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GLOBAL REGULATORY SOLUTIONS & SERVICES
AN ISO 9001 & 27001 COMPANY

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CONNECT

Freyr Global Expansion

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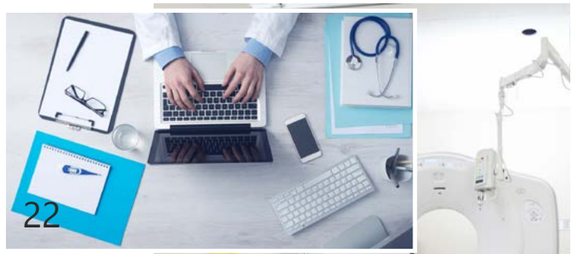
INSIDE

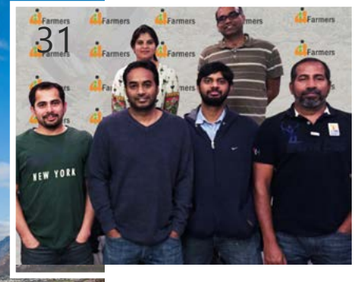
Lead Story

WHAT'S INSIDE

Regulatory Stories



Freyr 360⁰



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Foreword

Hello Everyone,

Welcome to another chapter of Freyr Connect!!!

Through this newsletter, we would like to announce that Freyr has emerged to be bigger and better than before. It gives us a great pleasure to announce that Freyr is expanding its EU presence with a 2nd operations center in Germany (after its Maidenhead , UK operations, established 3 years back), leading the company's effort to address the challenges in the ever-evolving regulatory arena in the region.

Every quarter we see remarkable transformations in terms of business prospects, that help us deliver excellence to our customers. This quarter witnessed significant momentum with the fast paced, broad-based, colossal developments. The highlight wins of the quarter were across the IDMP, Labeling & Artwork and Publishing regulatory segments. Freyr is delighted to provide expertise and services to the Top 2 of the Top 20 Global Bio-pharmaceutical companies - Forbes, one of the Top 5 Most Innovative Pharmaceutical companies - Forbes, a leading US-based biopharmaceutical company specialized in Drug Discovery, Development & Commercialization and one of the Top global consulting and evidence-based research firm.

We would like to appreciate everyone from Freyr team for their continued commitment to the company and growth.

This edition is special as it is the result of great employee contribution in terms of our featured articles. Shuffling through the pages you will come across how Freyr's CSR initiative i4Farmers got recognized by a leading Indian daily: The Hindu. Don't miss out the interesting Freyr 360° overview of all the roll-n-romp that took place in the house.

Lastly, we would like to thank everyone who contributed to this chapter of Freyr Connect. We hope this edition will enlighten your day.

Happy Reading!!!

Best Regards,

Rajiv Rangan
Co-CEO

Suren Dheenadayalan
Co-CEO

Upcoming Major Generic Drug Labeling Rule: What Should GDMs Know?

The wait is over. In a recent announcement, the US FDA has asserted that the proposed rule of

labeling pertaining to generic drugs will be released in July 2016. The much-anticipated rule is expected to ensure that utmost importance would be given to the patient safety while securing the rights of generic drug manufacturers. Before mulling over how the proposed rule would affect the generic manufacturers' dependency, let us try getting some facts about the patient safety and the labeling status-quo.

Influence of the Present Rule

As per the current regulations for updating the drug label, the guidelines are different for branded drug manufacturer and generic drug manufacturer that creates a timeline difference (which is generally more for generic drug manufacturers) for both manufacturers, to update and implement any safety related information on the packaging. Such a delay may cause health complications for a patient who is buying a generic drug whose safety information has not been updated on the package.

Corresponding to present guidelines, generic drug manufacturing companies cannot update product labels independently for any new safety information associated with new drug applications (NDAs), abbreviated new drug applications (ANDAs) and biologics license applications (BLAs). This situation poses threat to patients' health as companies cannot warn users about any safety issue identified, which is yet to be specified on the reference product's label.

What would the New Rule Entail?

After final considerations, if this rule comes into force, generic drug manufacturers will be able to issue a labeling update related to any safety information change in short timelines. It will entail a process that would allow the discrepancies to exist on temporary basis among the brand name reference products, generic drugs and approved generic drugs. When companies are filing applications to FDA for labeling change, they need to provide relevant information that describes the basis for label change along with:

- New data to be implemented after the change
- Published literature
- Adverse event data
- Epidemiologic studies

FDA says:

"The rule may encourage generic drug companies to participate more actively with FDA in ensuring the timeliness, accuracy, and completeness of drug safety labeling in accordance with current regulatory requirements."

Whenever a new rule is proposed by FDA, apart from elaborated internal discussions, the agency also considers suggestions from public docket to create the final guideline. For this particular guideline associated with safety label updating process, FDA received approximately 2300 comments which will be taken into consideration together with the final financial implications and benefits.

Approach, Approvals and Beyond

Once the manufacturer has found some discrepancy or risk with the new drug, the need of the hour is to report the issue to the US FDA and get the approvals for necessary label changes. Following approvals, the manufacturer may update the safety in different ways:

- by submitting a New Drug Application (NDA); to reflect new indication for use
- a Prior Approval Supplement (PAS); to propose other substantial changes
- through Annual Reports; for minor changes regarding extension of expiry date
- by submitting Changes Being Effected (CBE-30 & CBE-0); for immediate moderate changes

In this scenario, generic drug manufacturers, on finding an issue, can notify the FDA by filing CBE – 0 to make immediate changes to the label information furnishing the below details.

- the basis of the labeling change
- data pertaining to adverse events and
- related studies

Though the CBE-0 differentiates the RLD and generic drug labels temporarily, regulatory mechanisms eventually will align both the labels as per the same standards.

The Pros & Cons

Maintaining the uniformity of the label as that of an RLD might seem advantageous for generic manufacturers:

- to accelerate approval processes
- to save much of the time without any need to get involved in the rigorous tracking of safety issues
- to safeguard themselves from failure to warn instances

However, with the fact that the proposed rule itself has some serious conflicts with that of the Hatch-Waxman act, the health authority has a long way in sorting out a legal deadlock to ensure the possibility of rolling out the mandate anytime, soon. Meanwhile, let us bring to you how this rule is going to affect both the end users and the generic drug manufacturers.

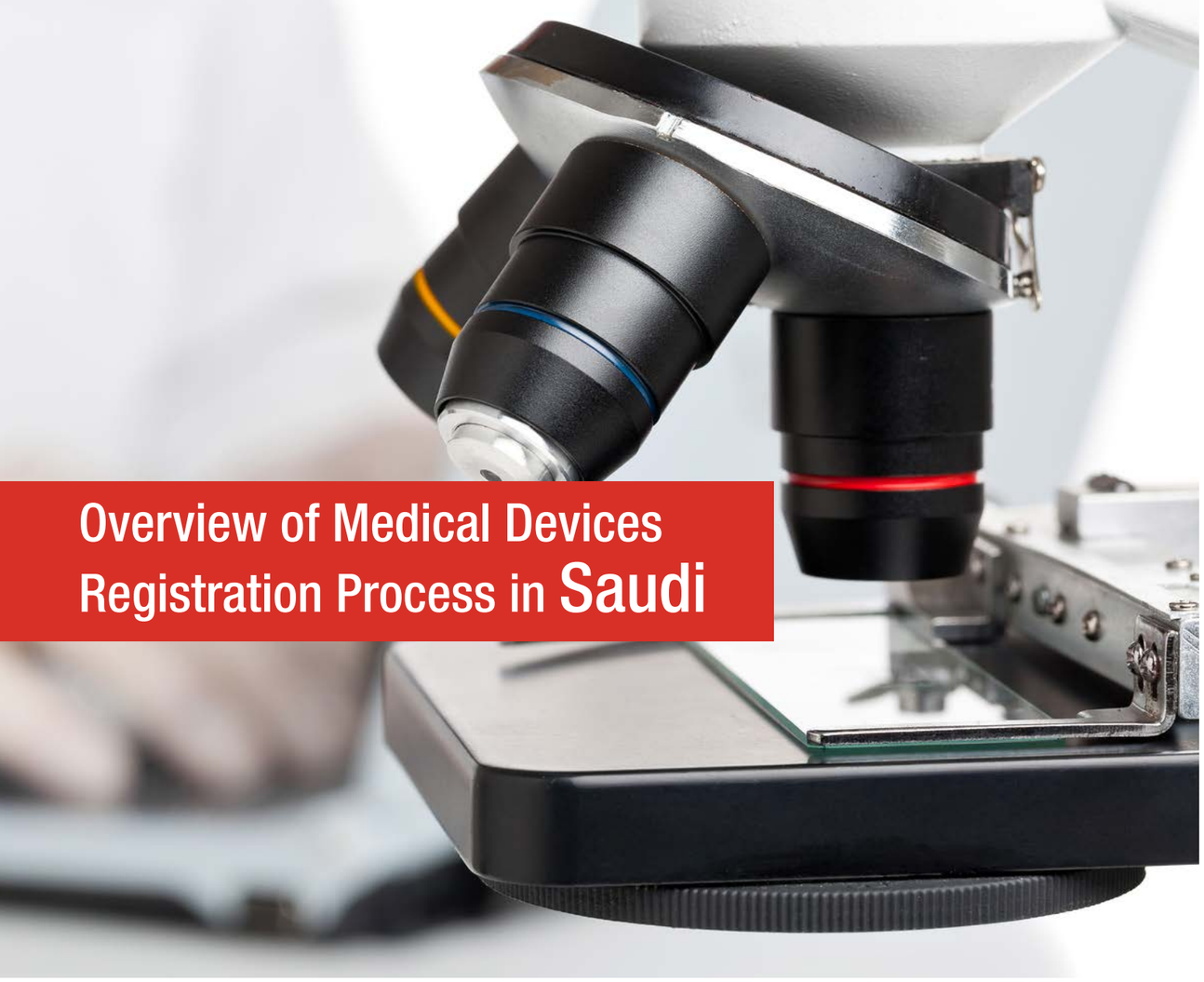
	Pros	Cons
Generic Drug manufacturers	• Freedom to track the drug Safety • Authority to update the safety labels with prior approvals • Cut down review time	Liable to 'failure to warn' instances, in case the US FDA approvals are missing
Customers	• Updated drug safety	Increased product costs

Disagreements Witnessed For the Rule

Lot of disagreements were unveiled in generic industry against the proposed rule, as some sponsors believed that new legal liabilities and delay in announcing the final rule would bring financial instability and lead to loss of billions of dollars to generic companies. They proposed that FDA should be quick in making final decisions intended for this rule and ensure that updated safety information is accessible by patients on time.

In Conclusion: A Challenge Ahead for GDMs

As generic drug industry awaits for the new rule to be released by FDA, manufacturers should get ready to have a quick response time in case of any change in safety information. This will be a challenging task, as presently, the complete information about the final guideline is not known to generic drug manufacturers.



Overview of Medical Devices Registration Process in Saudi

Saudi Arabia Medical Device Market has grown extensively in the past few decades and is expected to reach US$ 1.5 Billion by 2018 from the US$ 1 Billion in 2012. According to the recent surveys based on forecasting strategies of Medical device market in Saudi Arabia, majority of the devices are acquired by imports. Saudi Arabia is one of the largest and emerging markets for medical devices and associated products in the Middle East region. Favourable growth in medical device market is primarily driven by public sector spending with more than 60% share contributed by the Ministry of Health, the remaining being dominated by the private sector and other public providers.

Saudi Food and Drug Authority (SFDA) Medical Device Approval Process

The initial step to market the medical devices in Saudi Arabia is to get the medical device registered under Medical Devices Marketing Authorisation System (MDMA). Manufacturers must have the approval from at least one of the GHTF countries (US, Canada, Europe, Japan or Australia), before the registration.

Steps to Consider

1. Medical device must be approved for sale in one of the GHTF countries.
2. Manufacturers' medical device type of classification will be same as classified by the referring jurisdiction country (manufacturer referring GHTF country).
3. Local manufacturer/importer/distributor needs to be registered electronically through the Medical Device National Registry (MDNR) in order to get the Establishment Registration.
4. Manufacturer must appoint a KSA Authorised Representative (who is registered and licensed from SFDA) in order to register and communicate on behalf of the overseas manufacturer. In addition to that, the KSA Authorized Representative license must be renewed every year.
5. Local Manufacturer/KSA authorized person should fill the application form, details, and upload all the required documents.
6. Once applied device is approved, SFDA will issue the Medical Device Marketing Authorisation after which the manufacturer can distribute the device in the market.
7. The manufacturer can market the medical devices before getting the approval from SFDA, for Class I devices.
8. **Changes/Variations:** Local manufacturer or authorised representative may provide the written information on the changes/variations in previously provided documentary evidence (during the original MDMA submission). Subsequently, the updated information should be provided using the electronic form available on the MDMA portion of SFDA website.
9. **Renewal or Extension:** Local Manufacturer/Authorised Representative shall apply for medical device extension using the electronic form in MDMA portion of SFDA website. This extension will be applicable for 60 days before the medical devices' marketing authorization expires.

Note:

1. Extension applies where there has been no change to the device, with respect to safety or performance, ever since the authorization was previously issued. This procedure will be applicable when the authorization in the Founding Member jurisdiction on which the marketing authorization application was based, has been updated without further technical evaluation of the device.
2. In all the other situations, the renewal procedure application and updated documentation must be submitted through the MDMA for verification by SFDA.

Industry Challenges

The key challenges that industry comes across are majorly related to the regulatory requirements for medical device registration. Some of the major industry encounters are discussed below:

1. Devices must be registered in one of the US, Europe, Japan, Australia and Canada countries (GHTF countries).
2. A lot of time goes into Legalization of Authorised Representative by country of origin (of manufacturers).
3. Some of the documents must be submitted in the Arabic language.
4. Manufacturer must appoint a Local Authorised Representative, registered in SFDA.
5. Distributor/Importer needs to have Establishment registration.
6. Sometimes SFDA may ask for a GMP (Good Manufacturing Practice) certificate even though it is not a published requirement. This kind of situation happens mostly with medical devices that include pharmaceuticals.
7. SFDA is now requesting manufacturers to provide UDI compliant labeling with barcodes, as well as product names and descriptions in Arabic for medical devices (barcodes are currently optional for other type of devices).
8. SFDA is now performing an audit for the Authorised Representatives' (AR) office in order to ensure AR's ability to monitor post-market activities (this kind of audits are mostly associated with high-risk medical devices). SFDA mentioned that AR can be a scientific office with some experience in medical devices. The manufacturer may also appoint one AR per category of relevant devices (low-risk, high-risk separate ARs) rather than appointing one AR for all kinds of devices.
9. Applicant must comply with the KSA's National Centre of Medical Devices Reporting (NCMDR) requirements that are related to Field Safety Corrective Action affecting manufacturers' medical device to be reported to KSA authorities and this statement needs to be confirmed by the manufacturer.

In Conclusion

MDMA registration for medical devices is comparatively simpler in SFDA as the entire process goes through online application, but we need to have exact documents and appropriate information to fill the form. However, manufacturers are trying to meet SFDA requirements with the minimum documentation, but the SFDA is demanding that manufacturers must be absolutely compliant with the regulations. If the manufacturer fails to meet the meticulous SFDA requirements (though the SFDA reviewers are willing to accept explanations or justifications for certain issues with provided documentation), it can lead to a complicated approval process.

eCTD Module 1 V3.0 For EU

What Should Companies Know About The Revised Specification?

Are you currently submitting eCTDs (electronic common technical documents) to European Union (EU)? Or planning for the same in near future? Then we suggest it's time to pull up your socks as the EU is taking its turn in 2016. As we could decode the details from EU M1 eCTD specification – V 3.0, which was published in the last quarter of 2015, the final version is set to take effect from 1st July 2016 and is set to be mandatory from 1st October 2016.

What companies should realize about the new specification, Module 1 change, is the complexity for it's:

Additional submission types which are going to support specific regulatory activities. The updated specification includes the submission of clinical data reports for redacted publication and supports applications on Certificates of suitability (CEP) which are directed towards EDQM.

Granular insights based on the concept of US FDA's submission unit. While the current submission type exclusively describes regulatory activities on a broader spectrum, the inclusion of submission unit describes the content at a granular level in relation to defined regulatory activity. In simple terms, submission unit gives much more clarity on sequences and their relation in specific. The valid values defined in the new specification includes, initial, validation-response, response, additional-info, closing, consolidating, corrigendum, and reformat.

As it has been said that the new mandate is all about giving importance to the term VALIDATION, the new specification requires UUID (Universal Unique Identifier), a 32 digit hexadecimal number which links sequences and eCTD applications. With this, the European regulatory agencies are expected to validate the new sequences based on the uniqueness across applicants and applications. However, older sequences and applications are not expected to assign the same UUID.

Conclusion

The deadlines are set. With the major change anticipated, the only solution with your organization's regulatory operations and IT support teams is the software upgradation. The new specification is expected to affect your eCTD publishing, review and validation software. If your software is not upgraded/updated to comply with eCTD Module 1 V3.0, we advise you to consult a global regulatory partner for submission and publishing with an exclusive and updated eCTD submission solution.

Let us help you plan your eCTD M1 V3.0 transition right away!

Email: sales@freyrsolutions.com

Emerging Regulatory Trends in

Consumer Healthcare and Cosmetics Industry

The consumer healthcare industry is catching-up fast with the changing consumer behavior by delivering value driven product categories across consumer segments. Unlike before, where there was little data to support the strengths of claims, scientific studies and justifications backs up the brands today. Growing awareness among consumers with the trend of digital and mobile platforms across the globe is playing a dual role. At one end, concerns about personal wellness and health are growning among the consumers, at the same time, exposing them to myriad choices of products, based on information freely available online and peer recommendations. A consumer can easily check the quality of product by connecting with peers in another part of the world who have had used it. In this industry, consumer is the king who drives the key buying decisions.

The industry is adapting to a value-driven portfolio compared to volume-based approach focusing on benefits over price premium capitalizing on consumers' informed peer driven choices. This has put global players in a situation to meet fast emerging consumer needs while maintaining the quality in a continuously evolving global regulatory landscape.

In such a rigorous environment, a single adverse event related to a product can significantly damage a brand's image and its market. Organizations no longer are willing to risk a product without considerable clinical claims which not only ensure consumers' trust with the brand, but also enable brands to place their products as the best health management solution.

Challenges in Developed and Emerging Markets

The market dynamics of consumer healthcare industry favors consumer goods companies like Unilever, Reckitt Benckiser and similar organizations who have strengthened their regulatory teams to align with the changing regulatory framework while banking on their vast experience with consumer driven market.

Pharma companies, being well versed with complex regulatory environment, find it challenging to drive the consumer health divisions since the guidelines that monitor the pharma products often reduce the speed at which consumer healthcare portfolio should operate.

Developed markets have transparent and streamlined regulatory processes; however, it may not be same in emerging markets. Especially when industry is trying to maximize its profits over its portfolio by venturing into new markets, the local regulations pose new challenges at multiple levels.

Most of the health authorities worldwide follow the EU legislations with some degree of variation; however, the specific variance, timeline for implementation of changes and modality mostly remain unknown.

Often manufacturers face challenges during the export when they discover that a new regulation can affect their current batch. The available regulations published online is a challenge to comply with, as they pose language barriers. This is a common pattern witnessed across markets like Africa, Latin America, Asia, and some European countries. In such scenarios building a comprehensive market strategy for all Asian countries, becomes a challenge compounded by limited availability of online information and complex on-ground dynamics.

Cost

As the industry is facing new challenges in the evolving regulatory environment, cost continues to be a prominent hitch for the organizations. The fast-moving consumer health industry attracts diverse competition from niche market players like nutraceuticals, dietary supplements, and technology companies such as Google and Apple rolling out health management applications based on big data, resulting in increased cost pressure to maintain a healthy bottom line.

Recognized brands are striving towards capitalizing the price premium, based on brand loyalty, while other brands and products need equal resources and investment to sustain the operation margins. There is a need for striking a right balance across quality, benefits, and cost by implementing innovative, comprehensive, and intelligent models.

In Conclusion

Global organizations are moving towards centralization utilizing strategic inputs from stakeholders including industry thought leaders, global department leads and local market experts, regulatory and operational experts translating them into holistic roadmap for managing product portfolios, go-to market strategies, licensing and innovations.

Process transformations in conjunction with integrated, end-to-end regulatory information management technologies, data driven inputs for regulatory strategy and operations are a way forward for responding to global market needs.

Artwork Errors Affecting Enterprise Repute In Global Markets

The dynamic environment of pharma regulatory for packaging & artwork has set forth huge challenges for the pharmaceutical and life sciences companies in terms of meeting the latest mandates. Subsequent to the rapid updates in artwork regulations, companies are facing one of the most crucial phases in their life cycles. Where, on the one hand the existing product chain is running out of patent timelines leading to major financial challenges, on the other hand the traditional products are struggling to meet the regulatory compliance gaps due to regulatory changes. Moreover the growing global markets are giving rise to expansion of new markets around the globe, posing a threat to the passive traditional markets.

To fix the situation incepted as a result of dynamic artwork regulatory challenges, companies are manifesting manufacturing more variations and alternatives to their current products and launch their products in the emerging markets. Implementing this practice leads to changes in the physical packaging of the products as the components change, thereby making the artwork creation and maintenance, an intricate process to achieve.

For companies with an extensive product line distributed around the globe in different regions, a perfect balance between business process and product information management is required, to keep up with Artwork compliance. However regardless of the size of the organization, companies witness similar errors/defects throughout the Artwork creation, few of which are discussed below:

Content Defects

This is a direct error that is observed in the detailed Artwork information about the product. Errors like omissions or placing incorrect symbols in the information generally dive into this category.

Gross Defects

This is a major error that arise because of an important piece of information missing completely from the detailed product information. Such an information can be a recent regulatory update that entails changes in the Artwork.

Technical Defects

The technical aspects of packaging line, such as the barcode on the pack, may lead to these errors because of the incorrect specifications or information about the product mentioned in the barcode.

Context Defects

This error implies that the information on the Artwork is mentioned in an abstruse or an incorrect way that may mislead the perspective of the information. Such errors may appear because of inappropriate use of symbols or special characters.

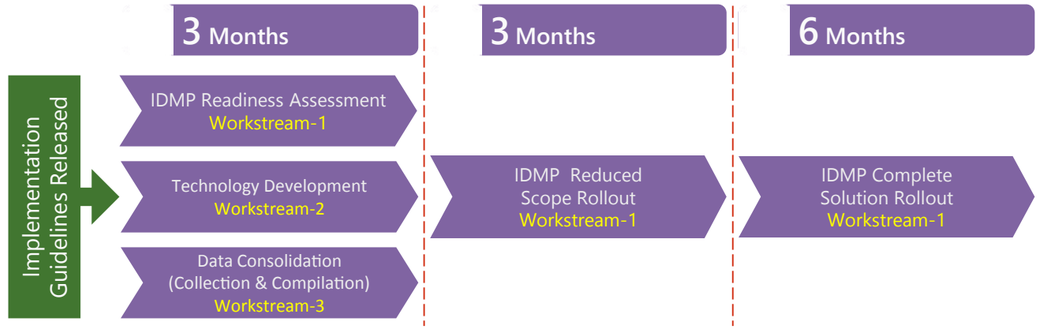
In Conclusion

These errors in packaging Artwork can bring about harsh implications for the companies in terms of revenue loss due to product recall if failed to meet the regulatory compliance or even put their reputation on risk in the global market. Regulatory experts around the globe recognize these risks and are dedicated to drive advanced operations that leads to error-free packaging artwork creation following the regulatory environment.

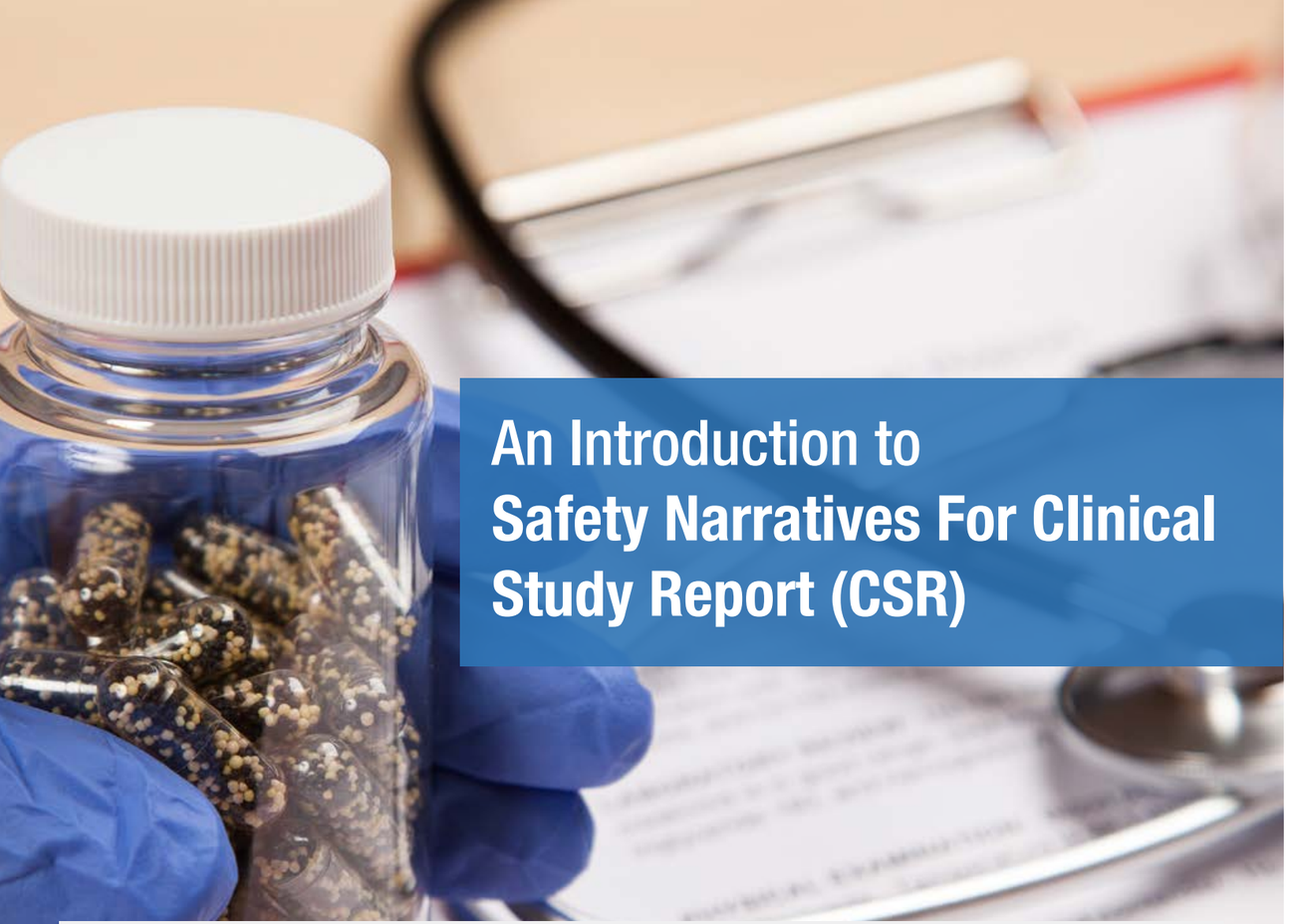
It has been observed that lack of good communication and competence are few of the major reasons for these errors to appear. So it is needed for companies to rely on trained specialists that are well acquainted with the latest regulatory updates and are proficient in managing the pharmaceutical artwork creation lifecycle.

Freyr IDMP Approach

Illustrative Timeline



Freyr - Consultants, Tech Teams, Client Team, Process Teams, Process Owners, BA	Freyr - Consultants, Tech Teams, Client Team, Process Teams, Process Owners, BA	Freyr - Consultants, Tech Teams, Client Team, Process Teams, Process Owners, BA
Workstream-1 ✓ Freyr consultants perform IDMP readiness, gap analysis and submit report **Workstream-2** ✓ Freyr tech team delivers a Pilot IDMP system with system/interface integration **Workstream-1** ✓ Freyr IDMP experts work with the client team and process owners to complete the data consolidation process	**(Scope – Fewer Products)** ✓ Freyr releases the initial IDMP Pilot system for data entry and consolidation ✓ Freyr drives this pilot through the various business functions for a small number of products ✓ Freyr and client teams collect the outcomes from the pilot drive ✓ Freyr builds the strategy for long term IDMP Solution	**(Scope – All Products)** ✓ Freyr's tech team delivers the long-term solution based on outcomes ✓ Freyr drives this system through various business functions for all products ✓ Freyr team performs data entry ✓ Freyr team builds and deliver the IDMP submissions to agency ✓ Client teams are able to track and generate IDMP analytics and reports



An Introduction to Safety Narratives For Clinical Study Report (CSR)

Safety narrative is a short story or a safety summary about a particular subject participated in a clinical study and experienced safety event which qualify under the criteria, such as Death, Serious Adverse Event (SAE), AE(s) leading to discontinuation of study, and AE of special interest.

As per the International Council of Harmonisation (ICH), E3 guidance for Clinical Study Report (CSR) structure and content, the CSR Section 12.3.2 or Section 14.3.3 should contain a brief subject narrative describing the event. The placement of the narrative in the CSR section depends on the number of narratives. The narratives count always depends on the type of clinical study, number of participants and the number of events that fall under narrative criteria; usually, the late phase studies have more number of narratives.

When the number of narratives is very high, they are prepared as a separate entity called as attachment to CSR section 14.3.3. The preparation of narratives is carried out as a separate narrative writing project either by the sponsor company itself or outsourced to medical writing group of a Clinical Research Organization (CRO). Safety narratives are prepared from Phase 1 to Phase 4 clinical studies.

Narrative and its Content

Narrative writing is an art that expresses the medical information clearly and effectively. It involves collating the relevant information from several source documents, and liaising with medical experts to describe the safety summary about a particular subject who participated in a clinical study.

As per ICH E3 (Section 12.3.2 or Section 14.3.3), a narrative should describe:

- Demographic data of the subject
- Medical history and concomitant medications
- Study drug administration timing
- Description of the event(s) (nature, intensity and outcome)
- Relevant laboratory measures
- Action taken with the study drug in relation to the event(s)
- Treatment for the event(s)
- Causality decision of Investigator and Sponsor

The above-specified information will be extracted from one or more source files as following: Council for International Organisations of Medical Sciences [CIOMS] form, Case Report Form [CRF], FDA Med Watch Form, Data Clarification Form [DCF], summary tables, and listings.

Challenges of Narrative Writing Projects

The narrative writing projects are executed as teamwork between the sponsors and CROs have to reach the goal of submitting the study results at the earliest. In most of the therapeutic confirmatory studies conducted for marketing approval, preparation of the narratives is the last and the most critical step in the dossier preparation. Listed below are the challenges that various stakeholders come across.

Challenges for the Clinical Research Organizations (CROs)

For CROs, completing narrative writing projects within a pre-specified timelines and budget while providing excellent quality can be a stringent task. Considerable effort of project management and resource management activities is involved before and during the narrative writing project execution.

These are short term projects (up to 3 months), and the CRO has real challenge in keeping and getting the trained resources along with:

- Maintaining/Providing MW resource count for the project
- Involving/allocating required resources in a short span of time
- Providing project/study specific trainings and updates
- Providing adequate communication channels
- Defining process flow and getting it approved by the Sponsor
- Identifying key person from the sponsor team who takes the ownership
- Using resources without affecting other MW projects
- Tracking and managing the entire project

Challenges for Sponsors

For sponsors, finding a CRO with an adequate resource count, hands on experience & capability and therapeutic area knowledge is a challenge. Getting high-quality documents within specified time, but without compromising company policies, SOPs and confidentiality are other major challenges in addition to:

- Identifying the number of narratives before the project (at least approximate number), to decide whether it can be executed in-house or should be outsourced to CRO
- Planning the activities and deciding the timeline
- Defining the responsibilities for CRO MW and in-house reviewer
- Template design/format of the narrative
- Deciding outsourcing cost and budget allocation
- Providing the reviewers, including clinical team and Medical experts
- Performing sponsor's quality check/ quality assurance, if any planned

Challenges for Medical Writers

Narratives describe the whole story of the subject/participant in predefined restricted format. It is quite challenging from the medical writer's perspective because different types of data such as demographics, study drug administration, medical history, event(s) description, associated lab, concomitant medications, outcome and causality assessment details are put together within the agreed template (might be full text, semi-tabulated, or automated narratives) which has to be completed in stringent timelines.

Rework is the biggest challenge in narrative writing projects due to inappropriate sources, intermediate change requests, updating template and adding the new requirements during the drafting stage. Other common challenges that medical writers come across are:

- Adapting to new style guide and the meeting the Sponsor's reviewer expectation
- Fulfilling the template and style guide requirements
- Delivering the narratives in stringent timelines
- Achieving daily target (number of narratives per day/week)
- Understanding multiple source documents
- Involvement of multiple reviewers
- Management of multiple drafts
- Unclear or illegible source data (hand written CRFs, CIOMS)
- Undergoing multiple project-specific trainings or attending multiple update meetings
- Complexity of the narratives (example: Oncology narratives consist of several numbers of events, multiple concomitant therapies and hospitalizations)

The narrative writing projects are executed as teamwork, and has several challenges as compared to the other medical writing projects. A proper forecasting, planning, coordination and execution is the key to success for Narratives.

An Overview of Companion Diagnostics And Personalized Medicines

The accelerating costs of drug discovery, development and drug promotion continues to concern

the pharmaceutical sector. This has been compounded by the initiation of personalized medicine and its demand for individualized products. In contemplation to satisfy the demands presented by this new prototype, the next generation of drugs needs to be safe & efficacious and the pharmaceutical companies must assemble more genotype and/or phenotype-engrossed therapeutic agents.

Personalized medicine is the adaptation of treatment, based on a patient's genetic or somatic heredities and holds the promise of transforming healthcare. Companion diagnostics, many of which are molecular genetics assays, are critical tools in the accomplishment of personalized medicine. Information resulting from these tests provides for customizing definite therapies based on the genetics of the disease.

Molecular genetic companion diagnostic assays are befitting more pertinent and imperative in an environment of amplified regulatory guidance in their development and application. The advancement of Companion Diagnostics seems to offer a set of tools as well as the presage of relevant biological and clinical information that concentrates on many challenges that the pharmaceutical companies must overcome.

Personalized Medicine

Personalized medicine is a therapeutic model using molecular profiling technologies for tailoring the accurate therapeutic strategy for the correct person at the right time, and determines the predisposition to disease at the population level and to deliver appropriate and stratified prevention. The vital concept in this definition is molecular profiling. Molecular profiling encompasses the use of a biomarker.

Biomarker

A biomarker can be defined as **"a representative that is empirically gauged and assessed as an indicator of normal biological processes, pathogenic processes or pharmacological responses to a therapeutic intervention."**

Various types of biomarkers can be classified as per their purpose:

- Predisposition biomarkers – to assess the possibility of a disease (e.g. BRCA1 for breast cancer)
- Diagnostic biomarkers – to identify a specific disease (e.g. HCV RNA after infection)
- Prognostic biomarkers – to predict the course of disease (e.g. HER2 for breast cancer)
- Monitoring biomarkers – to assess the track of disease progress (e.g. BCR-abl for monitoring the treatment response in patients with chronic myeloid leukemia)
- Predictive biomarkers – to predict the response or reactions to a pharmaceutical drug (e.g. BRAF-V600 for melanoma patients)

Patients react contrarily to the same pharmaceutical drug, at standard prescriptions. An assessment for a predictive biomarker that is allied with a pharmaceutical drug (Rx) is called a companion diagnostic (CDx). FDA defines a companion diagnostic as **"an in vitro diagnostic device that stipulates information that is necessary for the safe and effective usage of a corresponding therapeutic product."**

FDA has emphasized four areas in which a companion diagnostic may be indispensable to the protected and operative use of a therapeutic product to:

(1) Identify patients likely to benefit from the therapeutic product;

(2) Identify patients predisposed to compounded risk for serious adverse reactions as a result of treatment with the therapeutic product;

(3) Monitor response to therapeutic product for the purpose of correcting treatment (eg; dose, discontinuation) to accomplish enhanced safety or effectiveness; and

(4) Identify patients in the population for whom the therapeutic product has been effectively considered, and found nontoxic and efficient, i.e., there is sufficient info regarding the protection and efficiency of the therapeutic product.

Companion Diagnostics

"'Companion diagnostic' means a device precisely anticipated for the selection of patients with a previously diagnosed condition or predisposition as appropriate or inappropriate for a particular therapy with a medicinal product or a range of medicinal products."

Companion diagnostics are a part of personalized medicine and will likely endure to swiftly surge in number and application to disease areas. First companion diagnostics were sprung in the 1980s and in the face of substantial preliminary cynicism from drug developers in case of segmenting a drug's market through a diagnostic was advisable.

The viable accomplishment of drugs such as Gleevec® (imatinib) and Herceptin® (trastuzumab), which implicate testing with companion diagnostics beforehand they can be recommended, has proceeded the entire companion diagnostic field forward.

From an initiation of a handful of

oncology medications with consequent diagnostics, the field has augmented to include several therapeutic areas and the number of combinations has propagated by 12-fold.

Applications of Companion Diagnostics

The considerable application of companion diagnostics is to support the choice of most appropriate pharmaceutical drug for a given patient. Patients might react in a different way to the same pharmaceutical drug. One subgroup of patients may not respond, alternate subgroup might respond partially while a third subgroup might experience adverse drug reactions. Trial- and-error is one inquisitive to find which subgroup a patient belongs to. A trial-and-error approach can be tedious and prolonged, and patients with a life threatening disease may be despaired before the appropriate pharmaceutical drug is identified.

The potential of predictive biomarkers is the capability to ascertain patients who benefit or who are at threat of suffering from a pharmaceutical drug before initiation of treatment, thereby improving patients' health.

A second application of companion diagnostics is during pharmaceutical drug development. If the association between a predictive biomarker and a new pharmaceutical drug is discovered initially, subgroup-specific drug development is possible as patient population is expected to yield higher efficacy rates with smaller sample sizes and, hence, may also lower trial costs. In theory, even development time could be shortened, leading to amplified efficiency of the pharmaceutical drug development process

However, in practice generally subgroup-specific development is initiated only after a phase III study has failed and a subgroup analysis has revealed the prominence of the stratifying patients. In such a scenario, costs and development time would be increased. However, using a companion diagnostic may allow a moderately small group of responders to gain access to an efficacious pharmaceutical drug that would otherwise never have received a marketing authorization.

Regulatory Approval and Certification

In Europe regulatory pathways for pharmaceutical drugs and accompanying companion diagnostics are alienated. Marketing authorization applications for pharmaceutical drugs have to be submitted to the Committee for Medicinal Products for Humans Use (CHMP) within the European Medicines Agency (EMA). Based on the evaluation and endorsement of EMA, the European Commission then concedes a single marketing authorization valid in every member state of the European Union.

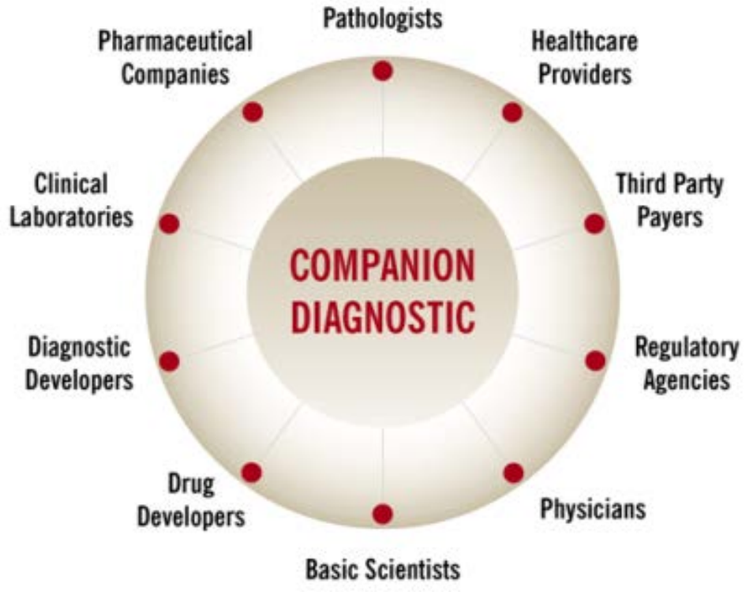
The association with a companion diagnostic test is stipulated in the pharmaceutical drug label. It is important to note that EMA recommendations on the pharmaceutical drug label do not specify a particular test and therefore any validated test can be used. A pre-marketing approval is not required for companion diagnostics. Commercial companion diagnostics are classified as in vitro diagnostics (IVDs) in Europe and consequently have to be in compliance with the respective 'IVD directive' (98/79/EC). Compliance with the IVD directive is indicated by a CE marking.

Self-certification by the manufacturer is sufficient in most cases to acquire a CE marking. Laboratories which develop their own biomarker tests for in-house use, so-called in-house tests or laboratory developed tests are exempted from CE marking requirements.

The IVD directive is presently under revision. The European Commission's proposal for a Regulation on IVDs introduces a risk classification that classifies companion diagnostics as Class C device (high individual risk and/or moderate public health risk). Class C in vitro diagnostics require a compulsory review by a notified body.

"Notified Bodies are the recognized third party bodies that can accomplish conformity assessments laid down in the relevant harmonized European standards or European Technical Assessment".

Manufacturers should submit a clinical evidence report to a notified body that demonstrates, analytical performance, scientific validity and where applicable, clinical performance. The review process of the clinical evidence report involves consultation with a national competent authority or EMA. The competent authority or EMA have 60 days to give their opinion which might be protracted once by further 60 days on scientifically valid grounds according to the proposal issued in September 2012 by European Commission.



Challenges

One of the considerable challenges to impending growth in companion diagnostics is aligning the inducements of all stakeholders. A major carter of growth will be the economic incentives for drug developers to brace their products with diagnostics. Diagnostic companies are caught between the contradictory demands of foremost stakeholders, payers/providers and pharmaceutical companies.

Regulators are also grueling in aligning development timelines between drugs and diagnostics. In order to endure and thrive, diagnostic companies must contemplate more broadly about companion diagnostics. They should also have to continue the process of global expansion and consolidation that the industry has by now instigated. Despite of potential obstacles, companion diagnostics became one of the dampest areas of deal making in the diagnostic space in recent times, and the future trends continue to look progressive.

Fig 1: Necessary alliances to develop a successful companion diagnostic

Benefits of Companion Diagnostics

Companion diagnostics stipulate individual, treatment-essential information; health care payors (both public and private) and patients stand to benefit considerably from the evolution of the companion diagnostic device industry.

The benefits include:

- Earlier therapeutic intervention,
- Hasty disease detection and risk characterization/classification/ assessment,
- Ability to execute enhanced disease monitoring and improved monitoring of therapies anticipated for chronic use.

Companion diagnostics additionally identify patients for those a therapy may be ineffective, produce serious adverse advents — thus hoarding payers the burden of

(i) Paying for a medicine that does not act and

(ii) Paying costs correlated with treating potentially serious side effects.

Conclusion

Companion diagnostic device and the personalized medicine market, endure to progress in extent and significance to health care providers, patients, and payers of health care, and the market will surge in value. Manufacturers of companion diagnostics will capitalize significant progressive resources and should therefore, confer with legal counsel to

1. Edifice an optimum regulatory pathway that will lead to FDA approval;
2. Obtain the widest possible patent coverage; and
3. Augment the benefit of any available patent term extension.

Aswin Kumar

Holding experience of 10+ years in the pharmaceutical, biotech and life science consulting industry, Dr. Aswin Kumar is a Medical & Regulatory Writing expert at Freyr. He oversees the clinical documents like CSRs, protocols, Investigator's Brochures, Summaries for medical review. He actively supports the presales team in RFIs, RFPs and bid defense in addition to GCP Audits and compliance activities. Aswin holds in-depth knowledge and hands on experience in all aspects of clinical development including medical writing, clinical operations and pharmacovigilance. He reviews medical safety documents like ICSRs, PSURs, PBRERs, and literature reviews. Aswin is experienced in project and operations management with hands on experience in resource planning, budgeting, forecasting, strategy management, team management, risk management. He has extensively worked in CROs, KPO and leading Pharmaceutical Companies.

Standardization And Disclosures In Pharmaceutical Industry- Role Of Niche Consultancies

Disclosure is now the buzzword in the pharmaceutical, consumer health and FMCG Industry. The advent of internet search engines, increasing literacy and unrelenting curiosity of people to have more information about the products and services they use, have led the companies and policy makers to encourage pharmaceutical companies to standardize the information with higher levels of transparency and disclose it to relevant stakeholders.

Across all sectors policy makers are encouraging companies and individuals to declare the details at granular level for public. Pharmaceutical and consumer health companies are taking steps to make the information available in clear and lucid way to patients. Some of the measures in this direction include Identification of Medicinal Products (IDMP), Clinical Trial Disclosures, Company Core Data Sheets and standardization of consumer health claims and unique device identification.

Described below are the key elements of few such initiatives.

Identification of Medicinal Products (IDMP)

IDMP is an overarching concept of standardizing and disclosing the information about any product to the highest granularity as per the ISO standards. Every company would be required to provide the information regarding the drug substance, pharmaceutical form, manufacturing steps, labeling and safety related information for each of the products being marketed. This would help in earlier detection of safety signals and quality issues which in turn would help in protection of public health.

Clinical Trial Disclosures

Pharmaceutical companies are disclosing the details of the clinical studies by registering them on ClinicalTrials.gov and other public disclosure sites across the globe like EudraCT and Clinical Trials Registry-India. The study protocol, status of the studies, whether started or recruiting or completed, the study results are few of the details which are published for patients and healthcare professionals. This will help the patients and physicians to know the details of ongoing research being conducted in the unconquered fields of medicine.

Company Core Data Sheets

The creation of core data sheets which is the overall company position on the safety and efficacy of any product is another such step in harmonizing the information. As the labels across different regions have differing information it is very important to have a clearly documented company core data sheet or company core safety information for every product for which it is MAH.

The Regulatory agencies are providing the companies with more tools and means to disclose the information to the public and periodic assessment is being conducted to track compliance of the companies to these standards. The frequent inspections and changing regulatory standards demand the companies to update themselves with the evolving standards.

It is challenging for small and medium sized companies with limited resources to be compliant with these requirements. It is equally difficult for large corporations with multiple products in various geographies to be compliant with requirements at every region, every country for every product.

Pharmaceutical Companies are looking up to the niche consulting firms to provide the support to tide over the regulatory challenges. The roles and assignments handled by these consultancies are both challenging and unique. Every assignment has a different goal, timeline and a situation to handle. It is wonderful to work with set of motivated consultants on these tasks along with new stakeholders to help the Pharmaceutical companies to be both inspection ready and updated on latest standards.

All of these exercises are undertaken with one end goal in mind i.e. to ensure that the quality of the medicines delivered is of highest quality and safety and well-being of patients is given utmost importance.

In the era of personalized medicine and precision therapeutics, it is mandatory that pharmaceutical companies and agencies disclose the complete details for Physicians and patients to choose what is best for them. The niche pharmaceutical consultancies like Freyr are helping companies achieve these goals.

Pharmacovigilance-Individual Case Safety Reports (ICSRS)

Bare Basics

PV360
Global Regulatory PV and Safety Services

Overview

Pharmacovigilance is a branch of Pharmacological Science, which deals with safety, detection, assessment, understanding and prevention of adverse effects of a drug.

History of Pharmacovigilance

1968
WHO drug monitoring program was laid

1964
UK "Yellow Card" system for reporting adverse effects was implemented

2000
WHO UMC provided guidelines for setting up a Pharmacovigilance Centre

Objectives of Pharmacovigilance

- Improve patient health care and safety
- Encourage safe, rational and appropriate use of drugs
- Promote understanding, education and clinical training in Pharmacovigilance

Statistics pertaining to Product Recalls due to Poor Safety

Drug	Year	Unexpected Events that Lead to Product Recall
Thalidomide	1965	Phocomelia
Practolol	1975	Sclerosing peritonitis
Clioquinol	1970	Subacute neuropathy
Benoxaprofen	1982	Nephrotoxicity, oncholysis, cholestatic, jaundice
Terfenadine	1997	Torsade de pointes
Rofecoxib	2004	Cardiovascular effects

Basic Concepts

Adverse Event

Any untoward medical occurrence that may be present during the treatment with a pharmaceutical product at any dose, but does not necessarily have a causal relationship with this treatment.

Adverse Drug Reaction

A response which is noxious and unintended, and occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function which necessarily has a causal relationship with the drug.

Source of ICSRs

Individual Case Safety Reports can be obtained from two sources, either from a Solicited Source or an Unsolicited Source.

- Solicited Reports includes reports from marketing programs, customer engagement programs, and surveys etc.
- Unsolicited Reports includes reports from patient, pharmacist, physician, lawyer, nurse, caregiver, social media, email and fax, literature, and journals etc.

Timelines for ICSR Submission

Fatal case: 7 days of MRD (Manufacturer Receipt Date)

Serious case: 15 days of MRD

Non-serious case: 90 days of MRD

Kindly Note: Every Adverse event irrespective of its seriousness has to be reported to the Regulatory Authority. Serious cases reporting will be expedited to the Regulatory Authority, whereas non-serious cases will go in the form of Periodic Safety Update Reports (PSUR) to RA.

All the adverse events reported will be documented in Adverse Event Monitoring Form and then entered into a Safety Database. From Safety Database, reports will be generated and submitted to the Regulatory Authority.

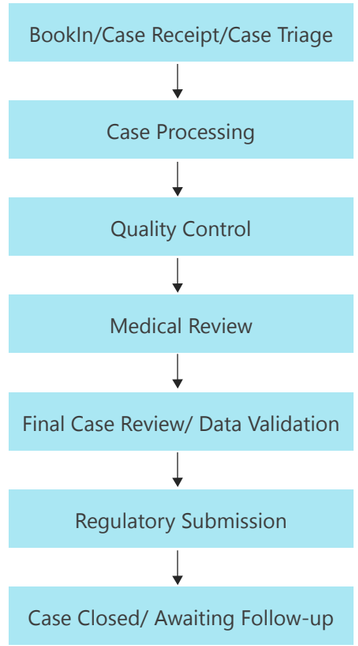
The different types of Safety Database are as follows:

- Argus Safety Database (created by Oracle)
- ARISg Safety Database (created by Aris Global)
- AERS (Created by Oracle)
- Clintrace

Kindly Note: Argus Safety Database and ARISg Safety Database are widely used, however AERS and Clintrace are the legacy databases which are still in use by few MAHs.

Flow Chart for Case Processing:

Let us discuss in brief about the steps involved in Case Processing:



1. BookIn/Case Receipt/Case Triage

In this step, the information received pertaining to AE will be analyzed to check whether the case is valid or invalid i.e. Case Triage. The case is valid if it fulfills the minimum criteria is processed and the minimum information required in terms of Patient, Reporter, and Suspect Drug and event, is present. The case is invalid if it does not fulfill the minimum criteria and is not processed. After entering this minimum information, a unique case number is generated.

Note: No two case numbers will be identical to each other. Every case number will be unique and different from others.

2. Case Processing

In this step, complete information pertaining to case will be entered into safety database. This step includes Full Data Entry which includes details like demography, previous and

ongoing medical history, concomitant medical history and brief narrative (case history) and laboratory investigations. Coding of events and Suspect Drug products with MedDRA (Medical Dictionary for Regulatory Activities) and "Company Drug Dictionary" (CDD) /WHODD (WHO Drug Dictionary) respectively is also undertaken. If there is any discrepancy or missing information, a query is generated, after which the case is routed to next step in workflow i.e. Quality Control or QC.

Note: If the Suspect Drug product is Company Product Drug (CPD), it will be coded with "Company Drug Dictionary" (CDD) and if the Suspect Drug Product does not belong to a particular company, it will be coded with "World Health Organization Drug Dictionary" (WHODD).

3. Quality Control

This is one of the integral part of Case Processing. This step deals with, "Checking the consistency of the information entered in database, hand written text with narratives, special characters in case, E2B validation errors and also appropriateness of any query generated". If any inconsistency is observed, it will be corrected promptly and the case will be routed for the next workflow i.e. Medical Review.

Note: E2B validation errors will lead to "Delayed Submissions". Hence, it is utmost important that all the validation errors are eliminated from the case.

4. Medical Review/Case Assessment

This is the step where, "Causality Assessment" is carried out. Medical Review can be only carried out by an allopathic physician. Based on the information available and confounding factors, medical review is done to determine the causality. It can be either, "Related or Unrelated or Probable or Not Associated". The Medical Reviewer can use his discretion and medical judgement to assess the causality. Once the Causality Assessment is done by a medical reviewer, the case is routed for a next workflow i.e. Final Case Review or Data Validation. If the medical reviewer has any comments or suggestions, those will be incorporated and addressed in the next workflow.

Note: The relationship between a Suspect Drug and an event is referred to as, "Causality". It can be either, "Related or Unrelated or Probable or Not Associated".

Causality Assessment directly impacts the Regulatory Submission.

5.Final Case Review/Data Validation

This is the step where Case Processor receives the case from a Medical Reviewer. The Case Processor in this step ensures that all the comments and suggestions are properly incorporated and addressed. Once every discrepancy and comment is addressed, the case is ready for Regulatory Submission.

Note: Final Case Review/Data Validation is the step where the case will be ready for Regulatory Submission. It is utmost important that all the changes and suggestions are properly addressed as given out by Medical Reviewer as there will be no QC after this step.

6. Regulatory Submission

This is the step where the case will be submitted to Regulatory Authority. Once the case is submitted, it will have a status of either, "Case Closed or routed for Awaiting Follow-up".

Note: The timelines for the case submissions to regulatory authority are as follows:

Fatal case: 7 days of MRD (Manufacturer Receipt Date)

Serious case: 15 days of MRD

Non-serious case: 90 days of MRD

7. Case Closed/Awaiting Follow-up

This is the final step in Case Processing. Once the regulatory submission is done, the case is either "Closed" or routed to "Awaiting Follow-up". If there is no pending information from a Reporter, the case will be locked and closed. If there is any information pending from a reporter, then the case will be routed to, "Awaiting Follow-up".

Note: If the case is Closed or Locked, and for the same case if additional information is received then, "the case is unlocked and the whole process of Case Processing continues till the report is submitted to Regulatory Authority".

REGULATORY AUTHORITIES 101

Bare Basics

Healthcare reforms and austerity measures, increased competition in the global marketplace bring in new and unique challenges to the Life science companies in marketing new drugs in the global regulatory landscape. Owing to this new development, companies are looking for innovative approaches to respond to the situation by focusing on emerging markets by collaborating with industry and academic partners. The companies intend to focus on operational efficiency while revolutionizing the traditional sales, marketing and research and development (R&D) operating models.

Pharmaceutical Industry: *Importance as a Global Sector*

The development, production and marketing of pharmaceutical products make up for a wide spectrum of global industry. According to an industry report total amount of pharmaceutical revenue worldwide had reached nearly one trillion U.S. dollars. It is said the North American region accounts for 40% of this revenue mostly due to the pivotal role played by the US pharmaceutical industry. On a global scale the Chinese pharmaceutical sector shows the highest growth rates over the last couple of years.

Asia-Pacific is expected to become the most profitable pharmaceutical market in future owing to its strong economic growth in major countries and large unexploited population. Brazil and Mexico are the next strongholds in the Latin American market. Furthermore growth of global pharmaceutical market in future may be confronted by diminishing drug pipelines and patent expiration of a number of blockbuster drugs.

Pharmaceutical companies invest 20% of their revenues in R&D measures as the sector is highly dependent on its research and development activities. Earlier companies used to develop few molecules and promote and market them extensively. However with the changing landscape its R&D productivity has gone down which is a cause of concern.

According to an industry report the global pharmaceutical market is expected to grow at a 9-10% annual rate through 2016. Loss of patent protection for leading products in developed markets and strong overall growth in the world's emerging markets are the causes of this increased growth rate.

Pharmaceuticals in Emerging Markets:

Currently, the global pharmaceutical market growth rate is 35% which is expected to rise to 50% in the second tier emerging markets by 2022. The key drivers account for aging populations, westernization of diets and increased government investment in healthcare.

Companies are now looking to relocate, shed assets and acquire smaller biotech firms to improve their competitive positioning in these new markets. It is a period of consolidation and de-diversification as increased competition and slow growth have forced companies to plan for the long term.

Regulatory Agencies And Organizations: *Play a Vital Role to Meet Requirements of Legal Procedures*

The pharmaceutical industry is considered as the most highly regulated industries worldwide. A regulatory body is in charge of drug product registration, manufacturing, distribution, price control, marketing, research and development and IP protection. A regulatory body currently ensures the proper enforcement of rules and regulations and issues guidelines for regulating drug development process, licensing, registration, manufacturing, marketing and labeling of pharmaceutical products.

Regulatory agencies are being established in various countries across the globe to aid life sciences companies meet the requirements of legal procedures related to drug development process in a particular country. The few regulatory agencies and organizations established in respective countries are the universal regulatory agencies and groups that play essential role in all aspects of pharmaceutical regulations. As a consequence of rapid globalization, the need for a coherent system of global health law and governance has never been greater than the current situation we see ourselves in.

List Of Country Specific Regulatory Authority:
USFDA(USA), MHRA(UK), TGA(Australia), CDSCO(India), HEALTH CANADA(CANADA), MCC(South Africa),ANVISA (Brazil) , EMEA (European Union), etc.

List Of International Regulatory Agencies And Organizations: World Health Organization (WHO), Pan American Health Organization (PAHO), World Trade Organization (WTO), etc.

Global Health Authority: *Major Challenges to Overcome in Delivery of Safe and Effective Healthcare Products*

A global regulatory authority will plays vital role in ensuring and increasing regulatory implementation in non-regulated parts of the world

- To ensure safety, quality and efficacy of medicines and medical devices
- To harmonize legal procedures for drug development
- To monitor and ensure compliance with statutory obligations
- To ensure and increase regulatory implementation in non-regulated regions for safety of people purposes
- To promote public health and protect the public from dubious drugs
- To establish proper legalization covering all products
- To increase worldwide regulatory growth to ensure safety of people.

Conclusion

Traditional clinical and corporate models may no longer gain power in a transforming marketplace as stakeholders must consider to address market and organizational issues in a bid to improve operational effectiveness and bolster health system sustainability.

Healthcare sponsors will need to function more competently, lower their unit costs, and identify ways to optimize the value of their limited resources to advance new care delivery models and targeted treatments. Stakeholders need to rethink traditional business models, redefine value propositions, innovate through new products and services as a recourse to adapting to market forces. A global regulatory authority can assess and address potential capability and localization gaps geographically, define a common vision and establish a unilateral governance process for risk-related decision making, thereby developing appropriate implementation and remediation programs. Some countries are working across governments and organizations to encourage a more methodical tactic to regulatory rule-making, monitoring, and enforcement.

The need of the hour is to establish more centralized procedures for improving drug regulation, harmonization of regulatory norms on a global scale. A global authority will offer a more stringent regulatory pathway for approval of new drugs, as well as government scrutiny of the continued marketing of existing drugs. The core focus will be on improving patient safety while introducing new drugs in the market. .

However we find that creating international legal norms, processes and institutions offers an enduring and organized platform for states to develop a shared humanitarian instinct on global health. But the use of a global law with respect to effective global health governance has its own structural inadequacies and intrinsic challenges— including ambiguous standards, ineffectual monitoring, weak implementation and geographical differences.

CASE STUDY

End to End CMC Support in Africa

Freyr delivered streamlined process for Master Dossier Creation for Module 2 & 3 in African Countries ensuring Country specific variations from Master Dossier

CMC 360
Global CMC and Change Management Services

CLIENT
Top 3, Fortune 50, $40+ Billion Pharma / Consumer Company

GEOGRAPHY / LOCATION(S)
South Africa, Ghana, Kenya, Namibia, Zimbabwe, Zambia, Mauritius, Tanzania, Botswana, Nigeria, Uganda, Malawi

FUNCTION(S)
Regulatory Affairs – CMC

SERVICE(S) / SOLUTION(S)
Variation

THERAPEUTIC AREA(S) / INDICATION(S)
Hemorrhoids / Other Anorectal Conditions

PRODUCT(S)
OTC / Consumer

TECHNOLOGICAL ENVIRONMENT
Documentum, Lorenz DocuBridge, EURS Validator, Lorenz Validator

BENEFIT HIGHLIGHTS
- Over 60% Savings on Cost of Compliance
- Established and Streamlined Master Dossier Management Process

Business Imperatives
- 24 CMC Variations (amendments) for established medicinal product for treatment of hemorrhoids and other related anorectal conditions in 12 African countries

Challenges
- Coordination across local markets
- Distributed country specific source documents
- Coordination with the proposed drug product manufacturing sites
- Country specific publishing requirements

Freyr Solutions & Services
- Harmonizing country-specific dossiers for 12 African countries
- GAP Analysis
- Assessment of dossiers across all countries
- Assessment and remediation of gaps between current drug product manufacturing and the proposed drug product manufacturing changes
- Master Dossier Creation for Module 2 & 3
- Country Variation
- Country specific variations from master dossier - Applications forms, cover letters and GMP documentation from respective Module 1

Client Benefits
- Cost Savings of 60% and upwards
- Established streamlined process for managing future change controls impacting the African countries

Legacy Product Management
End-To-End Regulatory Lifecycle Ownership

Freyr 360

End-to-End Regulatory Life-Cycle Management

To know more, reach us at **+1 908 483 7958 / +44 2037 012379**
Drop a mail at **sales@freyrsolutions.com**

Freyr Expands Its Global Footprint in EU

"I see it as another feather in our cap and it's the result of the collective effort of every individual associated with Freyr."

As an integral part of its global expansion strategy, Freyr establishes its 2nd operations center in Germany (Hanau, Frankfurt-Main) in EU after Maidenhead, UK, leading the company's effort to address the challenges in the ever-evolving regulatory arena in the region. Freyr Life Sciences GmBH will provide client services, localized regulatory strategies and tech-driven solutions in addition to the complete spectrum of Regulatory Solutions and Services to our clients and prospects in the EU. Freyr has touched another milestone with this new endeavor following the remarkable growth over the past years.

Freyr will embark its focus on emerging business opportunities with the new customers in the region as well as fostering the regulatory requirements of the existing ones. Equipped with best-in-class infrastructure and trained experts, Freyr aims to provide its customers, accelerated value-added solutions. Leveraging on its Centre of Excellence, Freyr anticipates catering to a wide spectrum of critical regulatory functions in different geographies, for small, medium and large companies in the EU. Freyr's strategy is to provide continuous compliance services to meet the challenges of the dynamic regulatory space by collaboration of high-quality service and low delivery cost.

"I see it as another feather in our cap and it's the result of the collective effort of every individual associated with Freyr. With the opening of this new office, we would help our European customers to handle the dynamic regulatory requirements and expand their business ventures across different regions in the EU. We hope to address the needs of companies seeking a reliable regulatory partner with our consistent approach. Freyr Life Sciences GmBH is an evidence of our aspiration to building a deep-rooted presence in the European Pharma Regulatory market and to invest in enduring customer relationships", said Rajiv Rangan, Co-CEO, Freyr at the opening ceremony.

i4Farmers, a Freyr's Corporate Social Initiative, featured in THE HINDU Paper

THE HINDU Hyderabad, 17 February, 2016

Freyr got recognition in The Hindu for its exceptional guidance to farmers on cost-effective agricultural approaches. Not only that, to lay a strong foundation for growth, Freyr supports education opportunities in rural areas for the underprivileged.

The Hindu quoted, "A group of NRI software professionals is adopting families of farmers who committed suicide and providing them social security."

i4Farmers is a joint initiative taken by five NRI software professionals that emerged as a ray of light for the families of distraught peasants who have taken their lives failing to cultivate abundant crops and paying the rising debts. On behalf of Freyr, Srinivasa Sadhu and Srinivas Ranabothu are doing their bit by adopting a family each and addressing their basic trepidations. In the interview with The Hindu, Srinivas Ranabothu, one of the founder-members of i4farmers said, "We try to get to the root cause of a farmer's death in each adopted family and give social security to the wife and children."

The incoming monetary support is capitalized in a very effective manner that not only addresses their basic troubles but also arrange for agricultural training to make best out of what they have. The tribal farmers who were inclined to cultivating BT cotton were given advice to shift towards food crops like jowar and rice that eventually turned into a blessing for them.

As another part of this program, the team is sponsoring the education of a total of 110 students from different regions of Telangana and Andhra Pradesh. Going forward i4Farmers will bring together some alternative resources of livelihood along with practical trainings, teaching the traditional farming practices for farmers and help them get a decent price at the market for their produce.

The end result of this venture has surprised everyone. An idea that originated over a cup of tea, spread like a ray of hope for these families. It is a sheer outcome of altruistic efforts, no-family weekends and resolute commitment of the team that brought million dollar smiles on the faces of those broken houses.

CELEBRATING NEW CLIENT WINS

As an organization, we at Freyr, have always placed the highest value on our business associations and partnerships.

It has been our guiding principle to identify newer opportunities and create exceptional engagement excellence for our clients that transform into long-term relationships.

As always, it is a great pleasure to announce the **new wins** of this quarter.

EFFECTIVE AND STREAMLINED IDMP SERVICES FOR A JAPAN-BASED PHARMACEUTICAL COMPANY

CSR PUBLISHING SERVICES FOR A LEADING GLOBAL HEALTHCARE CONSULTING & ADVISORY FIRM

SUCCESSFUL HARMONIZATION OF LABELING UPDATES FOR A US BASED, GLOBAL $50+ BN, PHARMACEUTICAL COMPANY

STRATEGIC ARTWORK SERVICES FOR US BASED, GLOBAL $50+ BN, PHARMACEUTICAL COMPANY

IDMP IMPLEMENTATION FOR A LEADING US-BASED BIOPHARMACETICAL COMPANY

STRATEGIC RESOURCE ALLOCATION FOR CMC SERVICES TO A GLOBAL TOP 3 CONSUMER HEALTHCARE COMPANY

- Support for CMC staff augmentation by providing ample resources for filling strategic and key roles in a Global top 3 consumer healthcare company.
- Focusing to help clients effectively meet their CMC regulatory requirements with a clear understanding of expectations.

END-TO-END ASSESSMENT SERVICES FOR COSMETIC CLAIMS TO A UK-BASED, FAST GROWING COSMETIC PRODUCT COMPANY

- To review cosmetic claims in the US for 45 products across multiple markets

STRATEGIC SUBMISSION SERVICES IN CANADA FOR UK-BASED COMPANY

- Freyr bags a strategic submission and publishing project from a leading UK based pharmaceutical company. We will be providing NeeS submission and publishing services for Canada.

END-TO-END ASSESSMENT SERVICES FOR COSMETIC CLAIMS TO A UK-BASED COSMETIC COMPANY

- Freyr to provide assessment services for Cosmetic Claims to a UK based, Fast growing Cosmetic Product Company. We are helping the client in reviewing cosmetic claims in the US for 45 products across multiple markets.

COMPREHENSIVE SUBMISSION AND PUBLISHING SERVICES IN OMAN FOR US-BASED COMPANY

- Freyr to deliver end-to-end submission and publishing services to a US based healthcare company, helping them to shift from NeeS to eCTD submission in Oman.

Client Visit

1

Freyr was pleased to welcome the 5th Largest Specialty Generic Pharmaceutical Company for Quality Audit of Labeling Process.

2

It was an honor to welcome 4th of the Top 10 Pharma companies in India for understanding Freyr's competencies in the regulatory labeling arena.

3

Freyr welcomed a South Korea based, Global $ 600 MN+ Pharma company and discussed the existing CMC project and new business prospects related to Medical Writing, Labeling and Artwork, Audit & Compliance and Regulatory Intelligence Services.

4

One of the largest Canadian-owned Pharma company visited Freyr facility to explore Freyr Artwork capabilities and discuss business standpoints.

5

Freyr was glad to welcome a UK-based, fast growing cosmetics products company to discuss business facades for Cosmetic Claims Review services across multiple markets.

Rewards & Recognitions

Freyr conducted Rewards and Recognitions for Quarter 1 to acknowledge employee efforts towards accomplishment and implementation of projects successfully. These appreciations were handed over to employees who went an extra mile in different categories like Target Oriented Performance, Critical Incident Performance, Deadline Meeting Performance, Innovative Performance, and Client Appreciated Performance.

Annual Awards














Funtastic **Pongal**

Freyr began it's yet another year howling Pongal-O-Pongal. The blend of rice, jaggery, cashews, raisins and that generous splotch of ghee was brought together in the form of a Rangoli competition. As always our fervent Freyrians stepped out in the full glory of festival through vibrant colors of rangoli. It was incredible to see how everyone apart from the participants spliced in the fiesta feel in their own ways by decorating our Freyr House with their exquisite artistic tinges.

Sieze the **Moment**

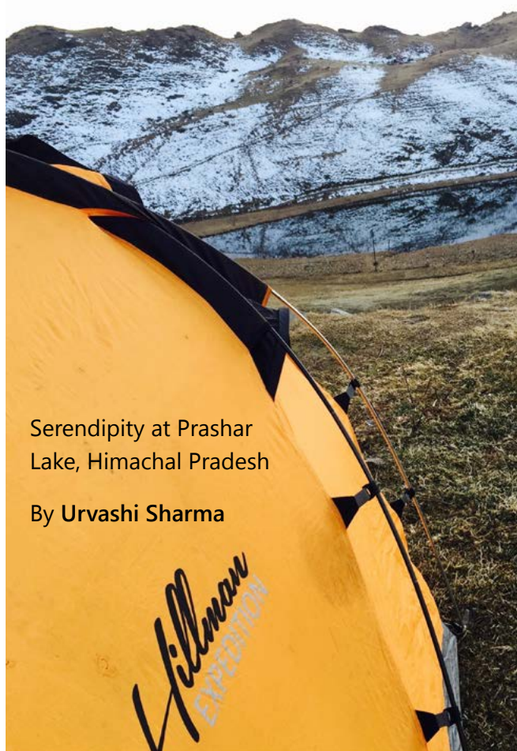
For, some photography is a passion, for some a profession and for the rest, a way to capture a moment to be cherished all their lives. Heading with the idea of seizing the moment, Freyrians shared some of the breathtaking moments captured in their cameras with us. Enjoy the snapshots.

The Mighty Himalayas

By **Urvashi Sharma**

Be happy for no reason & spread smiles where ever you go

By Sindhuja.M



Serendipity at Prashar Lake, Himachal Pradesh

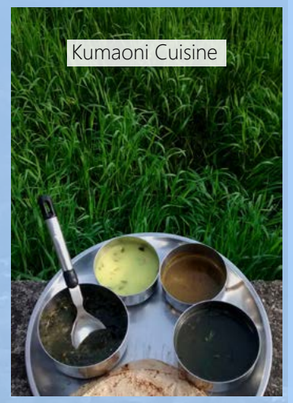
By **Urvashi Sharma**

Travelogue

Postcards from the Mountains

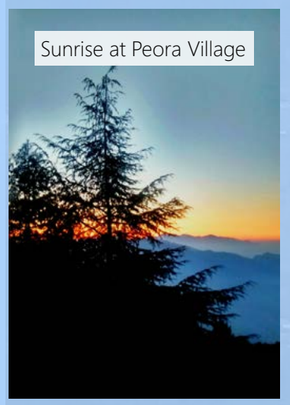
If only pictures could speak, they would languidly tell you mist-laden tales of what it felt like to be in toy-bright lesser known villages of Kumaon, Uttarakhand. This winter; miles away from the touristy hotels and baggage and chatter, I sipped the divine tonic of wilderness. Watched the dawn blossom into light, breathed in the musty smell of crushed leaves while walking through the woods, stuffed my hands with pine cones, picked bright yellow flowers and magpie feathers and intricately woven nests, and slept under a clear star-lit sky watching the distant hills wrapped in fairy lights. And even though my humble camera couldn't do quite the justice and I'm yet to spot just the right words, this is all I have for now. To inspire you all to go there, be there, and walk gently and quietly deep within those profound surroundings.

Kush Mukherji



Kumaoni Cuisine

Peora Dak Bunglow



Sunrise at Peora Village

How did I reach there?

Board a train/ flight from Hyderabad to New Delhi. Take the Ranikhet Express to Haldwani. Bus or shared taxis would take you to my first stop Kanda village (Bageshwar district), approximately 100 kms beyond Almora. My next destination, Loharkhet & Chaura village, lay almost 80 kms beyond Bageshwar town towards the renowned Pindari glaciers. A shared taxi from Kanda would take you there. Peora village lies close to 50 kms from Almora town towards Haldwani.

Places I Went : Kanda

With the concept of 'voluntourism' picking up fast in India, I indulged in one such travel volunteering project during this trip. A local NGO named R.O.S.E (Rural Organization for Social Elevation) works at grassroots level in a cluster of mountain villages close to Almora to improve health, education and the quality of life of rural

Kandha Village

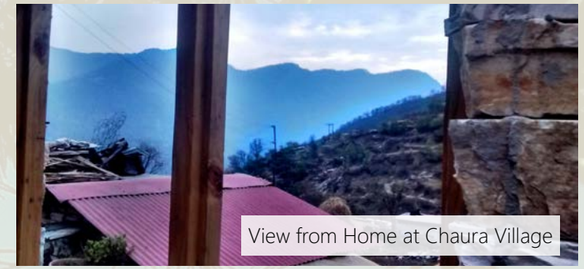
Kumaon. Teaching a happy bunch of enthusiastic kids, participating in myriad community services, exploring the scenic landscapes and spending long evenings chatting away with ever friendly villagers

Kandha Village Children

was all part of the delightful combo. The lovely hosts, Mr. Verma and family, besides serving us with delectable Kumaoni special meals and organizing nearby sightseeing tours, walked an extra mile to ensure we had a comfortable stay all through. Just in case I managed to pique your interest, here's where you can contact the host: **jeevanverma@rosekanda.org/ 08954868561.**

Kandha Village

Loharkhet/ Chaura: The sheer joy of being in a quaint little village sandwiched between the mighty mountains and lofty meadows, dense conifers and sprawling mustard fields, 8000 ft above sea level, is impossible to put into words. The Loharkhet



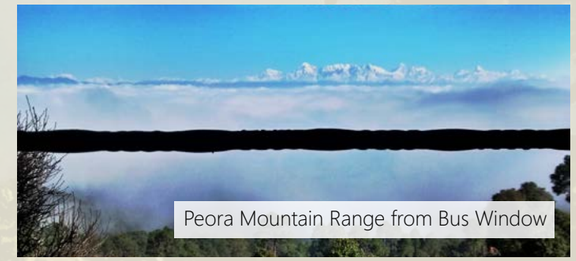
View from Home at Chaura Village

and Chaura villages may be mere pit stops during the daunting Pindari glacier trek, but its magnificent unspoiled terrain remains a thing of beauty and a joy forever. I stayed with a local family, and needless to say, it was an experience of a lifetime. Amidst the bursts of clouds and patches of sun, smell of wood fire lurking in the air, a humble meal of spicy egg curry and mountain rice, low thatched stone roof, a 100 watt bulb in my humble room, and villagers gathered around the bonfire for an evening deeply soaked in folk music and eerie ghost stories, I wondered what else is true contentment if not this. In case this place sounds enchanting

Top of Mukteshwar Mountain

enough, there's a KMVN resort out there as well at your disposal.

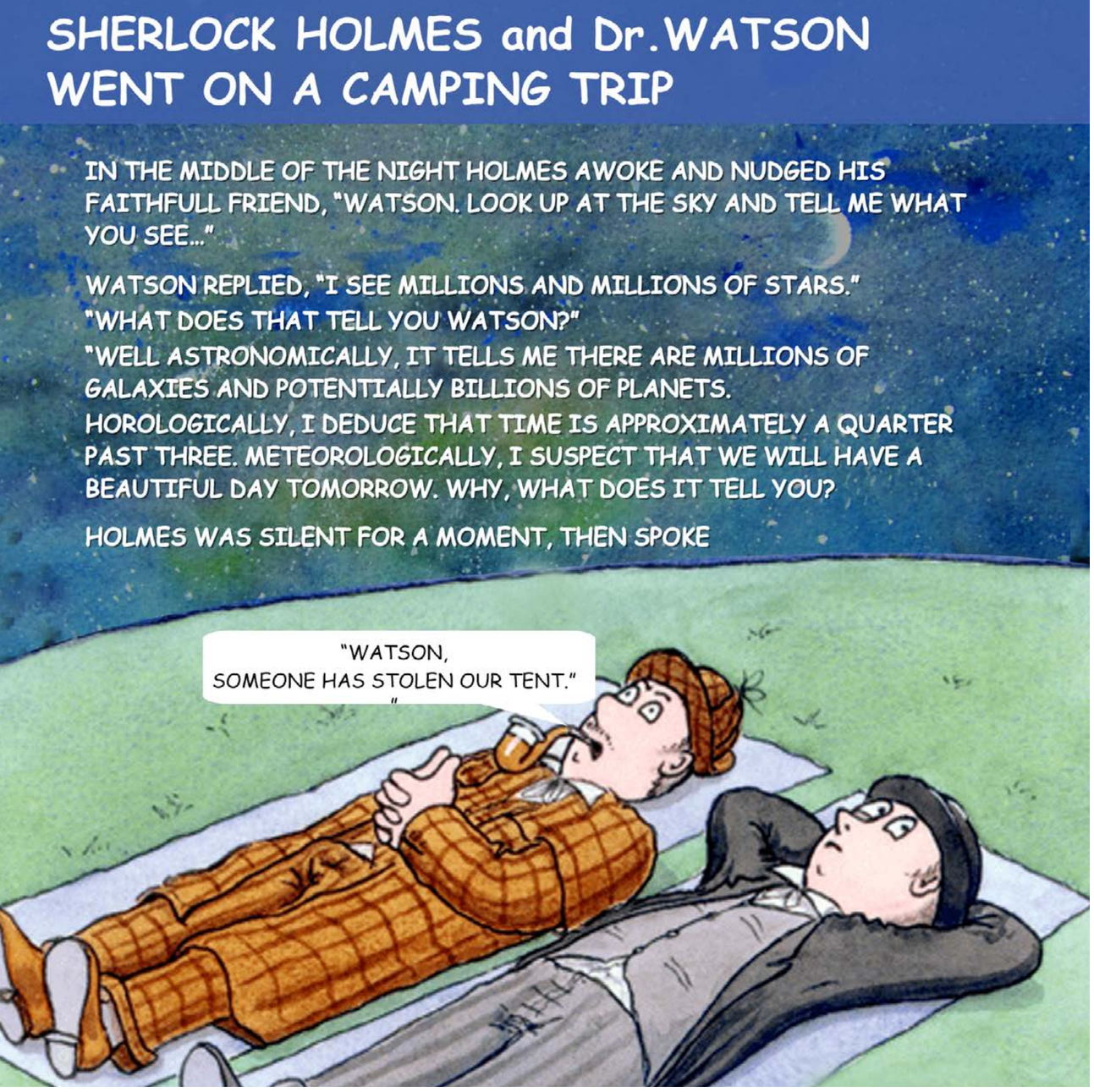
Peora : If you want to spend a laidback holiday soaking in views of the majestic Nanda Devi, Trishul and Panchachuli peaks, having soupy Maggi in the balcony of Mama's shop, playing carom with the locals, taking long walks through the dense coniferous forests, trekking to nearby villages, day trips to Mukteshwar (approx 17



Peora Mountain Range from Bus Window

kms away), stargazing or volunteering with Aarohi- a reputed local NGO since 1992, this sleepy hamlet is your place to be. I stayed at the tastefully restored century-old Dak Bungalow out here in the company of my lovely hosts, Pradeep & Shubha. For more details about the place,

email: untravel@indiauntravelled.com.



by **Kush Mukherji**

Regulatory Intelligence is not just about knowing the correct information;

it is actually about...

Accuracy, Relativity & Actionability of the information

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