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Organisation of Pharmaceutical Producers of India

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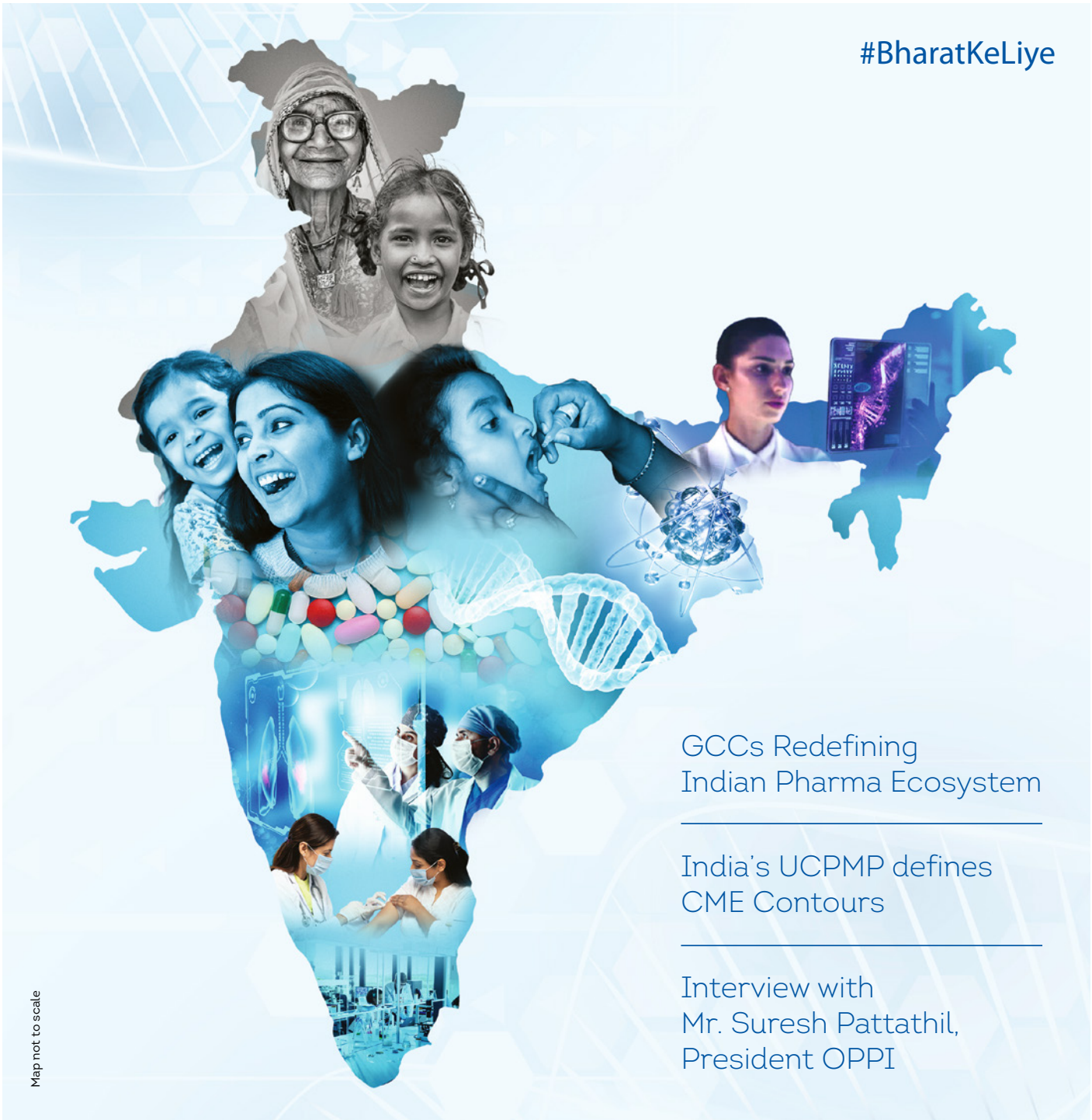
Inaugural Issue - September 2024



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Foreword

Anil Matai
Director General, OPPI

Welcome to the First Edition of The OPPI Quarterly Newsletter!

I am pleased to present the very first edition of the Organisation of Pharmaceutical Producers of India's (OPPI) Quarterly Newsletter. This marks the beginning of an exciting new chapter for OPPI as we launch this initiative in collaboration with Citeline. This exclusive newsletter aims to inform you about the latest developments and strategic priorities within our dynamic industry.

Each edition will bring you valuable insights from industry experts, updates on the ever-evolving regulatory landscape, and a closer look at OPPI's advocacy efforts to drive innovation, uphold quality standards, and ensure ethical practices with the key trends and innovations shaping the future of healthcare in India. Our goal is to keep you connected with these trends and innovations.

I am confident that this newsletter will serve as a valuable resource for us all as we continue to work together toward a healthier and more innovative future.

I look forward to sharing these insights and embarking on this journey together.

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India's Revised GMP Norms: Can It Separate the Wheat from the Chaff?

India has recently implemented revised Good Manufacturing Practices (GMP) norms under Schedule M of the Drugs and Cosmetics Rules, raising the bar for quality and compliance in the pharmaceutical sector. These updated norms are set to weed out non-compliant players and improve the overall standard of pharmaceutical production in the country.

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Gaps Found in Most Pharma Trial Diversity Policies

A recent study has highlighted significant gaps in the diversity policies of pharmaceutical trials. While most large pharma companies have a publicly available policy on clinical trial diversity, many still fall short of incorporating key recommendations from regulators like the FDA. The findings suggest a need for more comprehensive policies to ensure trial enrollment better reflects the patient populations that will use these medicines.

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EU Helps Firms to Prioritize Submission of Data on Critical Drugs

The European Medicines Agency (EMA) has introduced a new list of critical medicines to help companies prioritize the submission of essential product data. This initiative is part of a broader effort to ensure standardized product information across the EU, particularly for managing drug shortages during health crises.

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WHO Invites Vaccine Manufacturers to Join Fight Against Growing Mpox Outbreak

In response to a growing Mpox outbreak in Central and East Africa, the WHO has initiated an emergency use listing (EUL) for two vaccines. This move aims to expedite the availability of these vaccines in lower-income countries, including those where the vaccines are not yet licensed.

GCCs Redefining the Indian Pharma Ecosystem

By Anju Ghangurde,
Executive Editor, APAC at The Pink Sheet, part of Citeline

Key Highlights:

- Expansion of major pharma GCCs in India
- Strategic roles played by GCCs in clinical trials, drug discovery, and digital operations
- The future potential of GCCs in boosting India's biopharmaceutical innovation

Foreign firms across a range of sectors are fortifying their India-based global capability centres (GCCs) as they leverage the talent base, innovation capabilities and cost advantages in the country.

Pharma is no exception and there's been a flurry of activity over the years, with leading multinational companies establishing or expanding their GCCs in India.

Anil Matai, Director General of the Organization of Pharmaceutical Producers of India (OPPI), maintained that with the establishment of new captives of GCCs by renowned multinational corporations, alongside substantial expansions of existing ones, India is now a pivotal hub for critical functions ranging from clinical trials to drug discovery.

"What sets India apart in this new narrative is its unwavering commitment to embracing cutting-edge technologies such as Gen AI, AR/VR, and IoT, thereby redefining the contours of pharmaceutical research and development," Matai observed in a recent report that encapsulates the activities of 13 leading global pharma GCCs in India.

Most leading research-based multinational companies including Pfizer, Sanofi, Roche, GSK, Merck, MSD, Novartis, Novo Nordisk, Ferring, Eli Lilly, Bayer, Bristol Myers Squibb (BMS) and AstraZeneca have invested in GCCs in India. These centres are versatile and engaged in a range of activities spanning the complete R&D value chain, drug commercialization, manufacturing and supply chain, physician and patient engagement, business strategy, and digital operations.

Here's a snapshot of activities at the GCCs

- Novartis was among the early birds setting up a GCC in Hyderabad around 15 years ago. Recently renamed the Novartis Corporate Centre (NOCC), it contributes to the Swiss group's purpose of 'reimagining medicine'. The centre provides specialist support services across multiple functions and capabilities including drug development, data, digital & IT, manufacturing supply and quality, finance, risk and compliance.

- The Lilly Capability Centre India (LCCI), set up in 2016, similarly supports and provides solutions for various functions, including clinical trials, technology, commercial, and core services. The technology functions at LCCI, for instance, provide cloud, automation, advanced analytics, data science, artificial intelligence, software product engineering and information security solutions and services to support the digital transformation and innovation of Lilly's business units and functions.

- Bayer's Center of Excellence for Pharmaceuticals in Hyderabad caters to surging global demand for data sciences and analysis enabling the German multinational to focus on excellence in the execution of clinical trial deliverables and also contribute to industry leading solutions in analytical trends and methodologies. India also contributes to AI/ML projects for Bayer's global R&D.

- The GSK Global Capability Centre, India supports a range of global functions and pharma R&D. With over 2500 employees, the GCC boasts talent across R&D, digital & technology, people services finance, procurement, legal contracting network and transformation. Activities at the Bengaluru centre also encompass critical R&D aspects such as data management, medical writing, study delivery of assets, system validation, quality control framework and laboratory management support within the clinical operations segment.

- The Merck Healthcare R&D India hub established in 2020 as an Excellence Center is focused on leveraging the talent pool and technological advances in India to empower and accelerate innovation, ensuring that more medicines reach patients faster. It supports the global team in a range of disease areas such as oncology, fertility, endocrinology, neurology, immunology, and general medicines. Several key functions that are critical across R&D are supported by the hub including global regulatory affairs, global patient safety, global development operations and statistical programming.

- MSD's dedicated Insights, Analytics & Data centre in Pune, India catalyses the power of data and analytics to improve patient and business outcomes worldwide. Set up in 2022 at an investment of over $16m, the hub provides a range of near shore capabilities. These include driving personalized engagement, strategic forecasting, application of digital and web analytics, driving health equity work, optimizing investment, and providing market performance analysis to businesses in the Asia-Pacific, Europe, and Africa at MSD (known as Merck & Co Inc in the US and Canada).

- The Novo Nordisk Global Business Services in India began as a transactional service centre for finance, patents, and data management way back in 2007 but has since evolved to encompass core services pertaining to commercial affairs, supply chain, quality and development, among others. With over 4000 full-time employees supporting global business needs, the centre offers solutions in a range of areas including medical/regulatory affairs, safety operations, clinical reporting, biostatistics, drug development and supply chain.

- Pfizer's Global Drug Development Centre in Chennai functions as a crucible for the development of complex sterile injectable formulations and device combination products, driving the US multinational's quest for groundbreaking medical solutions. It is spearheading transformative research tailored for global markets, with a thrust on small molecules, innovative formulations, and active pharmaceutical ingredients. With an expansion in headcount and capabilities lined up, Pfizer expects the centre to redefine healthcare paradigms in the coming years.

- Roche is leveraging India's engineering talent

and robust technology ecosystem to advance in the digital sphere, with innovative solutions that resonate on a global scale. The Roche Information Solutions (RIS) at Pune, is a key site for RIS globally, and has emerged as the company's healthcare digital Centre of Excellence (CoE). The Swiss group's Offshore Development Center (ODC) in Chennai, partnered with ZS Associates, consolidates existing data and analytics business operations services of all Roche Pharma affiliates at one place, while Roche Services and Solutions (RSS) India, an analytics and technology CoE, buttresses expertise around technological advancements in the healthcare space, via utilization of AI/ML concepts.

- Sanofi's GCC in Hyderabad supports the medical, digital, commercial functions, among others. With 800 employees on its roster and plans for further expansion, its current key capabilities span scientific writing, data analytics, biostatistics and statistical programming. In addition, R&D activities at Sanofi's Goa site and ongoing research at this CoE covers new product development, lifecycle management of established products, new dosage forms and formulations for easy administration, supports R&D projects and delivers technology transfer to commercial sites, troubleshooting for industrial sites, product harmonization, process improvements and robustness, amongst other functions.

- The Ferring Hyderabad Product Development Centre (FHPDC) in Genome Valley, Hyderabad, counts as one of the group's 10 global R&D sites. With a thrust on Ferring's key therapy areas namely reproductive medicine and maternal health, uro-oncology and gastroenterology, FHPDC has been working on the concept of "local to local" and "local to global" product development and its capabilities also extend to areas like innovative packaging solutions, clinical and non-clinical development and regulatory submission.

More GCC Action – India at The Fulcrum

Further momentum appears to be building up in the GCCs space as they drive efficiencies, contribute to innovation and derisk operations.

In February this year, Bristol Myers Squibb announced the official opening of a new facility in Hyderabad which is expected to expand the company's global drug development and IT and digital capabilities and take on board over 1,500 employees.

The new site, which entails an investment of over $100 million, expands Bristol Myers Squibb's global footprint and will serve as an innovation hub, as the company "writes the next chapter in its history," the US multinational said at the time. Bristol Myers Squibb already has an R&D site in Bangalore, in partnership with Syngene International, which supports target identification, lead discovery and optimization, among other activities. Close to 1000 people are engaged in activities at the R&D centre.

More recently AstraZeneca unveiled plans to expand its Global Innovation and Technology Centre (GITC) in Chennai, Tamil Nadu, a move which is expected to create close to 1,300 highly skilled job opportunities by 2025. AstraZeneca is investing $30 million in the expansion effort.

Currently, about 38 pharma GCCs in India are estimated to employ over 75,000 people. A report by OPPI- EY Parthenon earlier underscored that GCCs also contribute to India's innovation ecosystem by fostering talent and skill development across the value chain, especially in "intricate and strategic domains".

McKinsey & Company senior partner and lead, life sciences practice (Asia), Sathya Prathipati, believes that India can build on the GCC momentum and talent base to boost the wider biopharmaceutical innovation ecosystem in several ways.

He called for an increase in collaborations between the global leaders and local players so that "there is a way to develop the knowledge institutionally."

"The GCC opportunity is a real here and now for India. Not just because of the advantage that GCC's provide on cost and a lift to margin, but increasingly because of the speed, agility and best in class ways of working as we are seeing across industries now," Prathipati told Citeline in an interview recently.

More widely across sectors, India boasts more than 1580 GCCs, which engage over 1.66 million professionals.

Last year, a report by Nasscom, the industry association for the technology sector in India and the global management consultancy and strategy advisory firm, Zinnov, outlined how the Indian GCC ecosystem had become a sandbox of innovation, technologies, and transformation for global companies that are driving organization-wide initiatives.

"GCCs are also being entrusted with the responsibility of setting up new centres in other locations, thereby diversifying and mitigating risks. This shift in strategy reflects GCCs' deep understanding of the intricacies involved in setting up newer centres from the ground up, but also showcases the deep autonomy that HQ organizations are tasking their Indian GCCs with," the duo's biennial report noted.

Interview with Suresh Pattathil, President OPPI

By Izabela Chmielewska,
Managing Editor, Custom Content at Citeline

Key Highlights:

- The inspiration behind the newsletter launch
- Regulatory changes impacting the industry
- The importance of ethical conduct in pharma
- OPPI's role in promoting higher standards of ethics and quality
- Future challenges and opportunities for the Indian pharmaceutical sector

In this interview, Mr. Suresh Pattathil, President of the Organisation of Pharmaceutical Producers of India (OPPI), discusses the strategic priorities and initiatives shaping the future of the Indian pharmaceutical industry.

He elaborates on the newly launched newsletter, regulatory changes and compliance, the industry's ethical conduct, manufacturing standards, and OPPI's role in fostering innovation and quality.

Mr. Pattathil outlines OPPI's three pillars of advocacy for the upcoming year, i.e., Healthcare Access, Quality, and Innovation while providing an outlook on future challenges and opportunities within the sector.

What inspired the launch of this newsletter and what are the key objectives you aim to achieve with it?

When discussing the newsletter, we wanted to ensure that it effectively communicated OPPI's work to key stakeholders. Our member companies need to know what we are doing in terms of advocacy and other work.

We also wanted to address external stakeholders who are not directly related to OPPI by ensuring they understand our key areas and initiatives. The newsletter aims to provide regular updates on our activities and future.

Through this newsletter, we hope to establish a regular touchpoint to share our activities and plans and foster a well-informed community around OPPI's initiatives. We also wish to promote our mission of achieving 'Healthcare for All' through collaboration and innovation.

Regulatory Changes and Compliance

Could you explain the recent regulatory change that has made the Uniform Code for Pharmaceutical Marketing Practices (UCPMP) to be followed by the entire pharma industry in letter and spirit, and what are its implications?

The UCPMP has been a voluntary code of conduct for the past few years. The Indian government has now decided to implement it, which is a welcome move. By introducing the UCPMP, the government has taken a pivotal step towards fostering transparency and ethical practices within the industry. These ethical and compliant marketing practices are crucial to ensuring patient interest is taken care of. This is an easy transition for multinational and global pharmaceutical companies, as they have always followed these standards.

The regulatory change is significant because it ensures that all pharma industry players meet high ethical standards. UCPMP 2024 is also aligned with international standards and incorporates stringent guidelines that companies must adhere to when engaging with healthcare professionals, promoting their products, and conducting educational and research activities. For smaller companies, this will enforce a higher standard of conduct, aligning them with practices that many global companies already follow.

Conduct and Industry Growth

How do you envision the new compliance code impacting the ethical conduct of players in the pharma industry and contributing to its growth?

The implementation of the updated UCPMP will significantly enhance ethical conduct within the pharma industry. By mandating strict adherence to ethical guidelines, the code seeks to mitigate unethical marketing practices, thereby fostering a more transparent and accountable industry environment.

The new compliance code will emphasize ethical practices and ensure all players adhere to UCPMP in letter and spirit.

Enforcing this compliance code sets a high bar for ethical conduct – We need to do the right thing every single time. This focus will build trust and integrity, which are essential for the sector's long-term growth and sustainability.

Manufacturing Standards, Quality Issues and Regulatory Actions

What challenges do Indian manufacturing facilities face in aligning with the World Health Organization's (WHO) standards, and how are these being addressed? Additionally, what recent regulatory actions are concerned with compliance with WHO's Good Distribution Practices (GDP) and revised Good Manufacturing Practices (GMP) in India?

OPPI has consistently advocated for minimum WHO GMP norms. The new Schedule M aligns with these norms and is now mandated by the Central Drugs Standard Control Organization (CDSCO). The challenge for smaller and mid-sized players is the investment required to meet these standards, including capital investments, training, and hiring capable people for quality functions.

Aligning with WHO GMP standards is crucial for ensuring the quality and safety of pharmaceutical products. While larger companies may already meet these standards, smaller and mid-sized facilities face significant challenges in terms of investment and training. The government and organizations like CDSCO are actively working to provide the necessary training and support to help these facilities comply with the new regulations.

OPPI's Role and Member Companies

How does OPPI contribute to promoting higher standards of ethics and good manufacturing practices among its member companies?

Most of our member companies either have their own manufacturing facilities or work with large contract manufacturers. We directly impact over 100 manufacturing facilities, ensuring they follow global quality norms that are often stricter than local regulations.

Quality and innovation are our bread and butter. We train our contract manufacturers and ensure that they are audited at regular intervals by global teams. These third-party audits ensure the manufacturing quality is on a par with products made in any other developed country.

For OPPI, patients are at the forefront of everything we do. By focusing on quality and ethics, we ensure that member companies and their contract manufacturers uphold the highest standards, thereby ensuring that patients receive the best possible products.

Our members have adopted UCPMP 2024 to ensure ethical drug promotions and marketing. We are consistently coordinating with the pharmaceutical industry and the government to ensure that the UCPMP 2024 Code is being adhered to and there are no hurdles in implementation.

Future Outlook

What are your priorities for the organization in the upcoming year?

We will continue to prioritise our three pillars of advocacy: Innovation, Access and Quality. Regulatory and policy changes are also in focus for OPPI.

Innovation

Intellectual Property

The first pillar is crucial because innovative global pharmaceutical companies invest billions of dollars to bring products from the lab to the market, a process that can take 10-12 years. Consequently, the effective patent period is reduced to about 8-10 years, making Intellectual Property IP protection vital to ensure that future innovation continues.

This pillar is essential for India to advance up the discovery ladder. While India is already the world's third-largest pharmaceutical producer by volume and fourteenth by value, there is a need for more innovation originating from India. For instance, Sun Pharma's recent approval of a new innovative product for alopecia in the U.S. is a positive development.

Access

The second pillar focuses on improving healthcare availability. We collaborate with the government on initiatives like Ayushman Bharat, which covers the

hospitalization costs. Expanding this coverage to include non-communicable diseases like diabetes and hypertension is essential. We also advocate for mechanisms to extend healthcare coverage to the segment of population known as the 'missing middle' which cannot afford private healthcare and is currently not covered by Ayushman Bharat. This 'missing middle' segment consists of 40% of the population and currently lacks sufficient health coverage.

When innovative products are launched in India, a small percentage of patients (around 5-10%) can currently access them due to their high costs. We are collaborating with the government to develop solutions that will increase access and ensure that a larger number of patients can benefit from these advancements in healthcare.

Quality

The third pillar is improving the quality of the manufacturing, ensuring that manufacturing processes meet international quality standards, and that the distribution of pharma products is conducted safely and reliably. OPPI member companies can significantly contribute to enhancing quality and fostering innovation within India.

Regulatory & Policy Changes

Operational efficiencies, regulatory processes, and key policy changes impacting patients are some areas that are being addressed by us. We remain committed to focusing on, access, quality, and innovation to ensure OPPI positively impacts patients in India. As the population ages, with approximately 100 million people over 65, addressing their healthcare needs will become increasingly important. OPPI aims to play a supportive and active role in contributing to the healthcare ecosystem and improving patient outcomes in India.

Recognizing the importance of pharmaceutical R&D, OPPI is dedicated to bolstering research initiatives. Central to this effort is the need to reward and incentivize innovation, which is essential for building a robust R&D ecosystem in India. OPPI emphasizes the three Cs–convergence, collaboration, and co-creation–across the pharma industry. This approach fosters a dynamic and unified sector, promoting shared progress and partnerships. We look forward to the government's continued support and strategic initiatives to foster a robust and innovative pharmaceutical sector in India. We are confident that these measures will accelerate R&D and innovation, ultimately leading to a healthier, more resilient, and self-reliant India.

The pharmaceutical sector in India needs to move from 'Make in India' to 'Discover and Innovate in India' making the country self-reliant and channeling our efforts towards sustainable healthcare solutions for ***Bharat Ke Liye.*** By focusing on these priorities, OPPI aims to significantly contribute to India's healthcare advancements and support the nation's journey towards innovation and self-reliance in the pharmaceutical sector.

India's UCPMP Defines CME Contours

By Anju Ghangurde,
Executive Editor, APAC at The Pink Sheet, part of Citeline

Key Highlights:

- Mandatory self-declarations for companies
- Prohibition of CME/CPD programs in foreign locations
- Enhanced disclosure requirements for CME expenditure

Months after India put out its revised Uniform Code for Pharmaceutical Marketing Practices (UCPMP), dozens of leading domestic and multinational firms have made the requisite self-declarations, signalling compliance with the new requirements.

The updated UCPMP 2024, which essentially builds on the 2014 version, expands disclosure requirements for industry's interactions with healthcare professionals and lays down a framework for continuing medical education (CME) programs that includes enabling provisions for an audit of such initiatives.

The new norms required executive heads of companies to submit a self-declaration in a specified format within two months of the end of every financial year to their industry association for uploading on their website, or directly on the UCPMP portal of India's Department of Pharmaceuticals in case the firm wasn't a member of the industry body.

Dr. Arunish Chawla, Secretary, India's Department of Pharmaceuticals (DoP), at an interaction with the media at a recent industry event, maintained that industry was implementing the new norms "in letter and spirit".

"We've already started getting in declarations. We are setting up a portal where declarations can be filed. And the feedback that we get is that it is making a difference and going forward it will only strengthen," Dr. Chawla said.

New Code Is Quasi-Statutory

Importantly, while UCPMP 2014 specifically indicated it was voluntary in nature, the updated 2024 version has no reference to that terminology.

Legal experts pointed out that the tone and tenor of language used in UCPMP 2024 - phrases like "shall be," "must be" – lack a qualification as to the voluntary nature of the code and indicate a "more directive-oriented," rather than suggestion-oriented, approach. "The new code comes across as more mandatory than voluntary in nature," a note by Cyril Amarchand Mangaldas, a leading law firm, had earlier noted.

DoP's Dr. Chawla, in an interview with CNBC-TV18 on 1 April, stated that the new code is mandatory and quasi-statutory. "A reputational play is the best defence against unethical marketing practices – that's what the code tries to achieve," Chawla underlined at the time.

One industry veteran told Citeline that UCPMP 2024 will bring about "some kind of discipline and awareness" across industry, though strict enforcement will be pivotal in determining its effectiveness.

CMEs/CPDs In Foreign Locations Prohibited

Among a string of important requirements, UCPMP 2024 bars the conduct of CMEs and continuing professional development (CPD) programs at "foreign locations" and also requires pharma to come clean about the details of such events conducted by them, including expenditure incurred, on their website. Such activities can also be subject to an "independent, random, or risk-based audit, " as per the new UCPMP.

Entities incurring expenditure on such events, as well as participants and speakers, must comply with the relevant provisions of India's Income Tax (IT) Act, the updated code adds.

Some senior pharmaceutical industry officials have expressed concern about the potential for misuse of such data; More so the new code keeps the door ajar for IT scrutiny or interpretation, they pointed out, while supporting the enforcement of the code overall.

UCPMP 2024 also requires organizers of CMEs/CPDs to "explicitly spell out" the procedure followed to select participants and speakers, while displaying a statement of their funding sources and expenditures on their website, which may be subject to a "special audit."

It remains to be seen how the new CME requirements, especially disclosing expenses in the public domain on websites, is implemented and whether the government will specify the scope and granularity of disclosures required given industry's apprehensions.

In addition to pharma companies (including their trusts/associations), the updated UCPMP permits medical colleges and teaching institutions, hospitals, professional associations of doctors, the National Institutes of Pharmaceutical Education and Research, laboratories of the Indian Council of Medical Research, Department of Biotechnology and the Council of Scientific & Industrial Research, among others, to conduct CME/CPD activities.

Some industry experts expect pharma companies to stop direct sponsorships for healthcare professionals (HCPs) but maintain that they can issue research grants to organizing committees or collaborate with physician associations, just as they do in the US.

The new Indian code, however, stipulates specific requirements for research support, including that the engagement of HCPs for research purposes must be for "bona fide" services, with consultancy agreements and also subject to the relevant provisions of the IT Act.

Such engagements are required to ensure that patient interest is not compromised and that the integrity of the HCP is maintained in line with India's National Medical Commission (NMC) regulations.

Industry insiders note that pharma, in general, tends to have a large pool of consultants on its roster, and the updated code could likely bolster the symbiotic industry-physician relationship in multiple ways.

Brand Reminders

UCPMP 2024 also sets limits in terms of the value of "brand reminders," while capping the value of drug samples provided to physicians.

For informational and educational items, including books, calendars, diaries, journals (including e-journals), dummy device models and clinical treatment guidelines for professionals used in healthcare settings, the code lays down that the value cannot exceed INR1,000 per

item. Such items should not have an "independent commercial value" for the HCP, it specifies.

Whether this can lid practices where expensive gifts masquerade as brand reminders remains to be seen, though some industry observers claim that requiring the giver and recipient of brand reminders to comply with the relevant provisions of the Income Tax Act, 1961, perhaps, just indirectly formalizes the practice.

Moreover, Section 5.2 of UCPMP 2024 also maintains that brand reminders from pharmaceutical companies to HCPs may not be construed as endorsement activity "if it does not amount to recommendation or issuance of a statement by a HCP with reference to use of the respective brand".

This, some industry experts claim, could give pharma some leeway to not classify their promotional items as brand reminders if endorsement action is not sought from a HCP.

Free Drug Samples

UCPMP 2024 also prescribes that an "adequate system of accountability and control" be maintained with respect to free drug samples provided to physicians.

As in the 2014 code, companies are required to maintain details such as product/doctor name, quantity of samples given and the date of supply of free samples to HCPs. In addition, the new code stipulates the monetary value of such samples should not exceed 2% of the domestic sales of the company per year.

Sample packs are to be limited to prescribed dosage for not more than three patients for the required course of treatment (as in the 2014 code), while companies cannot now offer more than 12 such sample packs per drug to any HCP per year.

Companies cannot supply a sample of a drug which is a hypnotic, sedative, or a tranquillizer – the 2014 code also covered anti-depressants in this category.

UCPMP Impact

While the UCPMP 2024 is clearly geared to raise the bar when it comes to pharma's marketing practices, some stakeholders believe the revised norms don't go far enough to address unethical practices.

The Federation of Medical And Sales Representatives Associations of India, which had earlier filed a writ petition in the Supreme Court seeking guidelines to regulate unethical marketing practices by pharma, was reported in the local media as saying the revised code lacked the teeth to penalise those it sees as "paying for prescriptions."

There was also some disillusionment given that complaints under UCPMP 2024 are primarily to be handled and decided by an Ethics Committee for Pharma Marketing Practices (ECPMP) in each industry association - blurring the lines between the offender and enforcer of the rules.

A provision for appeal against any decision by the ECPMP will lie before an Apex Committee for Pharma Marketing Practices, headed by the secretary of India's Department of Pharmaceuticals, with a joint secretary and a finance officer dealing with the subject as its members.

DoP Secretary Dr. Chawla in his interaction with the media at the industry event mentioned previously pointed out that the 2024 code encompasses various laws including the Income Tax Act.

"When infringement is found, or complaints are received, then there is a mechanism to audit and there is also a mechanism for referring such violations or infractions to the competent statutory authority," he underscored.

India's Revised GMP Norms: Can It Separate the Wheat from the Chaff?

By Anju Ghangurde,
Executive Editor, APAC at The Pink Sheet, part of Citeline

Key Highlights:

- Stricter requirements for Pharmaceutical Quality Systems (PQS) and Quality Risk Management (QRM).
- Emphasis on senior management's role in ensuring effective PQS.
- New specifics for the manufacture of sterile products, biological products, and more.

India is implementing revised Good Manufacturing Practices (GMP) norms for the pharmaceutical sector, raising the bar for quality and compliance and setting the stage to weed out dodgy players who cut corners and flout standards.

The updated norms under Schedule M of India's Drugs and Cosmetics Rules, cover GMP and requirements of "premises, plant and equipment for pharmaceutical products," and lists out specifics in a range of areas, including the Pharmaceutical Quality System (PQS), Quality Risk Management (QRM) and handling of product complaints.

Among a string of requirements for PQS, the revised Schedule M stipulates that "deviations, suspected product defects and other problems should be reported, investigated and recorded" and an "appropriate level" of root cause analysis be applied during such investigations.

Appropriate Corrective and Preventive Actions (CAPA) should be identified and taken and the effectiveness of the CAPA be monitored, it adds.

"There shall be periodic management reviews, with the involvement of senior management, of the operation of the PQS to identify opportunities for continual improvement of products, processes and the system itself. Unless otherwise justified, such reviews shall be conducted at least annually," the rules stated.

The revised norms also underscore that the ultimate onus lies with senior management to ensure that an effective PQS is in place, "is adequately resourced, and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organisation."

PQS, it notes, has to be defined and documented, with a quality manual or an equivalent documentation established, containing a description of the quality management system including management responsibilities.

"Senior management's leadership and active participation in the pharmaceutical quality system is essential. This shall ensure the support and commitment of staff at all levels and sites within the organisation to the PQS," details in the notification said.

In addition to the general principles applicable to industry under the new norms, detailed requirements have also been laid out, among others, for manufacture of sterile products, parenteral preparations (small volume injectables and large volume parenterals) and sterile ophthalmic preparations; biological products; metered dose inhalers; phytopharmaceuticals; radiopharmaceutical products and active pharmaceutical ingredients (APIs).

"Regular, Periodic Or Rolling" Quality Reviews

Building on the existing rules, the revised norms include a number of new sub-areas of thrust, including those pertaining to QRM, complaints and change control.

For QRM, which applies both proactively and retrospectively, the new rules, for instance, call for "regular, periodic or rolling" quality reviews of all pharmaceutical products, including products for export only, aimed at verifying the "consistency" of the existing process and the "appropriateness" of current specifications for both starting materials and the finished product, to "highlight any trends and to identify product and process improvements."

Such reviews should also cover, among other aspects, the qualification status of relevant equipment and utilities, e.g. heating, ventilation and air conditioning, water or compressed gases and a review of the results of monitoring the output of such equipment and utilities, as well as technical agreements to ensure that they are up to date.

Handling complaints and adverse drug reactions are other areas where specifics are set out. It requires "all decisions made and measures taken" as a result of a complaint to be recorded and referenced to the corresponding batch records.

"Complaint records shall be regularly reviewed for any indication of specific or recurring problems that require attention and might justify the recall of marketed products," the rules stipulate.

Further, the licensing authorities are required to be informed if a manufacturer is "considering action" following "faulty manufacture, product deterioration, a suspect product or any other serious quality problems with a product," it adds.

Specifics pertaining to product recalls have also been detailed in the revised norms; the regulator needs to be informed of "any intention to recall the product because it is, or is suspected of being, defective," the rules underlined.

The revised Schedule M also incorporates aspects around auditing suppliers to ensure they make the GMP compliance cut.

Those responsible for quality control, alongside other relevant departments, are required to approve suppliers who can reliably supply starting and packaging materials that meet established specifications.

Audit Procedures Initiated

The updated norms, notified on 28 December 2023, are being rolled out in a phased manner. For large manufacturers (defined as those with a turnover of more than INR2.50bn ($29.9m)), the rules come into force six months from the date of publication,

while for small and medium manufacturers (turnover less than or equal to INR2.50bn) it goes into effect 12 months from the publication date.

At an industry event late June this year in Mumbai, Dr. Rajeev Singh Raghuvanshi, Drugs Controller General of India (DCGI), indicated that audit procedures under the revised GMP norms were being initiated from 1st July.

The regulator has also undertaken risk-based inspections across around 400 manufacturing units in the country, coming down hard on more than 36% of these "because there was reason to close them," Dr. Raghuvanshi said.

"But the good part is it has moved the needle - the perception and the reality, both are changing on the ground," the DCGI remarked at the time.

Industry experts told Citeline that the inspections under the new norms were underway "as per the law and the regulator is trying to bring about change" but did not rule out "resistance" from small scale players. "But it's very important to build quality standards and the quality agenda is a very high priority for the government," a senior executive asserted.

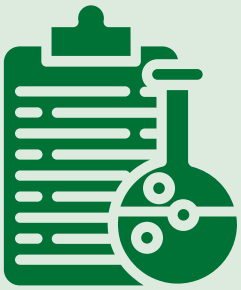
Support For MSMEs

Much of the concern around sub-optimal manufacturing standards lie in India's micro, small and medium enterprises (MSME) segment. Of the country's estimated 10,000 manufacturing units, about 80% are in the MSME space. It remains to be seen if the implementation deadline for smaller players holds or whether an extension could potentially be on the cards.

While the revised GMP norms are expected to weed out the non-compliant players, the government has also alongside initiated efforts to support medium and small firms via the Revamped Pharmaceuticals Technology Upgradation Assistance (RPTUAS) Scheme.

At the industry event mentioned previously, Dr Arunish Chawla, Secretary, India's Department of Pharmaceuticals, indicated that many medium and small units had come forward to improve and upgrade their quality and the government was set to approve the first tranche of applications.

Earlier this year, the RPTUAS scheme was expanded beyond MSMEs to include any pharmaceutical manufacturing unit with a turnover of less than INR5bn that requires technology and quality upgrades. The preference, though, remains for MSMEs and supporting smaller players to achieve high-quality manufacturing standards.



Gaps Found in Most Pharma Trial Diversity Policies

By Sarah Karlin-Smith,
Senior Writer at Pink Sheet

Key Highlights:

- Only 20% of non-large companies have a public policy on trial diversity
- Many large companies lack focus on patient input and broad inclusion criteria
- The study suggests industry groups like PhRMA could leverage more influence to enforce trial diversity

A study suggests industry groups like PhRMA could use more of their influence to hold members accountable on trial diversity policies. The average pharma company clinical trial diversity policy contains less than half of the commitments recommended by the US Food and Drug Administration, other regulators, and industry trade groups to improve the composition of their studies, a new BMJ study found.

The findings suggest the need for more comprehensive policies as the FDA is set to require diversity action plans for pivotal trials in an attempt to ensure trial enrollment more closely reflects the population of patients who will use medicines. (Also see "Diversity Action Plans Should Be Brief And Waiver Requests Filed Early, US FDA Says" - Pink Sheet, 26 Jun, 2024.) and (Also see "Diversity Enrichment: US FDA Guidance Suggests Sponsors May Need To Overenroll Key Groups "- Pink Sheet, 26 Jun, 2024.)

Despite Congress and the FDA 's new efforts, there are lingering concerns that more regulatory sticks will be needed to entice industry to prioritize trial diversity. (Also see "You Shall Not Pass:' Former Surgeon General On Why US Government Should Push Trial Diversity" - Pink Sheet, 5 Aug, 2024.) The BMJ paper stated that older adults and racially and ethnically minoritized individuals are among those still underrepresented in clinical trials. (See sidebar below.)

The study, led by Jennifer Miller of Yale University, reviewed trial diversity guidances from groups such as the FDA and the European Medicines Agency, the World Health Organization and the Pharmaceutical Research and Manufacturers of America (PhRMA), to create a reference standard with 14 components to audit industry diversity policies. (See table at the end of the story.)

Researchers looked for public trial diversity policies from 50 companies, selecting the 25 largest companies from the top 500 by market capitalization in 2021 and then randomly selecting 25 companies from the remaining 475.

Most Large Companies Had A Policy That Missed Some Areas

Twenty-six of the 50 companies selected had a publicly available policy on clinical trial diversity. Large companies had a policy 84% of the time (21/25) compared to 20% (5/25) of the smaller companies. Common gaps among large company policies included incorporating patient input and experiences into medical product development, which seems notable because patient-focused drug development has been a big theme among industry and regulators in recent years. (Also see "US Patient- Focused Drug Development Meetings Changing With The Times " - Pink Sheet, 7 Mar, 2022.) Only one-third of the 21 large company policies had the goal.

Only a few companies included using broad eligibility criteria in clinical trials as a goal, 4/21 policies, despite recent FDA pushes in the area. (Also see "US FDA Focuses On Labs, Concomitant Medication To Avert Needless Clinical Trial Exclusions " - Pink Sheet, 23 May, 2024.) Similarly, few companies focused on diversity in a multidimensional approach beyond sex, age, race and ethnic group (4/21). The FDA has emphasized that sponsors consider elements like geographic location and socioeconomic status as part of diversity goals.

Diversity elements more likely to be included in plans were using targets that represented the incidence, prevalence, or severity of the condition or disease in various populations targeted by a trial (15/21, 71%) and identifying and using trial sites with diverse populations and providers treating underserved or under-represented populations (12/21, 57%).
The non-large company cohort of publicly available policies tended to focus on different elements. The most common commitments were to use broad eligibility criteria in trial protocols and incorporate patient input and experience in the development of medical products and the design of trials, areas where the large company policies were lacking. (See chart at the end of the story.)

PhRMA Leverage

The study authors said the findings suggest pharmaceutical company policies could be better leveraged to promote diversity in clinical trials, noting that previous research has found that corporate polices can be effective in achieving policy objectives.

More companies should publicly communicate their trial diversity commitments to increase awareness and accountability. Companies with policies also should improve their comprehensiveness, the authors said.

The study suggests PhRMA could consider repercussions for members who fail to meet the trade association's trial diversity principles. In 2017, the trade association expelled 22 members who failed to meet investment requirements for research and development in new products. (Also see "Putting The 'Big' Back In PhRMA: New Membership Criteria Pares Ranks "- Pink Sheet, 9 May, 2017.)

Additionally, the authors suggested they may build portions of the trial diversity reference used in the study for the Good Pharma Scorecard, an annual index that evaluates, rates and ranks pharmaceutical company performance on bioethics and social responsibility. The scorecard already includes whether companies enroll representative patient populations into pivotal trials supporting FDA approval of new

EU Helps Firms to Prioritize Submission of Data on Critical Drugs

By Ian Schofield,
Executive Editor at Pink Sheet

Key Highlights:

- The EMA's Product Management Service (PMS) is key to building a comprehensive database for critical medicines
- Manufacturers are encouraged to submit product data by February 2025 to meet new regulatory requirements
- This effort supports the European Shortages Monitoring Platform (ESMP) for better crisis management

The submission of data for products on a new list of critical medicines is "a first step in achieving complete standardized product information for all medicines in the EU," says the EMA.

The European Medicines Agency has published a new list of "critical medicines" intended to help companies and national regulators map the drugs in its Product Management Service (PMS).

Manufacturing authorization holders (MAHs) can prioritize the medicines in the list for the submission of specific product information relating to pack sizes and manufacturing, while national competent authorities (NCAs) can use it to "facilitate the prioritization of product mapping within their national systems," the EMA said.

The PMS contains "master data" on packs of human-use medicines marketed in the EU, and is one of the four data management services for human and veterinary drugs called SPOR (substances, products, organizations and referentials).

The PMS is being introduced incrementally to allow the implementation in the EU of globally recognized ISO standards for the identification of medicinal products (ISO-IDMP). It comprises data on both centrally

authorized products (CAPs) and non-centrally authorized products (NAPs) that is "structured, standardized and authorized to be used by regulators and industry in regulatory and non-regulatory procedures," the agency said.

The PMS also "helps MAHs and NCAs to meet reporting requirements in preparation for the mandatory submission of data on supply and availability of medicines to the European Shortages Monitoring Platform [ESMP]," it added. The ESMP is intended to help monitor medicine supply, demand and availability during health crises such as pandemics. (Also see "EU To Launch New Platform For Tackling Shortages Of 'Critical' Medicines In Health Crises" - Pink Sheet, 30 Jul, 2024.)

Submitting Data On Products On The New List

The new "Union list of critical medicines: XEVMPD/PMS entries," dated 5 August, is based on the first version of the "Union list of critical medicines," which was published last December. It is a "high-level mapping" of the ACT (anatomical therapeutic chemical) codes of products on the December list as well as all products contained in XEVMPD/PMS as of 27 June, the EMA noted.

The XEVMPD (extended EudraVigilance Medicinal Product Dictionary) is the database of product information maintained by MAHs. Data in the XEVMPD are being migrated to the PMS, as are data held in the EMA's internal database, SIAMED II.

The EMA said that MAHs "can consider the submission of product data for products on this list as a first step in achieving complete standardized product information for all medicines in the EU."

"MAHs are advised to conduct this exercise until 2 February 2025" to support them in meeting their reporting requirements to the ESMP in the event of a health crisis or a preparedness exercise for a specific subset of medicines that will be published by the EMA as required, the agency added.

Need To Submit Information Now

The EMA has held a number of events this year to prepare MAHs and NCAs for the ESMP, which goes live for routine reporting of shortages by industry in November and for national agencies in February 2025. At those events, including webinars in June and July, companies have been encouraged to submit critical medicine pack information to the platform before February.

If they do not and a health emergency is declared, they will have only two weeks to do so once a specific list of critical medicines relevant to that health emergency is issued.

At the June webinar, the EMA's Marcos Fernández Gómez said: "What we are trying to do now is encourage you to submit pack sizes before February 2025 to avoid late submissions by applicants whenever there is a crisis, because then in 14 days, you will have to submit a lot of information."

By submitting this information now, "we will be ready in the ESMP team, and also the teams at EMA could start preparing and doing some analysis," said Fernández Gómez, who is the PMS product owner at the agency.

From the first quarter of 2025, MAHs will be able to provide additional information for NAPs "so we will request you to provide manufacturers data and also structured data on the pack sizes – what we want you to provide is the quantity and the units of measurement for those packs sizes," he added.

Concerns Over XEVMPD To PMS Migration

The pharmaceutical industry has expressed some concern about the migration of data from the XEVMPD to the PMS, citing "technical challenges," according to a 31 July report on the latest meeting of the industry stakeholder platform on the operation of the centralized procedure, held on 19 June.

Industry suggested "preferred alternative solutions" such as the creation of product entities directly in PMS, the report notes.

But the EMA said that because of "critical" ESMP timelines "and after consideration of different alternatives," it felt that XEVMPD submission was "the only solution available that supports creation and maintenance of package data without jeopardizing ESMP go live in February 2025."

After the meeting, the industry provided survey data from 46 MAHs showing that "13% have submitted the data in XEVMPD, 50% of MAHs (23 out of 46) are preparing them and 37% have not actioned yet," the report says.

PMS Support For Other Regulatory Products

As well as the ESMP, the PMS supports the electronic application form (eAF), electronic product information (ePI), the IRIS portal for the management of regulatory procedures, and the Antimicrobial Sales and Use (ASU) platform.

WHO Invites Vaccine Manufacturers to Join Fight Against Growing Mpox Outbreak

By Ian Schofield,
Executive Editor at Pink Sheet

Key Highlights:

- WHO triggers the EUL process for Bavarian Nordic's MVA-BN and KM Biologics' LC16 vaccines to combat the Mpox outbreak
- The EUL allows international organizations like Gavi and UNICEF to procure and distribute these vaccines in low-income countries
- The current outbreak has spread to countries neighboring the Democratic Republic of Congo, raising concerns about a broader regional spread

An emergency use listing means the vaccines can be approved for use in lower-income countries where they are not licensed, and will allow international organizations like Gavi and UNICEF to procure them for wider distribution.

The World Health Organization has triggered an emergency use listing (EUL) process for two vaccines against mpox after the current outbreak of the disease spread outside the Democratic Republic of Congo to a number of neighboring countries.

The two vaccines chosen by the WHO for the EUL process are Bavarian Nordic's MVA-BN and KM Biologics' LC16, which will undergo an expedited expert review once the relevant data have been received, a WHO spokesperson told the Pink Sheet.

MVA-BN is marketed as Jynneos in the US, as Imvanex in Europe and as Imvamune in Canada. LC16, a freeze- dried smallpox vaccine, was approved for use in Japan in August 2022.

An EUL helps to speed up the approval and availability of vaccines and other products in countries where they are not yet authorized – mainly lower-income ones – for use in the event of a public health emergency.

EUL status also allows partners such as the vaccine alliance Gavi and UNICEF to procure vaccines for distribution.

The WHO has also issued the first invitation to manufacturers of candidate mpox vaccines to submit an expression of interest for an EUL.

The moves have been prompted by the "serious and growing outbreak" in DRC that has "now expanded outside the country," the WHO said, adding that a "new viral strain, which first emerged in September 2023, has for the first time been detected outside DRC."

The current outbreak in eastern DRC is due to a new offshoot, called clade 1b, that causes more serious disease than clade 2. It has been confirmed in Kenya, Rwanda and Uganda, while the Burundi clade is still being analyzed. Cases of clade 1a have been reported this year in DRC, the Central African Republic and the Republic of Congo, while clade 2 has been reported in Cameroon, Côte d'Ivoire, Liberia, Nigeria and South Africa.

The WHO's director general, Tedros Adhanom Ghebreyesus, said the organization had decided to set up an emergency committee under the International Health Regulations to advise on whether the outbreak represented a "public health emergency of international concern" (PHEIC).

"The committee will meet as soon as possible and will be made up of independent experts from a range of relevant disciplines from around the world," Tedros declared. A PHEIC triggers the measures and obligations necessary for a coordinated international response to an outbreak.

EUL For Bavarian Nordic & KM Biologics' Vaccines

The WHO noted that the Bavarian Nordic and KM Biologics vaccines had both been approved for marketing by WHO-listed authorities (WLAs) and recommended for use by its Strategic Advisory Group of Experts on Immunization (SAGE). They were also approved for use in June by the regulatory authority in DRC.

"Now that the EUL process has been triggered, WHO is requesting the manufacturers to submit the full dossier to ensure that the vaccines are safe, effective, of assured quality and suitable for the target populations," the WHO spokesperson said.

"Once the data is available, an expedited review by relevant experts is planned. Following this expedited process to assess that the vaccine meets the EUL criteria, the technical advisory group (TAG) for EUL will be convened."

The TAG will be convened one month after the dossiers have been submitted by the manufacturers, the spokesperson said. Based on the WHO assessment report, the group will advise on whether the vaccine should receive an EUL and, if so, the

conditions for its deployment, including any post-approval/post-EUL commitments.

"It's important that information on the use of the vaccines continues to be collected after they are made available to all those involved, so that the decision may be reviewed on the basis of more data," the spokesperson added.

EOIs Invited For Other Vaccines

The WHO has separately invited manufacturers of candidate mpox vaccines to submit an expression of interest (EOI) for an EUL evaluation.

The criteria that must be met for an EUL include

The targeted disease is serious or life threatening and could cause an outbreak, epidemic or pandemic. Existing products have not been successful in eradicating the disease or preventing outbreaks.

The product is developed and manufactured in compliance with current internationally recognized standards such as good manufacturing practices, good clinical practices and good laboratory practices.

The national authority responsible for the regulatory oversight of the vaccine has been assessed and documented as a "WHO-listed authority."

In this invitation, priority will be given to candidate vaccines that "are expected to meet all or most of the WHO TPP [target product profile] characteristics," the WHO noted.

Manufacturers that meet the criteria and have submitted a complete EOI will be contacted to schedule a pre- submission meeting to discuss issues such as the assessment procedure, date of dossier submission, and readiness of the submission package.

Upcoming OPPI Event

About OPPI

The Organisation of Pharmaceutical Producers of India (OPPI) established in 1965, represents the research-based global pharmaceutical companies in India. OPPI has been an integral part of the healthcare journey of the country. We remain committed to supporting the nation's healthcare objectives, putting patients at the core of all decision making and collaborating with all stakeholders to find sustainable solutions to realize the collective vision of *Health for All*.

Our member companies have been serving the country's healthcare ecosystem since pre-independence and continue to remain committed to patient safety and providing quality care in the future as well. As an association, our advocacy decisions, patient commitment and work are always keeping the country first and we embody the spirit of working for '*Bharat Ke Liye*'; driven with innovation to find solutions for unmet medical needs, collaboration with government stakeholders, and co-creation with partners coming together to address the nation's healthcare challenges. We are committed to the Hon'ble Prime Minister Shri Narendra Modi-ji's clarion call of '*Jai Vigyan and Jai Anusandhan*'.

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