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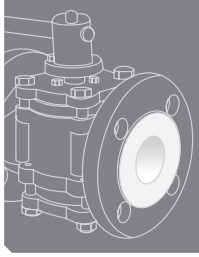

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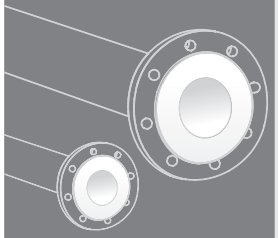

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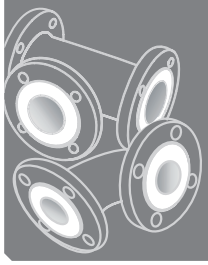

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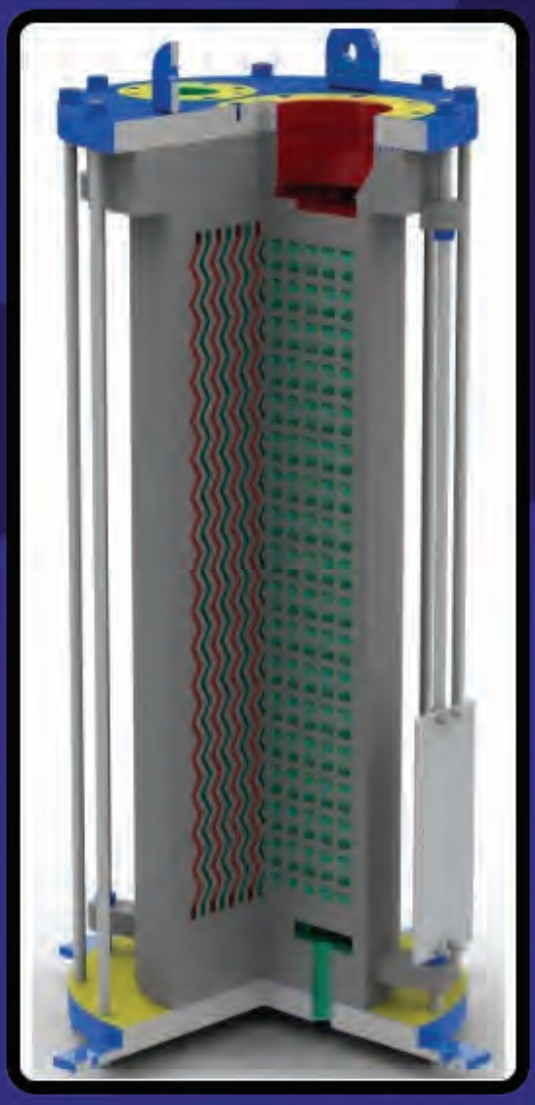

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Collaborative efforts between Bureau of Indian Standards and International Electrotechnical Commission for wider promotion of Standards

New Delhi, India: The Secretary-General & CEO, International Electrotechnical Commission (IEC), Mr. Philippe Metzger during a recent visit to Bureau of Indian Standards (BIS) emphasized on the collaboration between BIS and IEC. He had an intensive interaction with Shri Pramod Kumar Tiwari, Director General, BIS and encouraged Indian Standards community to take up further leadership positions in technical, policy and governance bodies of IEC.

Presently, India is a member of IEC Standardization Management Board (SMB) and Market Strategy Board (MSB), the highest policy-making bodies of IEC responsible for technical matters and for identifying relevant subject areas for future work respectively. India also contributes in the technical work of IEC through its participation in Technical Committees (TCs), Subcommittees (SCs) and their groups.

During the interaction, BIS officials discussed how both the organizations could have deeper engagements and can promote standards. Mr. Metzger had fruitful deliberations with Indian standards community to address needs and expectations of the community, members representing India in IEC Governance bodies. Representatives of relevant Industry associations discussed the significance of IEC from Indian perspectives, and prospects for further collaborations between BIS and IEC.

A drug delivery solution can improve cancer management and treatment

Jaipur, India: A novel site-specific drug delivery method using gold nanoparticles can improve management and treatment of cancer.

There are more than 200 different types of cancers known which are currently being treated through surgery, chemotherapy, and radiation therapy. Many of these cancers can be cured if detected early and treated effectively. However, the available treatments are time-taking, expensive, and trigger numerous other side-effects and the actual health benefits of the therapy do not reach to the cancer patients effectively.

Researchers at Amity University Rajasthan, Jaipur have developed therapeutic agents with the help of nano-biotechnological approaches using a unique solution of 'gold nanoparticles' that helps in improving the site-specific drug delivery for cancer disease management and its effective treatment.

JMP® introduces Quality by Design (QbD) SAAS for Pharma Industry

Cary, North Carolina: Quality by Design enables Pharma R & D to move towards a more scientific & risk-based approach to develop drug candidates. This new technology for the pharma industry was born out of trends such as the high attrition rate of drug

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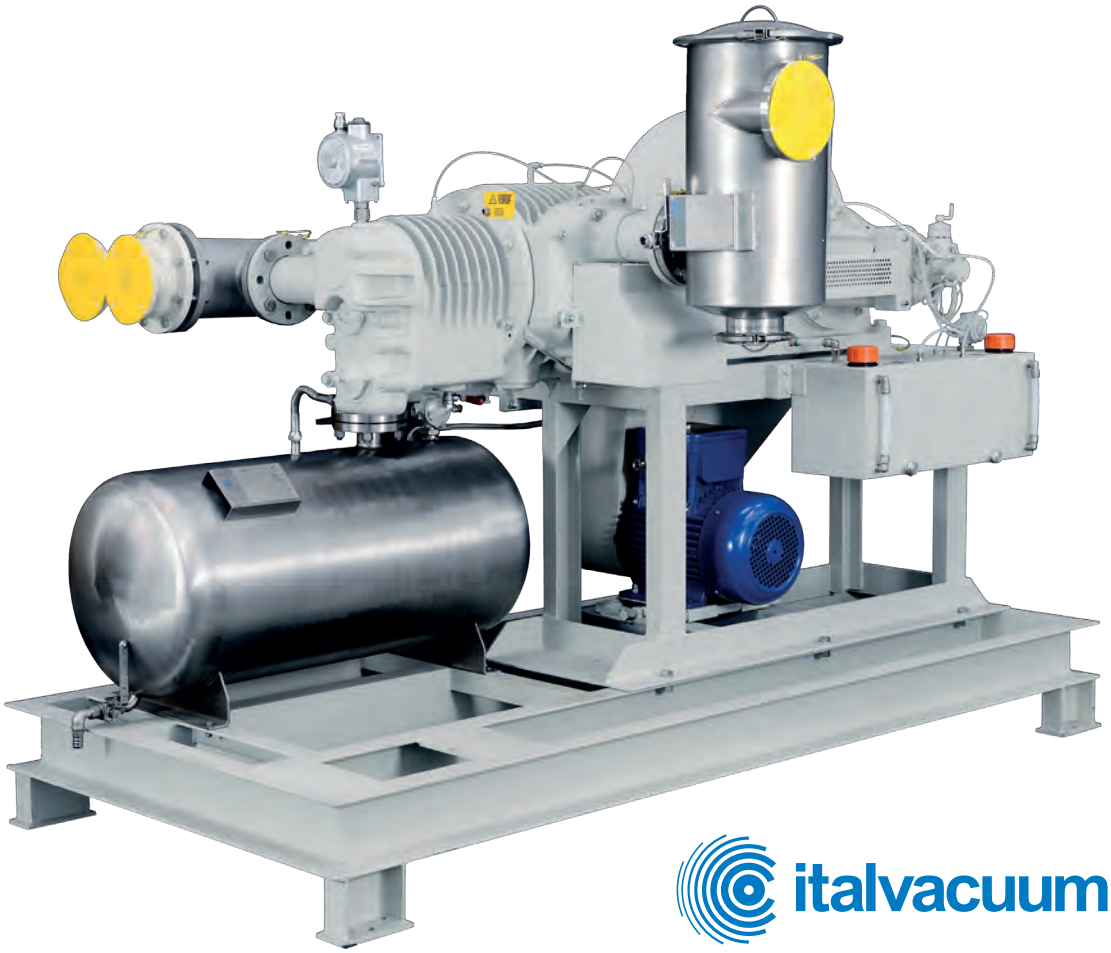

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candidates during development, the high value of pharma products, and the extremely high regulatory load. QbD will cause shifts in the pharma industry from the unstructured experimentation with usually considering one factor at a time & standard check-list procedures to a more data driven, digitalized approach which leverages the technological advancements in Data Sciences.

Recognising that more testing will almost certainly not improve the quality of a drug, the US Food and Drug Administration (FDA) started this paradigm shift through its imitative "Pharmaceutical Quality for the 21st Century: A Risk-Based Approach." Regulators are now placing process understanding centre stage, encouraging pharma companies to develop the ability to assess the dependability and robustness of their manufacturing systems.

Cipla leverages Digitalization & emerging segments to drive it's next phase of growth.

Mumbai, India: Towards generating shareholder & stakeholder value the drugmaker Cipla is leveraging digitalization and novel segments like biosimilars and mRNA-aided medications.

To drive its next phase of growth, Cipla is also looking forward on maximising value opportunity in the complex generics in the US market. It is also looking to scale up its US core formulations sales on the back of respiratory and peptide franchises while monitoring upcoming complex product launches in the second half of the current fiscal year.

Samina Hamied, Executive Vice-Chairperson, Cipla has said "Digitalisation in healthcare found its rightful place during the pandemic, and there is a need to expand and support the essential backup services to enable digital healthcare to function efficiently in all primary and secondary healthcare centres" in the company's Annual Report for 2021-22.

The drugmaker has also embarked on the digital transformation of the value chain across functions, including finance, R&D, manufacturing, supply chain, HR, customer outreach and stakeholder engagement.

CEPI and SK bioscience partner to advance mRNA vaccine technology

Oslo, Norway: Coalition for Epidemic Preparedness Innovations (CEPI) and SK bioscience today announced a new partnership agreement to advance the development of mRNA-based vaccine technologies to facilitate rapid response to unknown pathogens with epidemic and pandemic potential (referred to as Disease X).

CEPI will provide up to 40 million USD in initial funding to support the development of mRNA-vaccine candidates against Lassa Fever virus (viral family: Arenaviridae) and Japanese Encephalitis virus (Flaviviridae). The funding will support preclinical studies through to

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phase 1/2 trials. Pending results of these studies, a further 100 million USD in funding could be made available to support late-stage trials/licensure to further validate the mRNA platform and have it ready for use in outbreak situations.

This partnership is the first such agreement to be announced under CEPI's call for proposals, launched in January 2022, to develop RNA vaccine platform technologies and support development of a vaccine library against emerging and specific endemic infectious diseases.

CEPI aims to form a 'library' of vaccine candidates that are ready to be pulled off the shelf and swiftly adapted next time Disease X emerges. That way, valuable time is not lost creating a new vaccine from scratch when a new viral threat emerges.

Dr. Reddy's Hyderabad factory joins Global Lighthouse Network (GLN)

Hyderabad, India: Dr. Reddy's Laboratories announced the recognition of its largest manufacturing facility in Bachupally, Hyderabad, as part of the Global Lighthouse Network (GLN) by the World Economic Forum (WEF).

The GLN, a community of over 100 manufacturers that are showing leadership in applying Fourth Industrial Revolution (Industry 4.0 or 4IR) technologies to drive impact in productivity, workforce engagement, sustainability, and supply chain resilience.

Dr. Reddy's initiated the programme to 'digitise its core' around four years ago, this involved upgrade of infrastructure and digitisation of processes for robust and comprehensive data capture. Whereas OpsNext program was initiated two years ago which was aimed at transformation of the plant. into an Industry 4.0-driven 'Lighthouse' factory as defined by the WEF. The site saw the deployment of six of the eight technologies of 4IR – Advanced Analytics, Digital Twins, Robotic Process Automation, Augmented/Virtual/Mixed Reality, Digital Performance Management, and Industrial Internet of Things (IIoT).

AGC begins study to expand its Bio-CDMO capability in Japan

Yokohama, Japan: AGC, a leading manufacturer of glass, chemicals, and high-tech materials, has announced that the company has reached on 30th September 2022 the eligibility criteria and will be joining METI's "Developing biopharmaceutical manufacturing sites to strengthen vaccine production" project.

This inclusion of ACG in METI's project will accelerate its expansion planning of its biopharmaceutical CDMO capabilities at the AGC Yokohama Technical Centre to be operationally ready in 2025. The additional capabilities AGC is considering for the AGC Yokohama Technical Centre consists of CDMO services for mRNA pharmaceuticals, cell and gene therapeutics, and protein-based biopharmaceuticals made using mammalian

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cell cultures, which also can be applied for the manufacture of vaccines in the event of a pandemic.

During COVID-19, new types of vaccines utilizing biopharmaceutical technologies are being researched and developed around the world to combat new infectious diseases. Meanwhile in Japan there are limited production sites for biopharmaceuticals, including these new types of vaccines, and the development of production sites in Japan is an urgent issue.

Cadila and CII launches joint national campaign for rabies-free India by 2030

Ahmedabad, India: Cadila Pharmaceuticals and Confederation of Indian Industry (CII) have launched a joint national campaign for a rabies-free India by 2030.

As a part of the campaign to make India rabies-free by 2030, several activities for awareness and prevention of rabies will be undertaken at the national and state level under the aegis of the government of India.

Jawed Zia, CEO, Cadila Pharma said, "Lack of public awareness and the resultant failure to complete the vaccine regimen are key causes behind rabies deaths."

Rabies claims around 59,000 deaths globally a year, of which around 20,000 or just over one-third of the deaths take place in India alone.

Antibacterial Resistance Leadership Group (ARLG) begins clinical trial of phage therapy for cystic fibrosis

Washington D.C., US: The Antibacterial Resistance Leadership Group (ARLG) has begun a clinical trial of phage therapy for cystic fibrosis in adults who carry Pseudomonas aeruginosa (P. aeruginosa) in their lungs, according to a statement from the National Institute of Health (NIH). P. aeruginosa, a serious and sometimes deadly bacterium frequently acquired in healthcare settings, is the most common bacterial cause of CF exacerbations. Recently, multidrug-resistant P. aeruginosa infections are becoming increasingly common, and, in recent years, only a handful of new antibiotics have been approved to treat them.

The trial is evaluating whether the bacteriophage, or "phage," therapy is safe and able to reduce the number of bacteria in the lungs of volunteers. Investigators aim to enrol up to 72 adults at 16 CF centres across the US, the statement said.

It also said that phages are viruses that can kill or neutralise specific bacteria while leaving non-target bacteria and human cells unharmed. For more than a century, researchers have considered the potential use of phages as therapeutics, theorising that mixtures of bacteriophages might be used on their own, or in conjunction with antibiotics, to treat bacterial infections—especially those resistant to antibiotics.

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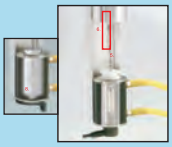
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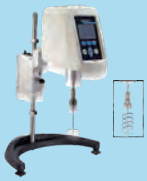
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RHEOLOGY VISCOSITY TEXTURE IN-LINE POWDER MOISTURE GAS

Johnson & Johnson's blood cancer therapy gets US FDA approval

New Brunswick, New Jersey: The US Food and Drug Administration (FDA) has approved Johnson & Johnson's therapy for treating a type of multiple myeloma, giving another treatment option to patients with the incurable blood cancer. J&J's teclistamab, branded as Tecvayli, is approved for treating adults with multiple myeloma that is hard to treat or has come back after receiving four or more prior lines of certain classes of therapies, the company said.

A company spokesperson said the therapy, which will be available on or around 4th November, will have a list price of $39,500 per month, with the overall pricing ranging between $355,000 and $395,000 for a nine-to-10-month course.

ProBioGen co-develops new Freedom ExpiCHO-S cell line development kit

Berlin, Germany: Following up on the success of the Gibco Freedom CHO-S Cell Line Development Kit, ProBioGen and Thermo Fisher Scientific have now developed an even better platform: the Gibco Freedom ExpiCHO-S Cell Line Development Kit.

It enables users to generate cell lines suitable for clinical development without their own starter cells, vectors, or prior experience in the field. ProBioGen has substantially contributed to the performance of Freedom ExpiCHO-S Kit by applying its strong expertise in cell line and process development.

Freedom ExpiCHO-S Kit uses Thermo Fisher's ExpiCHO-S cell line and a new powerful media platform specifically developed for it. The kit is based on a novel set of ProBioGen vectors equipped with strong promoters, selection markers and protective elements providing expression stability. Together with a simple workflow optimized by ProBioGen, the kit provides short development time, reproducibly high titers (3-5 g/L) and high expression stability.

Lupin launches generic Paliperidone Extended-Release Tablets in US

Mumbai, India: Global pharma major Lupin Limited (Lupin) has announced the launch of Paliperidone Extended-Release (ER) Tablets, 1.5 mg, 3 mg, 6 mg and 9 mg, to market a generic equivalent of Invega Extended-Release Tablets, 1.5 mg, 3 mg, 6 mg and 9 mg, of Janssen Research and Development, LLC.

According to IQVIA MAT August 2022, the Paliperidone Extended-Release Tablets (RLD Invega) had estimated annual sales of USD 112 million in the U.S.

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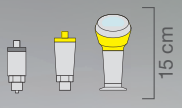

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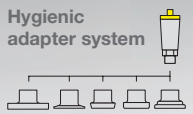

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Looking Forward VEGA

Glenmark launches Zita D for adults with Type 2 diabetes having comorbidities

Mumbai, India: Glenmark Pharmaceuticals Limited became the first to launch Teneligliptin (20mg) + Dapagliflozin (5mg/10mg) fixed dose combination (FDC) for the treatment of adult patients with type 2 diabetes, especially the ones with comorbidities.

Marketed under the brand name Zita D; it contains Teneligliptin (20mg) + Dapagliflozin (5 mg/10 mg) and must be taken once daily under prescription to improve glycemic control & prevent complications in adult patients with type 2 diabetes, especially the ones with comorbidities.

Lupin gets USFDA nod for generic version of Formoterol Fumarate Inhalation Solution

Mumbai, India: Lupin on Wednesday said it has received approval from the USFDA for Formoterol Fumarate Inhalation Solution, used in treating symptoms of chronic obstructive pulmonary disease.

The company has received approval from the US Food and Drug Administration (USFDA) for the product which is a generic version of Mylan Specialty's Perforomist Inhalation Solution.. By IQVIA MAT June 2022 data, the medication had annual sales of around USD 282 million in the US market.

CJ Shah Group opens new lab in Thane

Thane, India: CJ Shah Group recently opened its new technical service application lab in Thane, Maharashtra. This facility will concentrate and intensify its application activities in coatings, inks, personal care, and industrial specialities. This will eventually strengthen our commitment to cater our wide customer and principal base in a more definite and improved manner. Since 1961, CJ Shah has been offering, and continues to provide, the entire gamut of chemical products from APIs to break bulk chemicals to solvents to specialty and fine chemicals. The company caters to industries such as paints and coatings, agrochemicals, adhesives, flavors and fragrances, pharmaceuticals et cetera. ■

Marksans acquires capacity from Tevapharm India

Goa, India: Marksans Pharma entered into a Business Transfer Agreement (BTA) with Tevapharm India yesterday, to acquire its business relating to the manufacture and supply of bulk pharma formulations in Goa.

The BTA is expected to be finalised by 1st April 2023, subject to the usual closing conditions. Also, Marksans has agreed to retain the site employees with the existing terms of employment. It will continue to supply Teva's affiliates for certain products until the end of FY23 as part of the agreement, which can be extended further with mutual agreement.

Through the acquisition, the company plans to double the existing Indian capacity, which is currently 8 billion units per annum. Marksans plans to manufacture tablets, hard and soft gel capsules, ointments, gummies and creams from the new capacity. The new capacity is also scalable to manufacture oral solid dosage forms. This will be the forth facility in an addition to the three existing manufacturing sites in Southport (UK), Farmingdale (The US) and Goa (India). The manufacturing site is spread across 47,597 square metres, and has approvals to manufacture products from the EU, Health Canada and Japanese Health Authority.

Laurus Labs planning Rs. 2,000 Cr (around 260 million USD) Capex

Hyderabad, India: Laurus Labs Limited is planning a Capex guidance of Rs. 2,000 crores (around 260 million USD) across all the subsidiaries and divisions, says Dr. Satyanarayana Chava, Founder & CEO, Laurus Labs during the Q2 FY '23 Earnings Conference Call.

Dr. Satyanarayana Chava added "We have over 50 active projects at different stages and ongoing commercial supplies of 4 APIs and several intermediates. Our greenfield investment to set up a dedicated R&D centre for the Synthesis division at Genome Valley, Hyderabad and three manufacturing units in Vizag under Laurus Synthesis Private Limited is progressing as per our previous timelines. New sites for this division will have the capabilities to handle steroids, hormones and high potent molecules apart from medium and large volume products."

"On the Capex front, we have invested Rs. 416 crores in the first half and we are broadly in line with our guidance for the two years around Rs. 2,000 crores across all the subsidiaries and divisions. And we remain on course to strengthen our position as a cost-effective integrated pharma player." said V. V. Ravi Kumar, ED & CFO, Laurus Labs Limited.

"We are investing in the backward integration program and creating more capacity. The additional investments in the capacities we are expecting will be in the non-ARV sites. On the quality side, we are still bullish on the overall business of the company. The FDF ARVs are only a one-off kind of a thing in the second quarter, and we expect it to restore from the quarter three onwards," added Kumar.

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Kopran acquires assets of Abhinandan Rasayan

Ambernath, India: Kopran Research Laboratories Limited, a wholly owned subsidiary of Kopran Limited, has acquired the assets of an Active Pharmaceutical Intermediates (APIs) manufacturing Unit of Abhinandan Rasayan Private Limited located at MIDC- Ambernath, subject to certain terms and conditions as mentioned in the agreement.

Pursuant to the said acquisition, once the unit is made fully functional, it will help the company in increasing its API and intermediate production capacity.

Aragen to commence operations in Hyderabad formulation manufacturing facility by Jan 2023

Hyderabad, India: Aragen, a leading Contract Research Development and Manufacturing Organization (CRDMO), has announced that it will commence operations in its formulation manufacturing facility in the Mallapur campus, Hyderabad, India by January 2023. Once this facility becomes operational Aragen will be able to provide greater flexibility to deliver customers' clinical supply needs in multiple dosage forms, with process technologies and flexible batch sizes as low as 1,000 units to as high as 100,000 units.

The 12,000 square feet new facility will strengthen the company's ability to deliver clinical supplies to customers through its integrated drug substance and drug product development and manufacturing.

The new plant will include a wide range of dosage form capabilities for oral solids, liquids, topicals, films, and manufacturing technologies for granulation, film coating, spray drying, tableting – with expansion plans already in place to add nano milling and hot melt extrusion capabilities. These new capabilities at the Mallapur Campus will further enhance Aragen's New Chemical Entity (NCE) early-stage development offerings, providing customers the convenience to discover and develop drugs from a co-located facility.

Speaking on the development, Manni Kantipudi, CEO, Aragen Life Sciences said, "Aragen is investing in expanding capacities, extending capabilities, and widening its geographic footprint to meet the needs of the global bio-pharma industry. We understand that our customers rely on our expertise, track record, and solution offerings. With this facility, we will consolidate our drug product development solution offerings and strengthen our position as a one-stop shop for all their needs – transforming ideas into solutions for better health." ■

Transforming small batch production

With significantly smaller batch sizes, in some cases patient-specific, manufacturing is a key area requiring transformation. Organisations must meet increasingly stringent compliance standards and ensure the very highest quality and safety levels while consistently driving down costs through efficiency. Through flexibility, modularisation, automation, and digitalisation offered by ATMP platform technologies, the industry is finding solutions for some of the most challenging manufacturing challenges not previously faced.

With their one-and-done potential and pinpoint targeting capability, cell and gene therapies (CGTs) present huge promise in the fight against a range of previously untreatable diseases. Many advanced therapy medicinal products (ATMPs), such as CGTs, are now entering commercialisation. As developers embark on this next phase, new pressures emerge, with cost, accessibility and return on investment being ever present concerns.

No advancement without challenge

- **Recouping development costs**

The average cost to develop a new therapy stands at $1.3 billion, across 10-12 years of development. When a CGT gets to the commercialisation stage, there is enormous pressure to recoup this cost.

Already, we are seeing gene therapies pass the $1 million per dose mark, a situation that is unreachable for most patients and untenable for the market. Manufacturing efficiencies are critical here to provide the cost savings that deliver payback without transferring unnecessary cost burdens.

For highly targeted CGTs, reducing manufacturing costs is challenging. Very small batches require single-use fermenters; in the case of autologous treatments like CAR-T cell therapy, this might be one fermenter per patient and a complete upstream single-use fluid pathway. This costly, but robust, approach is necessary because every wasted millilitre could lose thousands of dollars.

- **Ensuring safety**

Contamination is a huge risk in the production of CGTs, and the

very highest standard of aseptic processing is needed to mitigate this. For autologous therapies, the chain of custody needs to be failsafe; each therapy manufactured could be a patient's only hope at a cure. In all cases, CGT therapies are often injected or delivered intravenously into extremely vulnerable patients, and sterility must be ensured.

But contamination is not just a risk to patients. Operators and the environment too must be protected against therapies, particularly with the use of bio-hazardous materials, such as Antibody Drug conjugates (ADCs) and genetically modified viral vectors.

The latest revision of the GMP Annex 1 addresses these issues in a holistic, risk-based, proactive way. These new requirements will increase the focus on ensuring each element of the manufacturing process accommodates the nuances of CGT manufacturing.

GMP Annex 1

- Increase Contamination Documentation & Control
- Consider technology barrier
- Increase automation to reduce risks

- **Quality without compromise**

As new processes evolve and adapt to manufacture pioneering treatments, manual tasks are often added to fill gaps in automated workflows; however, every manual step adds a quality risk. Combined with the challenge of transferring highly sensitive cells between manufacturing stages, it is easy to see how quality issues emerge and whole batches can be ruined.

CGTs require an evolution of current practices, yet seemingly small issues, such as part per million residues of vaporised hydrogen peroxide (VHP) in sterile containers, can destroy a sensitive therapy. Alongside chain-of-custody challenges, a new approach to manufacturing process design is required.

Safe, compliant, and cost-effective manufacturing

ATMP manufacturing platforms, drawing on the latest technology and industry experience, are ideally placed to build a manufacturing process that is compliant, safe, and cost-effective, but they must contain certain key attributes.

- **Flexibility**

CGTs are a broad and diverse range of therapeutics, so manufacturing platforms need to reflect this. There is strength in standardisation from modular equipment and single-use pathways, but this should not come

at the expense of flexibility, which is the only way to ensure the most efficient production. Platforms need to accommodate different therapies, batch sizes, container sizes and fill volumes.

▪ Modularity

Modular systems that are pre-validated, enclosed, and automated address many of the pain points of regulatory compliance, safety, product waste reduction and changeover between products. Far from restricting flexibility, these systems are often fully configurable and modular equipment often brings intensification benefits too. Connecting disparate functions and process steps into one intensified platform can better protect cells that need highly controlled conditions. Different manufacturing functions can be brought together in one integrated system, from bioprocessing through to formulation, aseptic processing, and fill/finish. Greater efficiencies, flexibilities and more robust quality control are realised, ultimately driving down the cost and time needed to produce the therapy.

▪ Automation and digitalisation

Managing the 'human factor' is central to meeting the 'contamination control strategy' element of the new GMP Annex 1 requirements. Human errors are mitigated by automation and human commensal contamination is further reduced by barrier technologies powered by automation. That said, automated systems should be fully accessible to humans. This means flexibility must be added to the design process so that interventions can be made without compromising the aseptic, grade A environment or ruining batches with subsequent loss of supply.

With automation also comes digitalisation, for both control and monitoring. Intensified systems should communicate seamlessly to ensure quality oversight monitoring and establish complete control over the chain of custody. Robust environmental and process monitoring should also be employed to measure the parameters of viable and non-viable contamination and include trend data for longer-term quality assurance and efficiency improvements

▪ Tried and tested

CGT manufacturing requires an evolution of existing methods, rather than a revolution. It is already known how to safely transfer cells in the biologics sector, using peristaltic pumps with fast, non-shearing processes, and we already use reliable bioreactors and suspension-based culture systems in biologics manufacturing. Where tried and tested equipment is fit for purpose, it can easily be incorporated into new CGT workflows.

Single-use technology is an obvious choice. Without clean-in-place (CIP) or sterilise-in-place (SIP) requirements, single-use systems can guarantee

sterility and meet small-batch and bespoke needs.

Single-use fluid pathways often come pre-validated, and this is extended into some automated, modular equipment too. Pre-validated, standardised systems bypass bespoke validation and design processes, provide a key part of a robust containment control strategy, and can lead to faster regulatory signoff.

Investing in a more efficient future

Whether manufacturing occurs in-house or through a CDMO, robust ATMP platforms are critical to meeting GMP compliance and optimising manufacturing to quickly recoup development costs.

Conclusion

As the CGT market evolves, modular, flexible, and automated platforms, along with their single-use pathways and connected data management, will meet the novel challenges of this growing sector. With collaboration between academia, developers, CDMOs, non-governmental organisations and regulatory bodies, this enabling technology can be used most effectively to deliver the best quality products to patients at the lowest possible price.

Safety, quality, efficacy, and assured supply will continue to be at the heart of all decisions as more CGTs progress from the laboratory, through commercialisation and to the patient. Only through close collaboration and sharing of best-practice and skills will the industry be able to achieve its primary goal: to drive down the cost of treatment so that more and more patients have access to these lifesaving therapies. ■

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Child Safe Packaging Today

With creative solutions abound in the packaging industry, manufacturers are able to address all manner of consumer and regulatory concerns, and health and safety is no exception. There's regular 'safe packaging', however, and then there's child-safe packaging: a sector with its very own demands and challenges. Richard Quelch, head of marketing at Origin Pharma Packaging, discusses child-resistant packaging and how to prevent incidences of medical poisoning.

As physicians become more reliant on prescribing medications to treat illness instead of advocating preventive measures, the risks associated with accidental medication poisonings is increasing. In the UK, approximately 50%[1] of our population take prescription medicine whilst in the US the figure is over 60%[2]. These figures are not quoted to in any way reflect on cases genuinely requiring prescription medication, they do however provide an insight into the volume of medicines in circulation and with this, the scale of potential risk to children. Poison centres in the US treat between 60,000 and 70,000 children each year for accidental ingestion.

Advancements in packaging technology such as soluble packs, films etc are undoubtedly to be viewed as a progression, it is questionable however whether there is a parallel effort in creating the child resistant packaging necessary to ensure these products are safe for the environments they occupy. Whilst Mercola[3] reports that pain medications are the single most frequent cause of fatalities from accidental medication poisonings in children, household products still present an alarming number of ingestion cases. In medicine terms the category of substances with the largest number of deaths across all ages (including intentional use of opioids in teens), are medications containing acetaminophen,

sedatives, sleeping medications, stimulants, and cardiovascular drugs. In terms of household products the most common issue is becoming the soluble packed alkaline detergents.

There is an abundance of information and even some creative solutions available to the packaging industry, with the ease of access to online information manufacturers are able to appraise themselves in consumer and regulatory concerns and safety is no exception. There is however possibly a lack of understanding what truly constitutes child-resistant packaging and also a preparedness to await regulatory obligation before introducing protection.

One question we hear raised from time to time is whether the effectiveness of some of the conventional child resistant packaging of today is to be assumed appropriate for today's world. Some of the established institutions will feel strongly that it is, however it is arguable whether the combined impact of freedom of information, intelligence of today's children, and the tragic increase in cases of diminished responsibility are effectively measured.

Non-medicine packaging

Whilst Origin's work of over 50 years has revolved largely around medicine packaging and drug delivery devices, there is perhaps a sharper increase in casualties from the non-medicine product categories.

The advance in soluble packaging is an example of a welcomed and convenient technological development, in our opinion it has been delivered upon with an apparent disregard of the potential harm to children. Soluble dishwasher tablets for example contain aggressive and corrosive alkaline salts. Ingestion of these products

is becoming a common occurrence yet apart from warnings printed on the box, there is no physical barrier provided in the packaging to protect children. These oftencolourful capsules are attractive to young children as is evidenced in the ingestion cases. How many of us in reality have these accessible to children in our homes? and how many of us have located and read the product information?

Unlike medicines, there are virtually no defined regulations to control the packaging of such products, guidance notes on packaging enforce only our impact on the environment but stop short of enforcing child safety values. If this situation continues little is likely to change on commercial scales to develop packaging to reduce these risks, yet without apportioning the burden unfairly, should we really wait for regulations to be imposed to meet the need? Regulation supports good practice and no doubt it will be pronounced on one day, in the meantime we wonder if our moral and ethical obligations are being fairly considered?

Child Resistant is Not Child Proof

An important consideration is the terminology used in matters pertaining to child safety, rarely if ever is packaging child proof. The balance between child resistance and senior accessibility restricts just how far we can restrain children and the senior friendly challenge is something of an interminable debate. Accommodating both aspects in design is a significant challenge, regulating such a conflicting scope is probably harder still.

Child resistance should, according to the ISO8404 Standard (non re-closable) be considered the last line of defence, not the first line. Whatever packaging is developed to meet the fine balance of abilities between children and seniors it should be always remembered that "child resistant" is never "child proof" and therefore the practise of keeping medicines out of sight and reach of children should be mandatory.

There will no doubt exist some interesting papers on child psychology that will substantiate this comment, but the fact is that for all our experience we still tend to underestimate the innocent, inquisitive nature of children. An article by VWA entitled "children see things differently"4 gives a simplistic message of how things appear to young children and provides thought-provoking questions about what consideration should be made when designing safety into these packages. Even the bright colours used as a means of retail marketing or shelf impact attract young children in an entirely different way to how they are intended.

Senior Friendly Child Resistance

Accommodating both Senior Friendly and Child Resistant values in design is a significant challenge, whilst regulating such a conflicting scope is probably harder still. In many ways, the senior accessibility aspect is less definable than the child resistance. With children, we have fairly prescribed parameters of ability in the child safe testing age bracket of 42 to 51 months. The scope of abilities present in the adult test panel however of 50 to 70 year olds presents a hugely different picture.

The loss of dexterity and in some cases the ability also to coordinate is often diminished in our latter years. The key principles required in achieving effective child resistance are by definition the same principles needed to enable the aging population. As our aging population is also increasing and advances in medicine is enabling us to retain our independence longer, questions could be raised as to whether 70 is still a relevant top end age for the testing protocol.

Storage of Harmful Substances

The storage of medicines and other potentially harmful substances therefore requires a responsible approach. As already stated, child resistance is the last line of defence. The most secure way without doubt to ensure children to not access these products is to ensure they never see them in the first place.

The deliberate misuse of opioid substitute has been the greatest cause of child ingestion of pharmacy-dispensed child

medicine ingestions in the UK that have led to actual fatality. It is important to recognise that these tragic instances have rarely (never in our experience) proved to be the result of non-compliant packaging.

A report from Alder Hey hospital, Liverpool5 found that of 30 methadone ingestion cases; 22 involved re-closable screw cap bottles and only 2 of these were found to be original and child resistant. Such evidence sadly proves that even compliant packaging cannot be expected to provide the intended protection if medicine is transferred to non-child resistant packaging. The cause of these breaches in security after police investigation have always proved to be the outcome of diminished responsibility on behalf of the adult. One simple measure that could be enforced easily in our opinion is to provide education to patients using such medication that the product must be stored in the container it was supplied in.

Regulations and Testing

We have effective and well recognised regulations for the safe containment of medicines and the necessity of a common test protocol has long been considered essential for these products. Reclosable packaging to BSEN ISO8317 and its American equivalent, 16CFR 1700.20 are still effective and the 2015 version of the ISO Standard has cleared up some areas of confusion.

To gain approval the complete pack must be tested – container and closure. Whilst many closures are produced to provide child resistance it is not possible to assume that because one pack combination passes another will pass also.

Testing in the UK is carried out at UKAS approved test centres in accordance with the relevant test protocol. Marginal differences apply between the European and US procedures but there is no meaningful difference in our opinion between the two with the exception of the re-securing aspect of the US test 16CFR1700.20.

Some test centres provide an expedited 'pre-application' test service providing a

smaller test panel for a lower cost (Origin can advise regarding this). The test conditions are as per the protocol and the results helpful in ascertaining whether there are any fundamental issues in the pack design. Successful pre-app tests can usually then be scheduled quickly to full protocol testing if there appear to be no issues. A further benefit from such preliminary testing is that we are able to 'weight' the test panel to include more or less of certain age brackets to create robust test conditions.

The official test protocol requires 200 able-bodied children between 42 and 51 months and can be carried out either with the full 200 contingent or by a method of sequential testing. For the adult test a panel of 100 is required between the ages of 50 and 70 years.

Compliance – how do I know?

With over 50 years' experience in child safe packaging we know there are an increasing number of packs in circulation that cannot be considered child resistant, as might be expected a number of these are imported. Research suggests to us that an assumption is often made that because a cap appears to have a push-and-turn mechanism it must be child resistant, however this is not a wise assumption.

We suggest a common practise should be to ask your supplier for a technical file and certificate of child resistance for the pack you are using. Remember that technically there is no such thing as a "child resistant cap" as for a pack to be child resistant you should have a certificate which specifies the container and cap.

If your product is sold within the UK and EU then the BSEN ISO8317 certificate is the correct document for your activities. If your product is to be sold in the US you will need the 16CFR1700.20 certificate to comply with the regulations currently in force in the US.

If you require support in design and supporting your packaging formation transition into child safe compliant packaging Origin Packaging Limited (originltd.com) can help. ■

Author

Richard Quelch
Head of Marketing
Origin Pharma Packaging

Improved Patient Outcomes through Innovative Packaging

Innovative packaging solutions could make a real difference for the brand and product. The demands placed on medical and healthcare packaging are intense. The packaging must protect its content from shock, puncture, temperature fluctuations, vibration, tearing and busting.

Gauri Chaudhari, Co-Founder of Brand Innerworld, a healthcare brand consultancy, who is also an author of the recently released book, 'The Perfect Pill: 10 steps to build a strong healthcare brand', explains about the importance of Innovative Packaging for pharma products.

"We are not in FMCG market, why should we have a special packaging strategy? Our packaging protects brands throughout the supply chain without hampering product quality. Is it not enough?"

I often hear this response from my pharma clients when I ask them about their packaging strategy. There are many reasons behind this response and I perfectly understand them.

Firstly, many brands in the pharma industry are under price control. This has made companies adopt cost conscious mindset. Keeping packaging to basic helps companies keep the costs under check.

Secondly, the pharma brands are promoted to doctors but are bought by the patients. Obviously the doctors don't get to see the sales pack unless patients show it to them. Hence companies doubt the ability of packaging to influence doctors.

Thirdly, unlike FMCG brands, those who buy the medicinal pack (patients) are not the decision makers. So even if the pack impresses patients, it cannot be purchased by them unless it is prescribed.

Yet, the reality of any healthcare ecosystem is that it exists only because

patients do. The purpose of any such ecosystem is to improve patient outcomes, and the only way to do so is to ensure patients take the right medicine at the right time and for the right duration. Packaging can play a significant role in this process if we adopt the right packaging strategy.

Packaging has the potential to create an ultimate win-win situation for all the three stakeholders of the healthcare ecosystem; patients, doctors and the pharma companies. Doctors breathe a sigh of relief when patients remain compliant with their prescriptions. Pharma companies make higher revenues when patients complete their prescribed course of medicine and give positive feedback to their doctors.

Closer home, in India, packaging has yet another important role to play. The Indian pharmaceutical market is crowded with branded generics. There are hundreds of brands operating in the same market with the same molecule. In such a scenario, a brand needs to create value-added differentiation to stand tall in the market. Packaging provides this much-needed opportunity. It can help not only in creating differentiation but also in improving patient outcomes. Such brands are often revered by the doctors and quickly get on to their prescriptions.

Improved patient outcomes through pharma packaging

Medicines don't help those patients who do not take them. Improved patient outcomes are achieved if and only if patients take their medicines as prescribed. There are many reasons why patients do not take medicines as prescribed. Lack of awareness, unclear instructions, forgetfulness or inertia are some of the reasons often sighted. But the list is long.

The first step is getting value-added packaging is to listen to the customers and understand their problems. "What are the pain points of patients, caregivers, doctors and other stakeholders? Which of those problems can be solved by packaging?" Brand development teams must brainstorm to get an answer to these questions.

A few years back, McNeil Consumer Company wanted to launch a Tylenol line

extension for arthritic patients. While listening to the patients, brand teams realized that the biggest hurdle for any arthritic patient is to open the pack of his or her medicine. Reason? Unbearable pain in finger joints.

The team decided to resolve this problem with innovative packaging. Instead of packing the medicine in a strip or a bottle, the brand team created a unique pack. As shown in the adjacent fig , the pack was designed with a hole in the cap. A pencil could be easily inserted in the hole and the bottle could be opened without bending fingers. Such pack was a huge relief for an arthritic patient. It was not an expensive innovation. All it needed was to have empathy towards patients and commitment towards improving patient outcomes.

Closer home, in India, Human Mixtard is yet another example. Human Mixtard is a brand of Insulin. The insulin market has many players with similar formulations. Yet Human Mixtard, a leading brand of Human Insulin, stood apart by creating a simple but highly effective packaging solution.

While talking to chemists, the brand team realized that the insulin formulations across the brands were available in multiple strengths. There was a significant chance for patients or even chemists to mix up the strengths. Insulin is a highly potent drug. A wrong dose of insulin can be fatal to the patient. Human Mixtard figured out a simple yet highly effective packaging solution to resolve the problem. It coded the caps of different strength vials in different colours. Now, the patients and chemist could recognize their Human Mixtard strength just by looking at the cap of the vial. A simple change in packaging ensured that the right medicine with the right dose reached the patient.

This simple but effective packaging strategy aimed at improving patient outcomes, changed the fortunes of the brand. Doctors saw great value in this packaging. They preferred Human Mixtard over other similar brands that were not color-coded. Human Mixtard went on to become the number one prescribed brand in the pharmaceutical industry.

Each disease and its treatment has a unique challenge. Need is to listen to patients and other stakeholders with empathy and create solutions.

Improved patient outcomes through Packaging Design

In addition to rational or functional needs, patients have emotional needs. Illness is an emotional subject. We feel sick. We feel better. There are a lot of feelings

associated with illness and treatments. Understanding these emotions is critical to developing a strong bond with patients which often results in better patient outcomes.

The colours, fonts, visuals, mnemonics and symbols used to design pack together help brands create an unbreakable bond with the patients.

Research has shown that the colour of packaging has a positive impact on health outcomes. For example, a patient suffering from anxiety and depression is positively inclined towards medicine, which is packed in soothing colours. Yellow packaging design for an antidepressant performs a lot better on patient acceptance criteria than dull brown packing. An analgesic that is expected to be strong and effective performs better when given in a red colour pack.

Fonts, too, have an important role to play. There are numerous fonts available for packaging designer. Each font makes a statement about the brands personality. While the sharp, bold font helps patients receive medicine as strong and powerful , a softer, curvier font gives a feeling of it being gentler and smoother.

Ulcikit, a brand for peptic ulcers, came up with a unique design. The strip of Ulcikit

comprises six tablets; three to be taken in the morning and three at night. The pack is designed in such a manner that patients instantly understand the regime of administration. The pack design colours and fonts bring out the friendly personality of the brand. Such designs often build a strong bond with patients and improve overall treatment outcomes.

Voveran, a leading analgesic brand, is meant for the skeletomuscular pain in the

body. It uses blue and red colour on its pack to communicate effective yet gentler brand personality . The mnemonic used on the brand provides much-needed sense of mobility. Moov, another topical analgesic gives the same sense of mobility through the fonts it uses on the pack.

Improved patient outcomes through therapy Adherence

Packaging can play an important role in ensuring patients' adherence to medication. It has been estimated that one third of the Indian patients are non-adherent to the prescribed treatment. Non -adherence often leads to complications and results in higher economic burden.

Medicines for chronic illnesses require long term therapies. Remembering to take medicine every day, ordering a new pack before the previous one is over can be challenging for many patients. Often such lapses result in poorer health outcomes.

Packaging has a unique role to play in providing solutions that improve adherence. There are several examples of calendarized packaging designs wonderfully acting as pill reminders.

Exforge HCT, a cardiac medicine manufactured by Novartis, comes in an interesting monthly pack. It labels not only days but also weeks of the month. It also has instruction for patients to reorder medicine by clearly indicating 'Time to reorder your prescription' above the fourth week. This definitely enhances patient's compliance with treatment.

Non-adherence to medicine to therapies, at times, puts the entire society at a disadvantage. India has a unique problem of antibiotic resistance. Since the patients often stop their antibiotics without completing its full course, antibiotic resistance in India is on the rise. By 2050,antibiotic resistance is expected to be the leading cause of death.

Packaging played an important role in educating/ warning patients to complete the prescribed antibiotic dose. Every strip of antibiotic has a red line indicating this medicine cannot be self-medicated and the patient is mandated to complete its entire course as per doctor's advice.

Improved patient outcomes through technology

Technology often makes the most complex problems simple. Today's technology can

add several features to packaging that aid in improving patient outcomes.

Patients often like to know more about their medicines. What is the dose? Should it be taken with food or empty stomach? What are the side effects? What precautions need to be taken while on the treatment. Putting all this information on the pack is practically not possible. But technology is here to resolve this issue. A QR code on the pack can give all this information to patients without taking up space on the pack. In India, CDSCO is advising pharma companies to print QR codes on the packs to inform channels and patients about the batch size, manufacturing date, expiry date etc.

Yet the application of QR code can be far more engaging.

- QR code can direct patients to brand website to know more about the brand.
- A patient education e-leaflet can be attached to QR code advising patients on various aspects of medicines.
- QR can open in a video. This can be a boon for complicated therapies like Insulin. Self- injecting insulin can be difficult. A video can instantly educate patients on various subjects including lifestyle modifications, exercises and diet.
- QR code can act as a pill reminder. On scanning QR code patients or caregivers can add recurring events to their calendar and get suitable reminders.

Future trends in Packaging

-Interactive pack: Technology can convert a pack into a content channel. An interactive sample pack can augment the efforts of the medical representative in a doctor's chamber

- Temperature sensor pack: Many medications are temperature sensitive. Digital technology today can alert chemists or patients if the medicine is

stored at the temperature outside the range.

- NFC technology to record when the pack is opened each day. If patient forgets to open the pack at the expected time of the day, alert is sent to his or her phone for reminding the dose.
- Microprocessors and conductive inks RFID can record the date and time at which the medicine is taken. Such packs are already available and being used in clinical trials to get the accurate data.

Of course, some of these inventions are expensive and are unthinkable in the country like India. Yet, technology tends to get cheaper over a period of time. Hence pharma brand marketers need to keep a tab on the latest technology.

In the coming decade, the packaging will become more and more important in the pharma industry. We are going to see packaging playing a critical role in improving health outcomes. Need is to put in sincere efforts to understand customers' pain points. Packaging strategy has the potential to build pharma product into a strong brand. But of course, that would be just a by-product. What would count the most? Blessings from patients. ■

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Gauri Chaudhari
Co-Founder of Brand Innerworld

New Frontiers of Growth in the Life Sciences Industry

The life sciences industry is on the cusp of change. While this change does give rise to some challenges, it throws open doors for new opportunities and possibilities. In order to capitalize on these opportunities, an organization must be on a dual mission of 'renew - new' – one that simultaneously focuses on renewing existing systems and processes for greater efficiency and adopting new advancements in technologies to gain value. In this paper, we discuss these opportunities and the way forward for the life sciences industry.

Recent scientific and technological advances coupled with an aging population, expansion in the emerging markets, and an exponential increase in mainstream adoption of digital technologies have set the ball rolling for the life sciences industry, providing it with a renewed platform to revive its fortunes.

With an explosion of digital data availability – electronic health records, social, genomics, clinical, insurance, and more digitally engaged consumers, the stage is set to derive benefits from an integrated drug development and manufacturing environment. Such an environment not only provides the best care for patients but also generates significant revenue growth. Furthermore, there is significant focus on personalized healthcare from both the Life Sciences industry and policy maker perspective. A case in point is President Barack Obama's precision medicine initiative. Personalized healthcare, however, would require a complete shift in how the industry evaluates the market (focus on an individual instead of a population), analyzes higher volumes of data, and puts in place newer processes and methods to complete their studies. The spate of recent investments in the immuno-oncology therapies is pointing towards a significant growth in the coming decade.

Technology is playing a massive role in enabling the industry to achieve these objectives, be it analytics in personalized medicine, cloud computing in collaboration, or wearable devices in remote and self-health monitoring. As the world becomes increasingly connected, information and communication technologies will fundamentally reshape both the consumption and delivery of services in life sciences. The industry must prepare for the future by embracing next-generation technologies and systems throughout the life sciences value chain.

We believe life sciences companies must adopt a more proactive strategy, one that allows them to maximize value from prior investments by renewing existing solutions and processes and generate new value by embracing new technologies, systems, and best practices.

Opportunities for 'renew' in Life Sciences

The Life Sciences industry is undergoing a major transformation. A large part of this is fueled by the integration of digital that has driven a powerful re-imagination of the Life Sciences industry landscape.

This transition has opened up new opportunities for development, but also comes with its own challenges.

- **Innovate through cloud:** Cloud's greatest impact is in facilitating innovation through increasing accessibility of both internal and external data. While initially the reasons for cloud adoption were centered on reducing the cost and the time for infrastructure provisioning, it is now providing many more strategic benefits such as enhancing collaboration and providing much greater computing power across the entire value chain from R&D, sales & marketing to enabling functions such as HR and finance.

  In pharmaceutical research where large volumes of data (notably next-generation DNA sequencing systems and genomic tools) needs to be mined and the cost of obtaining this sequence is rapidly decreasing, data has further increased the number of

both, instruments being used and labs using them. Through cloud's agility of provisioning and pricing (pay-per-use), setting up massive infrastructure resources for data crunching, analysis, or simulation is no longer an impediment.

Similar cases are happening in clinical research. A large pharma company is setting up a cloud-based solution to integrate clinical data across all its global trials and provide it to its global operations team for analysis. These big data solutions that receive clinical data instantly from all the current trails will reduce the time taken to analyze and predict the path of the trials, while decreasing the operating expenses substantially. On a broader application, the scope of collaboration is expanding to include R&D processes outsourcing, exemplified in virtual laboratories where thousands of researchers from contract research organizations can seek and provide help. Overall, by opening the doors of collaboration, exploding analytical power, and making information more accessible and manageable, the cloud is encouraging new practices such as open innovation in life sciences.

The industry must leverage these to

the fullest.

- **Smarter and transparent supply chains:** Due to globalization and the ever increasing size of organizations, the need to integrate supply chains and gain visibility into them has become critical. Wide diversity of the product mix (biologics versus small molecule) will further compound the need for supply chains that can handle this mix. Furthermore, regulatory policies on transparency are evolving and several states in the U.S. have passed product pedigree laws, and many others are contemplating such legislations. In summary, supply chains will need to transport an increasingly diverse range of products in a challenging environment with resources that are much more geographically scattered while simultaneously optimizing costs.

  As technology erases the distinctions between the virtual and the physical, it sets up the opportunity to create intelligent, analytics-driven, next-generation supply chains that provide real-time, end-to-end visibility and control. A smart supply chain, integrated across all business processes and systems, can also leverage real-time data and analytics to enable more accurate forecasting, shorter response times, optimized supply chain processes, and faster decisions.

  To enable transparency, pharma organizations are not only implementing global track and trace solutions but are also experimenting with cloud-based, leaner supply chain management solutions. While more prevalent in the CPG Industry, discussions in the pharma community on these lean solutions that can provide visibility on their products after they leave their warehouses have taken place. These solutions are being used in the developing nations that have a more complex network of distributors and wholesalers. Such solutions will promote growth by preventing stock-outs and allowing further optimization of inventory and support recalls.

- **Renew through automation and modernization:** Most large pharmaceutical organizations are born out of numerous mergers and acquisitions and have inherited portfolios of IT applications in various stages of modernization. In our experience, a substantial part of the legacy portfolio is either outdated or manual, creating high cost burden of managing them while ensuring they meet the complex and evolving regulatory compliance standards. While legacy systems are integral to the continued operational maintenance, they hinder the adoption of newer digital solutions.

Best-in-class companies are standardizing business processes, measuring manufacturing, focusing on visibility, and using the right tools. They are using automation to manage the processes and drive increased business value. Automation is being welcomed in the industry as an alternative to manual steps, especially across processes that have repetitive steps. Automation not only reduces the time taken to execute a task but also frees up time for valuable resources to focus on productive tasks. In manufacturing, Process Analytical Technologies (PAT) are being integrated across the assembly line to automatically capture unit operations data and integrate it with the plant quality equipment. This automation allows instant feedback on the batch quality based on the analysis of data while preventing waste and reducing costs. In R&D, numerous research labs are going paperless by integrating their critical solutions such as ELNs and LIMS with their high throughput chromatographs.

This has not only reduced the time taken, but also minimized errors and allowed scientists to collaborate more effectively leveraging digital data. Additionally, in core IT services, a novel use of automation is in enabling testing of large and complex enterprise solutions. Panaya, which was recently acquired by Infosys, uses artificial intelligence to provide impact assessment and execute automated testing of their enterprise solutions. As a result, it can achieve 75-80% reduction in time and resource consumption. This is now being utilized across a number of large organizations with substantial time and resource savings. Automation is also being effectively utilized in executing the many repetitive tasks in application support services resulting in greater than 35% efficiency savings for organizations.

We envision that the automation of IT processes will soon become a key component of the life sciences operations and new-generation leaders will mandate these efficiency savings within their lean organizations.

New opportunities for life sciences

Populations are aging. Chronic illnesses are increasing. New disease strains are emerging at an alarming rate. Add to this mix, the soaring number of patients in a greater spread of geographies. Top it with global regulatory mandates. Then, factor in the variable dosage needs. Think about the shelf life of pharmaceutical drugs and medications. And, we are looking at skyrocketing global healthcare costs. At the same time, there is pressure to

develop innovative drugs to save more lives.

Here are the opportunities that await the life sciences industry:

- **Connected patients and partners:** In today's socially connected world, pharmaceutical companies have a clear opportunity to play a greater role in delivering a better experience for patients and their providers. Patients are becoming demanding about how they want their care. This has precipitated a major transformation in business and technology and has led organizations to adopt a patient-centric model. Earlier attempts at creating these solutions were exclusively focused on adherence to the medication. However, an emphasis on continuity of care provides an opportunity for pharma companies to play a bigger role. Digital solutions are facilitating patient education, behavioral change, and better communication with clinicians. There is also a wide variety of solutions that facilitate this connect including web portals, body sensors, and apps. These help the patient self-monitor and get needed support, between visits to the physician.

  These solutions now provide health advice anytime, anywhere, by developing patient-centric smart tools and devices. These devices

also detect and track data regularly and accurately and relay the same to physicians.

Mobility is another key feature of these solutions, making it easier for the patient to communicate. A hospital network in Boston empowers patients to use their home devices to track and report data to their doctors. Patient and physician- centric portals, where comprehensive information about treatments and drugs is actively shared, are also on the rise.

In the future, pharma companies will design holistic Medical-health (M-health), platforms that connect the patients and physicians across the globe, drive patient and physician engagement, and activation – all with the objective of improved care experience for patients, better clinical outcomes, and lower total cost of care. In the new collaborative, omni-access data world, this will be a key factor in attracting and retaining patients, partners and clients. To keep pace

with a rapidly changing technology landscape, organization, would need to develop a deeper integration, collaboration, and synchronization of activities across all channels.

- **Adoption of IoT and wearables across the value chain:** Ubiquitous presence of smartphones and substantial investments in Internet-of-things (IoT) are providing an exciting opportunity to reduce the gap between the patients and the pharmaceutical industry. While still in its nascent stage, higher adoption of IoT has already started to facilitate at-home diagnostic testing, self-management of chronic diseases, and remote patient-health care provider interaction in the healthcare industry.

  For life sciences companies, the adoption of IoT can improve medication adherence and reduce time by capturing critical clinical indicators directly and sending them to the EDC system, produce better outcomes based on analytic insights such as in clinical trials where patient data through wearables has been found to be useful for tracking recovery from cardiac surgery, judiciously replace physical interaction with digital intervention, and lower the cost of treatment. Doctors are turning to wireless devices such as Fitbits to understand the factors that help the recovery of patients. A report published in the Annals of Thoracic Surgery says, "Wireless monitoring of mobility after major surgery was easy and practical. This opens the door for changing recovery models and improving outcomes in surgical practice."

  Early market movers already see the use of pill-shaped micro-cameras that traverse the human digestive tract, sensors in pills that track concordance, hip replacements that detect falls and send messages to care providers, and thousands of health-monitoring applications that send messages and data from the home to the hospital or patient to the HCP to improve early diagnosis and treatment solution.

  One critical innovation in this area is the advancement by Proteus Digital Health. It has created an FDA-approved small pill that consists of a pinhead- sized sensor embedded in the pill and a battery-powered patch that monitors various health indicators such as sleep, activity, respiration, and heart rate. The recent announcement by Novartis of partnering with Google on developing contact lenses that will monitor blood sugar levels and even correct impaired vision will further transform eye care and exemplify another frontier in adoption of IoT.

  The adoption of IoT is yet to pan out in

the life sciences industry. The industry must work cohesively to overcome the barriers to wearable technology adoption – concerns of security and privacy, data sharing and protection, regulatory compliance, among others – to take life sciences to the next level. In our view, companies that are proactive in using IoT will be the leaders of the future.

- **Effective big data utilization to generate insights:** From next-generation sequencing data and patient information to supply chain monitoring, pharmaceutical firms have been managing massive amounts of data for years. In recent years, rapid digitization has made access to larger volumes of data (EMR, clinical, genomics, wearables), an everyday reality. The need to design solutions that will systematically analyze and generate real-time insights from these mountains of data more effectively is critical for success. To develop and deliver the next generation of successful therapies, the industry must simultaneously minimize the cost of processing / managing data while maximizing its value. This is complicated by the need to continue integrating new data types and sources from around the globe and to glean insights from unstructured data, while complying with multiple complex regulations governing drug safety, supply chain security,

patient privacy, and other sensitive information.

Since early 2000, research units within biopharmaceutical organizations have been actively harnessing the powers of big data by leveraging the advancements in next-generation sequencing. This includes a variety of studies including whole-genome sequencing, targeted re-sequencing, discovery of transcription factor binding sites, and noncoding RNA expression profiling, among others. Organizations are now able to leverage the vast library of available molecular and clinical data, utilize predictive modeling techniques, and identify new potential candidate

molecules with a high probability of being successfully developed into drugs while ensuring efficacy and safety.

Clinical development now is also benefiting from big data solutions. We have already mentioned earlier how a large pharmaceutical company is creating a cloud-based aggregated clinical data solution that will house results from all of its global trials.

Faster access to and analysis of this data will reduce the time-to-market and enable rapid decision-making capability. We envision that a further integration of clinical operations data with safety data will allow near real-time monitoring of trials and provide the ability to rapidly identify safety or operational signals demanding action to avert adverse events and unnecessary delays.

We believe that the need to uncover valuable relationships within the existing data is the key to boosting innovation and driving new value. With computing power and storage becoming cheaper, as well as increase in cloud adoption, the life sciences industry stands to benefit tremendously from big data solutions.

Conclusion

There are several reasons for the conservatism of the life sciences industry. But given the current dynamism in the sector, occasioned by regulatory, market, and technological forces, life sciences companies can no longer hold back. We believe this is a time of great opportunity, albeit with some challenges, for this industry. As the industry looks to grow while managing existing investments, it must adopt a dual strategic approach towards technology- renew existing systems and processes for greater efficiency while adopting completely new technologies and practices for value creation. ■

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Making the Medicine Go Down: Specialized Oral Solids Delivery Technologies

In this article, Sandra Conway, Technical Lead at Pfizer CentreOne discusses some of the drug development technologies that provide a more specialized approach to oral dose delivery.

The oral administration of drugs in tablet or capsule form is still the most common practice for taking medicines today and oral solids accounts for a large proportion of drugs in the development pipeline. Most oral solid formulations are designed to release the drug immediately after swallowing for rapid absorption into the bloodstream. However, some products have been developed to release the drug in a specific way following ingestion and provide a "controlled-release" of the drug products.

Why controlled release?

Controlled-release products are considered by drug developers for the following reasons:

- To provide improved pharmacokinetic profiles compared with the immediate release product (i.e. steady state plasma concentration resulting in reduced adverse events)
- Reduced dosing frequency for improved patient convenience and/or compliance and improvement in overall efficacy. Controlled-release products are often adopted for drugs with short half-lives which are used to treat chronic conditions

Many marketed controlled-release products are hydrogel-based tablets or capsules containing coated beads, which can be produced using conventional pharmaceutical manufacturing equipment. However, to achieve particularly demanding drug release criteria it is sometimes necessary to adopt more sophisticated pharmaceutics, such as the use of osmotic pumps, which require more complex manufacturing strategies.

Osmotic pump technologies

Osmotic pump tablets are coated with a semi-permeable membrane which is breached in one location by a laser-drilled port. Water permeates through the

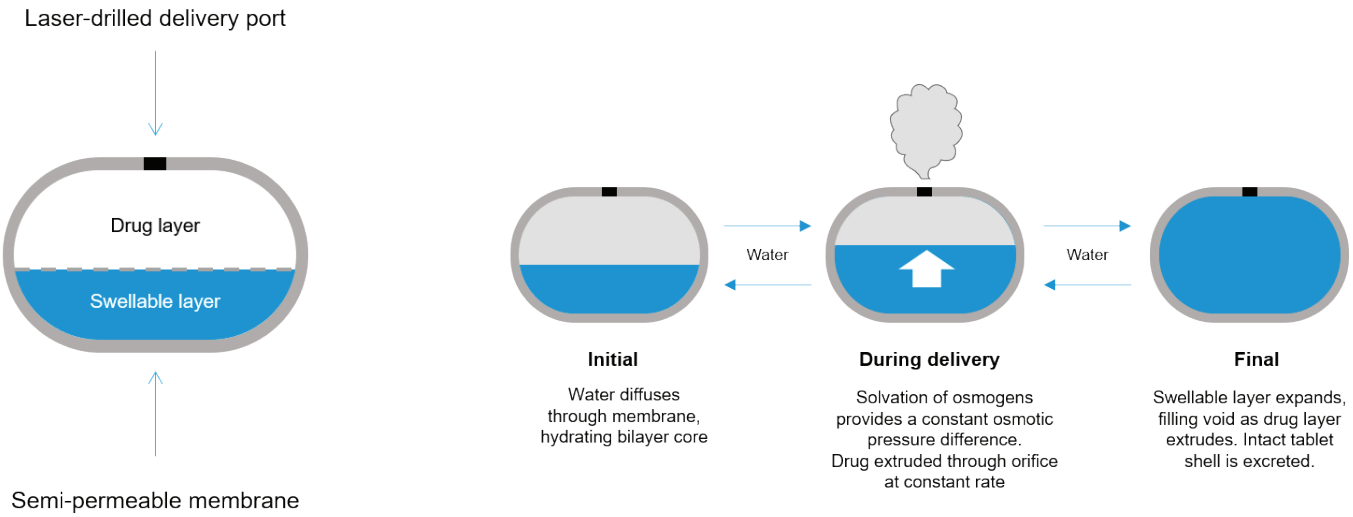

Figure 1. Schematic illustrating the working principle for the SCT. As water permeates the membrane the swellable layer expands, applying pressure on the drug-containing layer and hence forcing the drug through the port.

membrane, dissolving excipients in the core and thus raising the internal pressure. The raised pressure in the core causes the contents to be forced through the laser-drilled port at a constant rate.

The benefits of osmotic pump technologies for controlled drug release are:

- Zero-order drug release (i.e. drug is released at the same rate over a given period of time).
- The drug release rate is independent of the gastric pH
- The release rate from the delivery system is not affected by the presence of food (i.e. no food effect)
- High degree of in-vitro/in-vivo correlation with these kind of delivery systems
- Single daily dose is achievable

Pfizer CentreOne has two osmotic pump technologies within its Gastro-Intestinal Therapeutics Systems (GITS) portfolio. The Swellable Core Technology (SCT) consists of a round, bilayer core. One layer which contains the drug and a second layer which swells as water diffuses into the core, applying pressure on the drug-containing layer and thus extruding the drug through the laser-drilled port (Figure 1).

The Extrudable Core System (ECS) consists of a single-layer core containing both the drug and a polymeric viscosity enhancer. As water permeates the semi-permeable membrane the polymer hydrates and swells. The internal osmotic pressure increases and the viscous, drug-containing fluid is pushed through the laser-drilled port (Figure 2). The modified

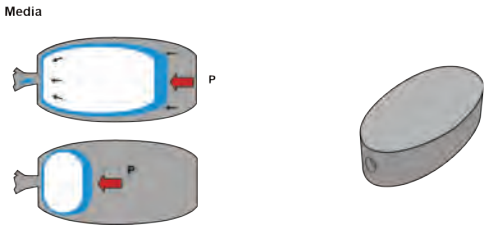

Figure 2. Schematic illustrating the working principle for the ECS. As water permeates the membrane the internal pressure (P) forces the drug-containing fluid through the port.

oval shape of the tablet helps control the release rate of the drug.

The single-layer design of the ECS allows higher drug loading compared with the SCT technology and the modified oval shape of the tablets make them easier to swallow compared with round SCT tablets. Single-layer ECS cores are also easier to manufacture compared with bilayer SCT tablets. The advantage of SCT tablets is that they deliver a more complete delivery of the unit dose from the tablet compared with ECS tablets.

For both the SCT and ECS osmotic pump tablet technologies, control of drug release depends upon the presence of a semi-permeable film with a laser-drilled port. The semi-permeable membrane is typically composed of a water-insoluble cellulosic polymer incorporating a water-soluble pore-forming agent. The permeability and thickness of the film are critical for achieving the required drug release rate. Film-coating of the tablet cores is therefore a critical process, particularly the intra-tablet coat uniformity to ensure coat integrity. Process analytical technologies (PAT) are employed to determine the process endpoint for

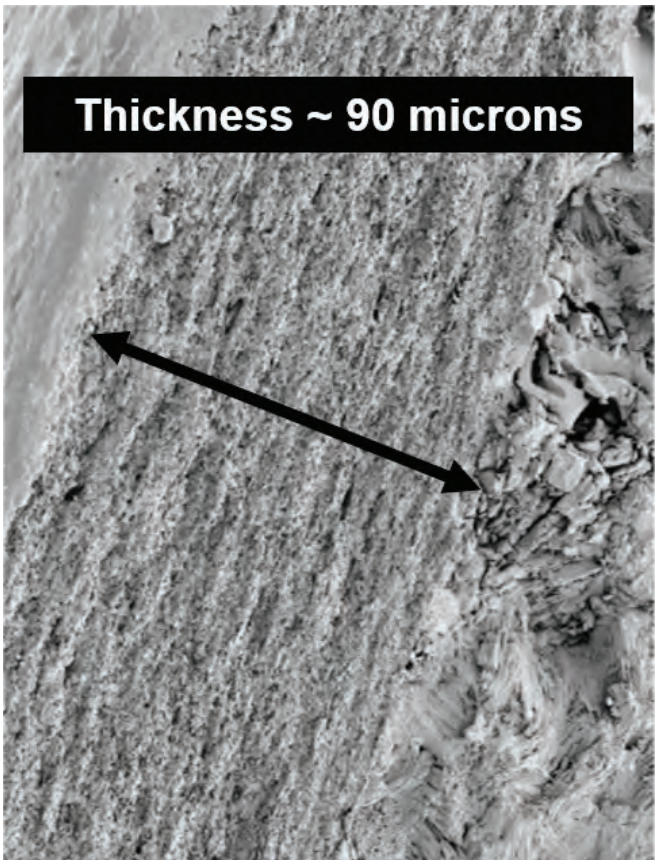

Figure 3. Cross-section of osmotic pump tablet showing semi-permeable film coat

coating and ensure the correct film thickness is achieved. A cross-section image of a coated tablet is shown in Figure 3.

The size of the port in the membrane is also critical for controlling drug release. Therefore, the laser-drilling process requires tight control. Vision systems are used for 100 per cent inspection of all laser-drilled tablets to ensure the presence, correct location and size of the port for all tablets produced.

Osmotic pump technologies have become popular for controlled drug delivery

Product	Drug substance	Dose (mg)	Indication	Manufacturer
Glucotrol® XL	Glipizide	5, 10	Diabetes	Pfizer
Minipress® XL	Prazosin	2.5, 5	Hypertension	Pfizer
Cardura® XL	Doxazosin Mesylate	4, 8	Hypertension	Pfizer
Procardia® XL	Nifedipine	30, 60, 90	Hypertension	Pfizer

Table 1. Commercially available SCT-type products

purposes and there are now many marketed products which utilise this approach. Some examples of commercially available osmotic pump products are given in Table 1.

Conclusion

Controlled release technologies provide versatile platforms for oral drug delivery. It is now possible to tailor drug release to match complex administration criteria in a single dosage form.

Osmotic pump technologies have become particularly popular due to their consistency of performance. In particular, the degree of correlation between in vitro versus in vivo performance is usually better with these osmotic controlled released forms than other conventional dosage forms. This is primarily due to the insensitivity of the release rate to food, pH and position in the GI tract.

There are now many marketed products that use this principle, for instance, they are used extensively for administration of hypertension drugs – providing accurate control of dose delivery and management of pharmacokinetics. They also offer the opportunity for extending the time between dosing intervals and thereby make life easier for patients on long-term medication, especially important for patients on multiple medications.

The use of controlled-release technologies in drug development will therefore certainly grow in popularity to meet patient needs. ■

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X-Ray Crystallography: A Revolutionary Tool in the Study of Solid Forms of Pharmaceuticals

X-ray crystallography is a powerful non-destructive technique for determining the molecular structure of a crystal and finding out how particles are arranged inside crystals. X-ray crystallography uses the principles of X-ray diffraction to analyze the sample, it is done in many different directions so that the 2D and 3D structures can be built up. It is a technique that has helped to deduce the 3D crystal structure of many materials, especially biological materials and revolutionized the field of solid state chemistry, especially in pharmaceutical landscape. William Bragg (father-son duo with same name), invented X-ray crystallography in 1912. At the time, all the calculations were done by hand – they won a Nobel Prize in 1915 for their work. The method has been used to solve the structures of many important molecules. In the 1950s Francis Crick and James Watson used pictures of DNA taken by Rosalind Franklin to solve the DNA structure. Dorothy Hodgkin determined the structures of the antibiotic penicillin (1946), vitamin B12 (1956) and insulin (1969), winning a Nobel Prize in 1964.

Key Principles and Instrument

When the X-ray beam hits the crystal, a pattern of spots is made on the screen at the other side. Complicated mathematics called Fourier transformation (FT) is applied using a computer to change the spot pattern into a picture showing how the particles in the crystal are arranged. In the instrument, the sample is mounted on to a goniometer, which is used to position the crystal into specific orientations so that it can be analyzed from multiple angles. X-rays are generated from an X-ray tube, and they are then filtered so that they are monochromatic, i.e. of a single wavelength frequency. The atoms in the crystal refract the X-rays and the X-rays are elastically scattered on to a detector, they have the same energy as the incident X-rays that are fired at the

sample. This generates a 2D diffraction pattern of the crystal in a single orientation.

Applications of X-Ray Crystallography in Pharmaceuticals

Solid State Characterization:

Powder X-Ray Diffraction (PXRD)

Powder X-ray diffraction (PXRD) measures the diffraction pattern of crystalline material in powder form as opposed to single crystal. PXRD is one of the most common bulk techniques used for the analysis of powders and is similar in concept to the single-crystal analysis, except the data is generated on the bulk powder instead of a single crystal. Each API produces a specific pattern depending on the structure of its crystal lattice. Each polymorph, salt, or co-crystalline material will exhibit its own specific pattern. For this reason, PXRD of the API can be done in controlled environmental conditions, using hot stage and/or controlled humidity environments in order to study the chance of any form conversions (e.g., hydration/dehydration). In addition to this, it can be used to determine if any change in crystalline form (e.g., hydration, salt disproportionation) in the drug product has occurred during the APS study. This relies on the presence of detectable diffraction peaks of both the ingoing API form and the forms to which it may convert at the formulated levels. In addition, the API peaks must be distinguishable from any crystalline excipient peaks. PXRD is also used for qualitative as well as quantitative determination of the degree of crystallinity of the pure API. Disorder leads to peak broadening in the powder pattern, and eventually an amorphous 'halo', a broad peak is obtained (see Fig-4).

Polymorphism and its Significance in Pharmaceutical Industry

Most drug molecules are highly functionalized and can self-organize in several ways in the solid state with nearly the same lattice energies. Due to this property, many drug substances crystallize in different arrangement of the molecules in the crystal. This ability of the substances to crystallize in different crystalline forms is called polymorphism. Screening for various solid forms of an API and selection of the right form is a critical step in drug development.

APIs may exist in multiple crystalline forms such as salts, hydrates, solvates,

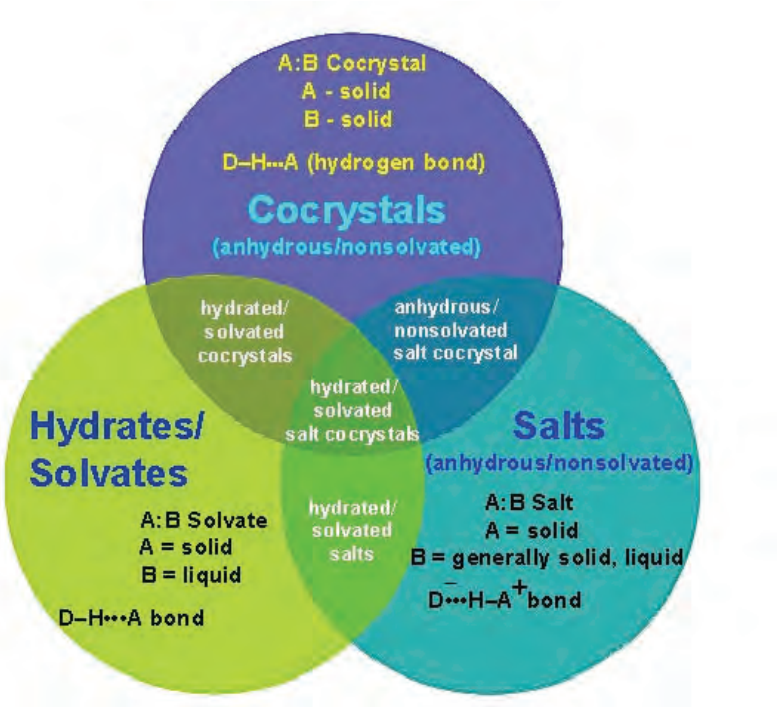


Fig-1: Inherent Overlap of Multi Component Solid Forms

co-crystals and their polymorphs (See Fig-1). These distinct solid forms impact physico- chemical properties of the API and offer solutions to solubility, stability, bioavailability, and patenting issues in drugs. Thus, polymorphism can affect the quality, safety, and efficacy of the drug product.

There are a number of methods that can be used to characterize polymorphs of a drug substance. Demonstration of a nonequivalent structure by Single Crystal X-Ray Diffraction is currently regarded as the most definitive evidence of polymorphism. X-ray powder diffraction (PXRD) can also be used to provide unequivocal proof of polymorphism. Other methods, including microscopy, thermal analysis (e.g., differential scanning calorimetry (DSC), thermal gravimetric analysis (TGA), and hot-stage microscopy), and spectroscopy (e.g., infrared [IR], Raman, solid-state nuclear magnetic resonance [ssNMR]) are helpful to further characterize polymorphic forms.

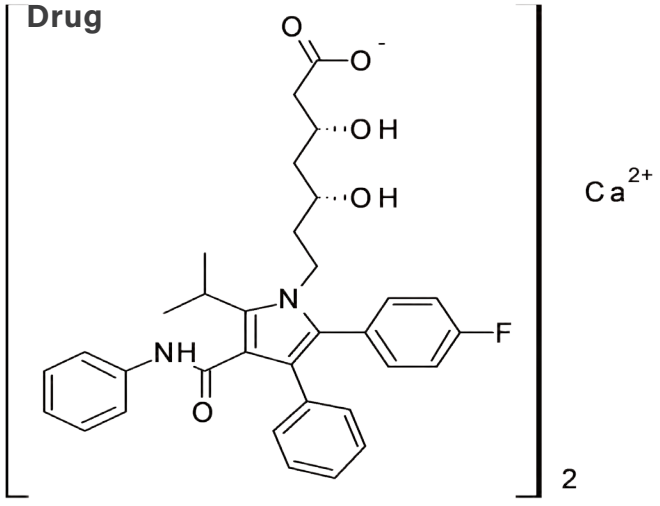
In fact XRD in combination with above mentioned techniques has revolutionized the solid state characterizations and brought useful innovations in the form of novel polymorphs, solvates, co-crystals and stabilized pharmaceuticals.

Solvates: Emerging Tool in API Development

Solvates are multi component crystal forms generally containing stoichiometric amounts of a solvent. If the incorporated solvent is water, the solvate is commonly known as a hydrate. Pharmaceutical chemists face many challenges in the lab and manufacturing due to issues related to scalability of various forms of a given solid form, and solid form inconsistencies.

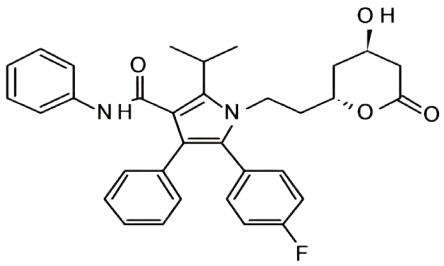
Due to difference in their physical

properties such as polarity and solubility, solvates sometimes also serve as tools in the purification of API. Recently, solvates of several drug molecules have been isolated with an aim to purify them, otherwise difficult to purify by conventional techniques. In



Atorvastatin Calcium

Intermediate



Atorvastatin lactone

atorvastatin, difficulty in the isolation of lactone is one of the reasons that Ca salt of the open dihydroxy acid is recommended as drug. The lactone form has not been described in the prior art with respect to the existence of polymorphism. We developed a process for the preparation of novel crystalline solvates such as DMSO solvate of atorvastatin lactone (DMSO content 17-22%, m pt 127-130 as supported by TGA). DMSO solvate (see Fig-2) was used for the isolation of lactone in highly pure form, leading to an efficient process technology for the removal of unwanted impurities from the API.

Solvates of anti-cancer drugs Sorafenib and lenalidomide have been well established and used as purification tools for API. There are many drug molecules in which solvate formation is a common occurrence, therefore, some are recommended in the form of solvates. For example darunavir ethanolate and estradiol which forms solvates with 30 solvents. Desolvation leads to the formation of other form, atorvastatin lactone DMSO solvate leads to the formation of amorphous form after desolvation as confirmed by its PXRD (see Fig-4). As per the new US FDA guidance on Chemistry, manufacturing, and controls (CMC) information regarding polymorphic integrity of drug substance must be submitted to support the approval of an abbreviated new drug application (ANDA).

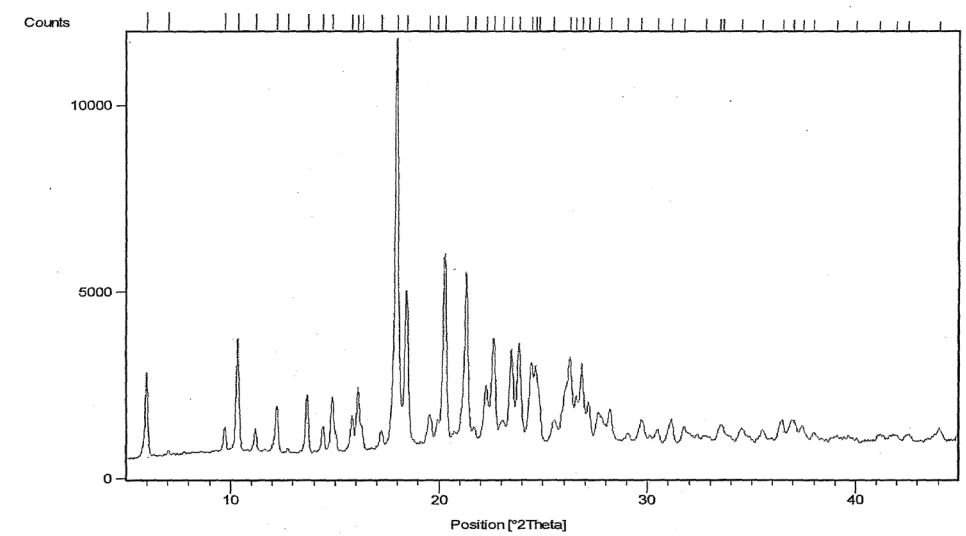


Fig-2: PXRD-Crystalline Atorvastatin Lactone DMSO Solvate

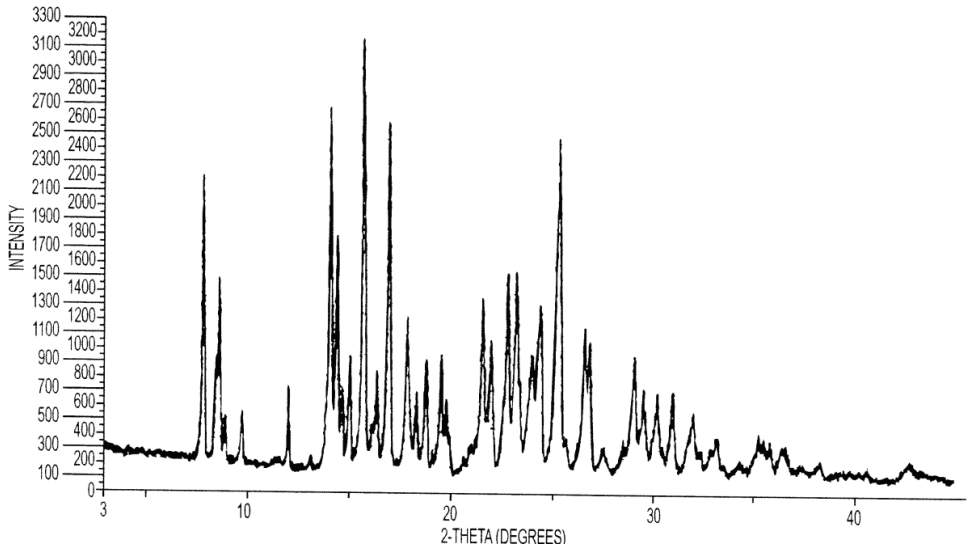


Fig-3: PXRD of DMF Solvate of Anticancer Drug Lenalidomide
DSC shows endotherm at 263 deg TGA: weight loss 13% at 146 deg C

Polymorphism and Patents: From Innovator and Generic Perspective

Polymorphism is playing an increasingly important role in establishing and protecting intellectual property rights in the pharmaceutical industry. As in the analysis and characterization of polymorphs a variety of analytical methods may be used in patent specifications. The preparation, prosecution and protection of a patent involving polymorphs is a challenging scientific and legal activity.

Generic's Perspective: Reverse Engineering is being extensively used by generic pharma companies for the determination of Polymorphic Forms of API in Innovator Tablets. Powder XRD (PXRD) is the handy main identification tool for the polymorph determination in innovator tablets because of non-availability of pure API used by the innovator and absence of samples of pure polymorphs. Discovery and development of alternate or novel polymorphs other than innovator's morph of a patented drug by a generic

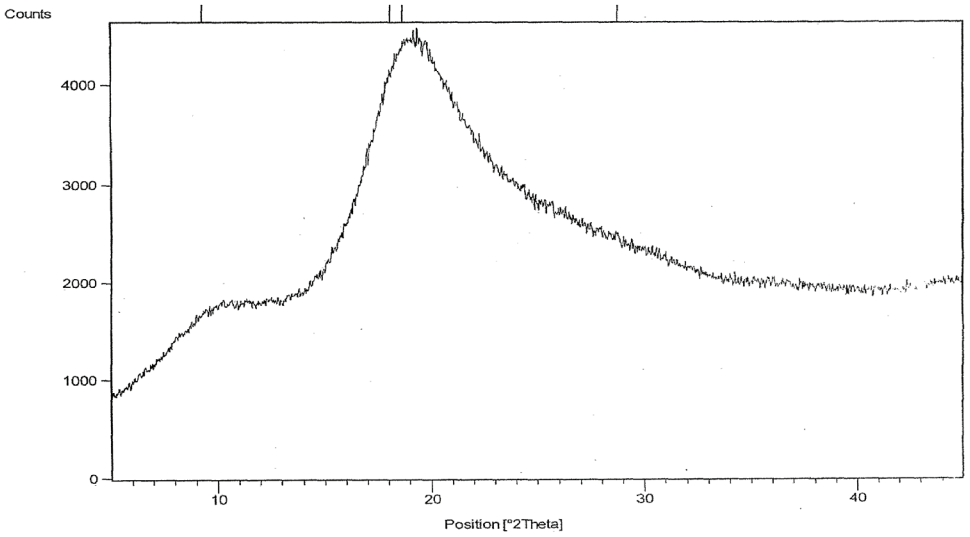


Fig-4: XRD of Atorvastatin Lactone Amorphous

company provides an opportunity for paragraph IV certification: the first ANDA approved with P-IV certification is entitled for 180 days marketing exclusivity. Novel or alternate polymorphs are also developed to block other generic launches with the help of marketing exclusivity and patent protection for some time.

Innovator's Perspective: Innovator companies extensively study the polymorphism of new drug molecules to identify the most suitable form with respect to solubility and stability as early as possible. Other objective of this study is to delay generic entry by filing patents, covering solid forms in the Orange book. By this innovator gets the advantage of 30 months stay in case of generic ANDA's para IV certification. This strategy is called IP Fencing.

Latter enhances the product life cycle by blocking generic entry by building a product portfolio around different forms- also called "ever greening of patents".

Drug Design: Investigating protein function and interaction, as well as developing direct drug design strategies requires structural information provided by X-ray crystallography. The Nobel Prize in Chemistry 2009 was awarded to V. Ramakrishnana, T. Steitz and A. Yonath for their work in the field of structural and functional studies of ribosomes wherein they applied X-ray crystallography most often during these studies.

Protein Structure: The elucidation of a macromolecular structure at the atomic level by X-ray or neutron diffraction analysis requires the compound to be formed into relatively large single crystals without any inclusions. Though protein crystallization is very difficult because of the fragile nature of protein crystals, many soluble proteins, membrane proteins, nucleic acids, and

nucleoprotein complexes have been obtained in a crystalline form suitable for crystallographic investigation. When a solution of a biopolymer is brought to supersaturation, the biopolymer may form crystals suitable for X-ray diffraction analysis, an amorphous precipitate, or any physical form between these two extremes. Parameters such as pH, temperature, chemical composition of the crystallization solution, and the rate of supersaturation determine whether an amorphous precipitate or crystals are formed. Supersaturation is often achieved by increasing the concentration of precipitating agents in the crystallization solution. Auxiliary substances may improve crystallization or may initiate crystallization in otherwise static solutions.

Conclusion

X-Ray Crystallography has emerged as a powerful tool in the last few decades for the accurate determination of molecular structure at atomic resolution. Principles of Powder X-Ray Diffraction in combination with DSC, TGA, Raman, etc. have revolutionized the solid state characterization of pharmaceuticals. Single crystal X-ray diffraction and PXRD are currently regarded as most definitive evidence of polymorphism and are used to determine the polymorphic integrity of drug substances as per US FDA guidance. Innovator and Generic companies must continue to evolve this area to innovate novel Polymorphs, Co-crystals, Solvates and Stabilized Products to meet the medical needs. ■

About Author:

Dr Rajesh Kumar Thaper has held several senior R&D positions in top pharmaceutical organizations like Ranbaxy, Lupin, Dr Reddy's and Jubilant. He has over 27 years of rich experience in Technology, Innovation and Execution. He has about 120 Patents and several scientific Publications to his credit and developed over 100 molecules.

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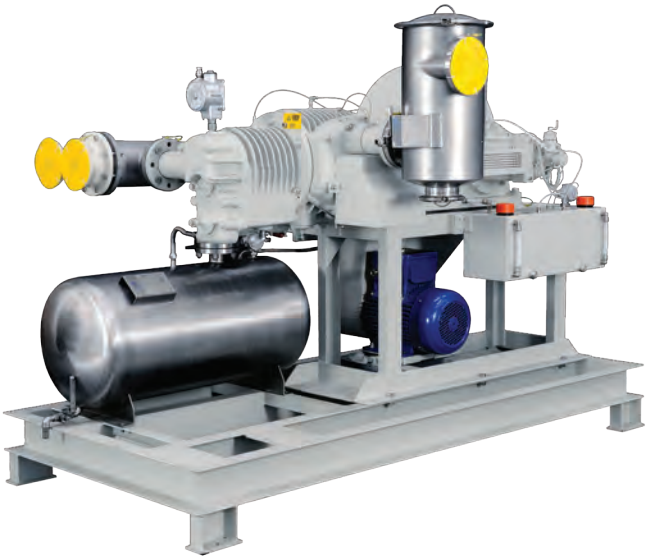
ITALVACUUM
Improving drying processes since 1939

Italvacuum is one of the leading international manufacturers of vacuum pumps and vacuum dryers since 1939 mainly used in production processes in chemical, fine chemical and pharmaceutical companies. Striving to serve its customer's needs all around the world, the firm offers multiple versatile turn-key solutions, as well as tailor-made equipment and systems, according to the client's individual process requirements in the chemical, specialty chemical, agro-chemical fine-chemical and pharmaceutical industry. Moreover, their original and patented product selection complies with all the general international regulations (ATEX, UL, PED and ASME) and with the latest FDA and cGMP norms.

Saurus939® - Italvacuum's trademark

The vacuum piston pump that guarantees best performances, ensuring total recovery of extracted solvents, even in severe operating conditions. A simply designed machine, that combines traditional robustness and reliability with the most evolved technology.

Resistance, strength and consumption



of oil virtually eliminated thanks to the innovative LubriZero® system. A solution which guarantees perfect operation and optimum results with total respect for the environment. Saurus939® has no fear of aggressive and corrosive solvents, powders and condensates, nor distillation by-products.

But above all it does not fear confrontation because it is designed and manufactured to work 24 hours a day with a constant excellent performance and minimum operating costs, thanks to a low-energy motor, negligible oil consumption and easy, immediate maintenance.

Powerful, efficient, but absolutely safe: Saurus939® guarantees optimum safety

Some moments of the last training held in September in Italvacuum facilities that had technical - operational parts and technical - documentary parts

through the whole process and complete purity of the final product.

In other words, ensures an uncontaminated vacuum. Saurus939® has a wide range of use and could be employed in different sectors: Chemicals, Pharmaceuticals, Cosmetics, Oil & Gas, Plastics & Rubber, Bioscience and Waste Management. Especially effective in the processes of drying, reaction, distillation, crystallization, filtration, evaporation and polymerization.

Tradition, Innovation and technical support

Since 1939 Italvacuum produces vacuum pumps with great technical know-how and a thorough knowledge of the needs of its customers, which has also progressed along with the developments in chemical and pharmaceutical industries. The company's awareness on those changes over time, enabled its engineering services to build up unparalleled expertise in vacuum processes.

Focusing on individual needs, pilot tests can be arranged at the manufacturer's headquarters to determine the best possible solution for the clients.

Since efficiency and safety are of highest

priority, Italvacuum's qualified personnel provides the following services after an installation

- Scheduled Preventive Maintenance
- Technical Assistance
- Service Parts
- System Upgrading and Overhaul.

In giving assistance in all of these areas, the firm ensures the proper function as well as durability of the product and a fruitful production process.

Not only Saurus939®: the dryer series

Multispray Cabinet Dryer®, tray vacuum dryer with C.I.P. (Clean in Place) Multispray® patented fast-washing system.

Criox® System, rotocone vacuum dryer / powderer with electric lump-breaking units.

LaboDry®, laboratory-scale tray vacuum dryer.

Planex® System, patented horizontal vacuum dryer with ZeroFriction® planetary movement eccentric agitator.

CosmoDry® System, patented horizontal vacuum dryer with concentric agitator

Italvacuum presence in India – 20 years of cooperation

Over a thousand vacuum pumps from Italvacuum has been installed in India in just 20 years. This fantastic result has been possible thanks also to the cooperation with Vacuum Drying Technology India LLP, based in Mumbai, sole agent for Italvacuum in India, since many years.

The goal is to always provide the best support to our customers, in India as well as anywhere else in the world, with the support of our long-time partners. Vacuum drying technology can provide local technical assistance, Local after sales support and presence for every need; spare part management; Engineering and Commissioning.

Italvacuum provide constant training provided by to all the salesmen and technicians, Vacuum Drying Technology technicians receive regular courses at Italvacuum headquarters.

Visit us in P-mec Exhibition!

Booth 15A.C74 | India Expo Centre, Greater Noida, Delhi NCR | 29 November – 01 December

Italvacuum and Vacuum drying technology team will be glad to introduce you the company, the vacuum dryers and pumps range and will exhibit a mock up of its vacuum pump model VVB double stage. ■

Contact Details

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Sanosil Biotech's aerial disinfectant & fumigant for Pharma & Healthcare Industry

Non-carcinogenic, non-mutagenic, non-toxic & non-irritant

Sanosil Biotech's Virosil Pharma is a revolutionary, eco – friendly fumigant a strong replacement to Formalin Fumigation. The tried and tested patented formulation includes a complex compound which kills all forms of bacteria, viruses and spores, rendering spaces perfectly safe and sterile.

Features:

- Being a clear, colourless, odourless, liquid disinfectant that is non-carcinogenic, non-mutagenic and non-toxic, it can be used where other chlorine-based disinfectants are ineffective.
- Does not have a foul odor.
- No irritation to the eyes.
- Requires no de-fumigation.
- Very easy to handle.
- No fears of overdosing and no residual effects.

- Thoroughly tested in Western Europe, Australia, the Middle East and India.

Active Constituents:

- Hydrogen Peroxide (12%)
- Silver Nitrate Solution (0.01%)

Mechanism of action

The combined action of hydrogen peroxide and silver nitrate attacks the cell wall of the pathogen upon direct contact. Nascent oxygen denatures the cell wall

and disrupts the cytoplasmic stability of the pathogen, thereby neutralizing it and rendering it harmless to humans.

Virosil Fogging in Pharma Industry

Why is fogging required in Pharma industry?

Microbial contamination and pollution play a significant role in Pharma Industries. Control of microbes has always been the biggest challenge to these industries. Load of microbes are present in areas such as Production, Warehouse, Cold Storage / Packaging, R&D, Q.A / Q.C., Filling etc. They are present everywhere in the air, surface, cip, water, instruments, linens etc.

Hence the disinfectant used should be so precise that it should not only take care of the microbial contamination but also be user & eco-friendly. Virosil Pharma meets all the require standards for the Pharma industry.

What is Formalin Fumigation?

Fumigation is a conventional method in which formaldehyde and potassium permanganate chemical are mixed in a predefined ratio and this reaction generate fumes which effectively kill bacteria, fungus, viruses and their spores.

Drawback of formaldehyde and potassium permanganate chemical:

- Different regulatory agencies banned fumigation with formaldehyde solution and potassium permanganate as formaldehyde is carcinogenic (Cancer causing) in nature and there is risk of cancer associate with this to the personnel who is handling formaldehyde.
- It is not safe for the personnel & there are also other drawbacks like fumigation with formaldehyde causes irritation to the eyes and nose.
- After fumigation with formaldehyde there is requirement for de-fumigation of area in which AHU (Air Handling Unit) must be continuously run for few hours without any activity to remove the residues from the air and cleaning and moping of equipment's and area is also required.

The trend in Pharma industry relatively shifted from Formalin Fumigation to use of ecofriendly Fogging as United Nation Environment Protection Agency (UNEPA), and Occupational Health and Safety Agency (OHSA) declared Formaldehyde as Carcinogenic.

Why VIROSIL PHARMA?

Virosil Pharma when sprayed in sterile areas completely inactivates all form of bacteria, fungi and viruses within 60 minutes. It also very widely used for disinfection of Air Handling Units, Air Shafts, Ducts and Filters which are common breeding ground for bacteria and biofilms.

Virosil Pharma effectively disinfects all critical surfaces that comes in contact with Pharma products. Complete surfaces/ wall disinfection of production, packing, filling, storage and other desired facilities where micro free environment is required. Also, all instruments, Equipment's, machinery, storage tanks, pipeline, etc. can be made completely pathogen free

An area of 1,000 cubic feet can be completely sterile within 60 minutes of spraying without causing any irritation to the eyes, nose and skin – unlike conventionally used formulation.

Virosil Pharma thereby increase the productivity by cutting down disinfection time while at the same time totally providing microbe free environment.

The recommended ULV fogger gives a very fine mist which allows the formulation to be suspended in the atmosphere for a longer period guaranteeing 100% kill on all air-borne bacteria and fungus.

Single disinfectant multiple applications

- **Surface / Instrument Disinfection:** Apply 10% solution of Virosil Pharma on floors, walls, tables, and linen. Dip the instruments in a 10% solution.
- **CIP/Loop System Disinfection:** When used in recommended dosages it eliminates Biofilms.
- **Resin and Filter Disinfection:** Dip in a 1% to 3% solution to control foul odor & contamination
- **Storage Tank Disinfection:** Spray the surfaces of the tank with 5% solution

Virosil Pharma caters to the disinfection demands of major industries like:

- Pharmaceutical Manufacturer's
- Vaccine Manufacturers
- Life Sciences
- Research Labs
- Tissue Culture Labs
- Ayurvedic & Herbal Product Manufacturers
- Medical Devices Units
- Nutraceuticals
- House Keeping / Facilty Management Teams

Certifications:

- FDA Drug License
- ISO
- Halal Certification
- WHO-GMP
- Efficacy Validation Reports ■

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