

ON-TIME LITERATURE MONITORING SERVICES IN THE USA

Client
Pharmaceuticals/Consumer product company

Health Authority
US FDA

Freyr CoE/Product
Pharmacovigilance

Service Offering
Literature monitoring

Industry
Pharmaceutical

Service Region
USA

Client Location
South Korea

Therapeutic Area/Indication
Multiple

BENEFIT HIGHLIGHTS

- Streamlined process with submission ready documents
- On-time delivery of the reports
- Cost advantage

FREYR CONNECT

Business Imperatives

- The client approached Freyr to perform the literature monitoring

Challenges

- Lack of clarity on actual Regulatory requirements and process flow to be followed by the client
- Stringent timelines

Freyr Solutions & Services

- High quality and first-time right document delivery
- Streamlining the process
- Excellent quality control process
- Proper planning and execution

Client Benefits

- Timely delivery
- Managed one-time peak activity by contractors
- High quality and compliance
- Decreased costs

SUNITHA ANUMULA

One of The 10 Most Impactful Women in Technology

With 19+ years of experience in Pharma services, consulting, IT and ITES industry, at various leadership positions, Sunitha Anumula, Managing Director at Freyr, has successfully managed organizations from both strategic and tactical perspectives. Ms. Sunitha is deeply rooted in technology, sales & marketing, operations, human resources and administrative functions of Freyr and has successfully led the same in other companies as well.

She has recently been featured by Analytics Insight in the 2021 listing of 'The 10 Most Impactful Women in Technology'. Here we bring you some of the excerpts from Analytics Insight feature with respect to why she has been listed.

Moving Ahead Through Self-Motivation

Every woman is a leader in her own way and this belief has played a key role in shaping Sunitha's career. She recalls, "I have always believed to be on my own and taken calculated risks." In her career, Sunitha deems that leading the most conservative side of the business itself is an achievement, especially in the Regulatory domain. Today, not only she is piloting this business but also driving the innovations and processes in the sector.

Rising Above Challenges to Create a Difference

Speaking about initial struggles in her career, Sunitha insists that she viewed them as stepping stones to her professional success. While the early phases of the transition have been challenging, Sunitha is proud of how far she has come today. The challenges she faced in her professional life were instrumental in helping her become a better version of herself, every time. Be it switching from the law background to an entrepreneurial role of technology and consulting organization-specific, to the Regulatory arena of life sciences or innovating and developing hi-end next-generation Regulatory solutions and services to enable accelerated performance, operations excellence, and high cost of compliance to clients, she never deterred herself from self-progression. At present, Sunitha is spearheading the initiative of core procedural automation across the Regulatory value-chain with customized, secured, cloud-hosted, on-demand & on-site Regulatory solutions.

She is familiar with the hesitation and paranoia people tend to counter when initiating to develop and sustain a business. However, Sunitha affirms that she thoroughly enjoyed them all through to make Freyr an end-to-end Regulatory software and solutioning partner.

Decisiveness and Persistence: Essential Leadership Hallmarks

Sunitha emphasizes that decisiveness and persistence are two vital attributes that every transformational leader must possess. As time goes on, success will not be a discussion point even if one is successful consecutively. But how

decisive one finds herself in the tough and challenging times matters the most. And that one decision has the power to transform the whole organization, if not the functioning of the entire industry. Beyond that, it is the leader's persistence that brings value to the decision. Sunitha adds that if a decision is made, the leader must be resolved to live with it till the end.

Building Solid Client Relationship

Freyr is focused on the customers' end goal, i.e., taking their product to global markets in a compliant way, within the timelines. Stressing more on that, the company asserts that the additional value it creates for its clients is through extended support which others fail to. Most of the time, the unconventional side of the Regulatory requirement is time consuming and an expensive affair. In such scenarios, for unique device/medicinal product classification and for unconventional market-tailored business strategies, Freyr has successfully offered end-to-end Regulatory support right from strategy to submissions and lifecycle maintenance.

Sunitha explains that the company continues to solve regional Regulatory problems for its clientele using its experts' on-ground knowledge, coupled with utmost attention to their needs and responsiveness. Freyr's work environment is entrepreneurial with the necessary empowerment of teams to ensure appropriate solutions for clients in a timely manner. Its patrons enjoy the attention they get and the proactive approach that its teams follow in solving complex Regulatory problems. Sunitha emphasizes that Regulatory is very natural to Freyr's teams, unlike its industry peers. The combination of Regulatory expertise, process experience, global perspective and constant effort for innovation has enabled significant value addition to all Freyr's programs.

Disruption to Emerge as Central Business Factor

The Regulatory function in the Life Sciences sector is held up with many manual processes impacting the organization-wide man efforts, quality standards and compliance best practices. Sunitha believes disruptive technologies like Deep Learning, Machine Learning, and Artificial Intelligence automate many of the life sciences' manual processes to spearhead rapid drug development and quick to market. She reveals that with a complete know-how on end-to-end processes of Regulatory, safety and clinical domains and respective traditional manual approaches, Freyr has developed dedicated CoEs for such disruptive technologies focusing mainly on the life sciences industry.

She assures that apart from the need to concentrate more on the simplification of things, disruptive technologies have not brought any principal changes in the role of business leaders.

Delivering Outstanding Services

According to Sunitha, Freyr is working on couple of technologies to simplify its clients' compliance journey. Some of the technologies are being used in few programs and latest versions will be available soon. Freyr's Regulatory services are entirely driven by customers and clientele needs and are highly customizable. She concedes that the combination of the unique requirements of the company's clients and team's passion to come up with a better solution every time, keeps the workforce excited every day.

Sunitha informs that the clients have the option to select from variety of service models, including hourly consulting, project-based delivery, FTE based model, unit-based delivery and on-demand services as per their requirements. Freyr offers great flexibility by enabling early intelligence activities performed before the project so its team could identify bundling opportunities for multi-country projects, and thus promote efficiency, harmonization and cost savings for clients.

Practice What You Preach!

Advising young talents, Sunitha suggests them to lead by example. She is strong advocate of the adage - "Do what you Preach"! She reiterates that doing so will ensures complete trust in one's company or business, from employees to stakeholders. She acknowledges that it takes a toll while a person faces new challenges every day. However, she recommends remaining persistent and accepting that failure is a part of the journey. She also encourages to put continuous efforts and strive till one achieves its desired goals as these challenges turn into opportunities.

Further, Sunitha persuades emerging women leaders to take smart chances and embrace new ideas, drive and lead the change from the frontline, as there is power in innovation and technology that can change the way things happen.

Client TESTIMONIALS

We've done it! Answers successfully transferred to MoH. Thank you very much for all the support last week and your incredible passion to cope with this.

- RA Specialist
A Global Biopharmaceutical Company

Thanks a lot for your extended support at last moment. We really appreciate your amazing dedication and efforts.

- Regulatory Affairs (Formulation R&D)
A Global Player in API Manufacturing

Thank you for your ongoing support with the RFA review process! We've moved a fair few forward recently, which is great to see! Given this, I was just wanting to enquire as to if you can take on 5 more Shower Gel RFAs that we have coming through for 1st review?

- Global Regulatory Affairs Associate
A British Multinational Consumer Goods Company

Freyr has been doing exemplary work in the QC Monitoring space for one of our workstreams. Continue the good work.

- Associate Director, Labeling Digital Enablement
One of the World's Largest Pharmaceutical Companies

Kudos to you all for the brilliant teamwork!! Alone, we can do so little; together, we can do so much. Looking forward to the next milestone and collaboration on new projects in future.

- SVP - R&D (Finished Dosage Form)
A Global Player in API Manufacturing

I take the opportunity to thank Freyr team for the great support in the registration of our devices with the MHRA. I appreciate that the activity has been completed within the committed timelines, in a very accurate, efficient and professional way.

- Director – Regulatory Affairs
A Global Medical Technology Company

It is good for submission. And I understand today is an Indian holiday, so I have to thank Freyr team in India for doing this. FDA called us and is trying to close out the CBE-30 filed in March and wanted these documents as soon as possible. So, I truly appreciate your assistance, even on a holiday.

- President
An Innovative Pharmaceutical Company

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

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

About Freyr

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

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