VOL. 17 NO. 5 PAGES 76 www.expresspharma.in

EXPRESS PHARMA

INDIA'S FOREMOST PHARMA & BIOTECH MAGAZINE APRIL 2022, ₹ 40

MARKET

Can an 'edge' of innovation empower pharma industry to scale global success?

INTERVIEW

Dr Rajeev Singh Raghuvanshi PhD, Secretary-cum-Scientific Director, Indian Pharmacopoeia Commission (IPC), Ministry of Health and Family Welfare

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+

STRATEGY

Tackling the rise of antibiotic-resistant infections:
The role of antibiotic subscription and pooled procurement
Gearing up for an era of innovation

ANALYTICAL DEVELOPMENT CONCLAVE 2022

PREPARING FOR AN ERA OF INNOVATION

Experts discuss different aspects of new-age analytical techniques and technology for increased productivity, product efficacy, and regulatory compliance in the pharma sector at the first-ever ADL Conclave

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CONTENTS

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Regd. With RNI No.MAHENG/2005/21398. Postal Regd.No.MCS/164/2022 - 24. Printed and Published by Vaidehi Thakar on behalf of The Indian Express (P) Limited and Printed at The Indian Express Press, Plot No.EL-208, TTC Industrial Area, Mahape, Navi Mumbai-400710 and Published at Mafatlal Centre, 7th floor, Ramnath Goenka Marg, Nariman Point, Mumbai 400021.
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Will a limited vaccine waiver limit future options?

After formulating and garnering the support of over 100 countries for a Trade-Related Intellectual Property Rights (TRIPS) waiver for COVID essentials, why did the governments of India and South Africa be part of a proposal to water it down?

A leaked draft of a World Trade Organisation (WTO) document, which reportedly emerged after discussions among India, South Africa, the US and the European Union (EU), is currently being discussed by governments of other WTO member states.

While it could be considered a much-needed break in the stalemate since South Africa and India first launched this campaign in October 2020, health NGOs feel this limited vaccine waiver could instead turn out to be the first step down a wrong lane, as it could set a bad precedent for the future.

Other experts feel that this negotiation is a start, as it will ease supply of COVID-19 vaccines. Would it be pragmatic to settle for just vaccines now, hoping either that the COVID pandemic becomes more manageable or that the waiver is expanded to medicines and diagnostics through further negotiation?

These concerns do seem valid. Firstly, the proposed compromise covers just vaccines. Though the document hints at including treatments and diagnostics at a later date, why not now?

A petition from the People's Vaccine Alliance points out that IP barriers are probably higher for treatment with only 427 of the 5,293 COVID-19 patent filings being for vaccines. Thus, 92 per cent patent filings were not for vaccines and removing IP barriers for treatments, tests and other medical technologies (such as genomic surveillance) will have an even faster impact (via generics) compared to vaccines. Thus, while vaccines are important for prevention of COVID-19, the importance of diagnostics and therapeutics cannot be ignored.

The Alliance, a global coalition of over 90 organisations and networks, has asked the Government of India's Ministry of Commerce and Industry to push the WTO towards waiving all forms of intellectual property (IP) on the COVID-19 vaccine ahead of WTO's General Council meeting.

Secondly, the proposed deal is geographically limited. India is eligible for this proposed vaccine waiver as its share of vaccine exports was 2.4 per cent as of January 2022, according to the WTO-IMF's COVID-19 vaccine tracker, which is well below the criteria of not exporting more than 10 per cent of COVID-19 vaccines in 2021.

However, doesn't this criterion defeat the entire purpose of allowing developing countries with large vaccine manufacturing capacities to make affordable vaccines and export as much as possible to all countries, including those with low or poor vaccine-making capabilities, which are susceptible to high COVID-19 infections and deaths?

As attempts to ring-fence markets and restrict access continue, will India and South Africa toe the WTO line?

For instance, as per an MSF analysis, this criterion effectively excludes Brazil and China from being able to use the waiver. The Alliance's petition highlights that 'limiting the scope of the vaccine waiver even in the third year of the pandemic is ethically, politically and medically ill-conceived.'

Thirdly, the proposed limited vaccine waiver covers only patents and leaves out other intellectual property (IP) barriers, such as trade secrets, which are critical for manufacturing of medical products. A case in point being that even while Moderna has offered to waive its patent on its mRNA vaccine way back in October 2020, it has not resulted in a slew of affordable safe vaccines equivalent to Moderna's original product.

Are such efforts to improve access doomed to be imperfect? Almost coinciding with the leaked draft of the proposed limited vaccine waiver, the Medicines Patent Pool (MPP) signed agreements with 35 manufacturers (including 19 from India) in 12 countries to produce and supply nirmatrelvir/ritonavir. This oral drug is considered the most promising one so far for treating high risk cases which could progress to severe/critical COVID-19. But as Felipe de Carvalho, MSF Access Campaign Coordinator in Brazil points out, the deal only covers 53 per cent of the world's population and excludes millions of people in middle-income countries.

Experts also point out that the proposed consensus document adds restrictions beyond TRIPS and could end up reducing previously available flexibilities, thus restricting, rather than increasing access. For instance, applicants need to list all patents covered by the authorisation. They also have to notify the WTO TRIPS Council when such rights included in the waiver are exercised by an eligible Member. In addition, the anti-diversion measure tasks eligible members to prevent re-exportation of COVID-19 vaccines.

These legal requirements make the process more cumbersome and seem designed to deter rather than encourage applicants. There is also some ambiguity on the duration of the waiver (three or five years) but this grey area could merely reflect the fact that the proposal is not final, and is still at discussion stage.

As attempts to ring-fence markets and restrict access continue, will India and South Africa succumb to the pressure to toe the WTO line? Or will they continue to stick their necks out to make affordable COVID-19 vaccines, medicines and diagnostics freely accessible in both the Global North and South?

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INSIGHT

Can an 'edge' of innovation empower pharma industry to scale global success?

Dr Anil Bansal, Former President, Delhi Medical Association, and Senior Joint Secretary, Indian Medical Association, IMA (National), traces down some of the important factors that would need a push to take the Indian pharma industry to greater heights

Indian pharma sector's growth has been sharp and resilient. With its valuation expected to touch $130bn by 2030, not only is the sector entering its golden period, but it also remains to be one of the biggest leaders of vaccines and essential supplies in the global market (by volume). To further make headway and gain ground as an impactful global leader, we need to factor in innovation and R&D critically. This is also essential to be on par with the global curriculum and modernise healthcare.

But where do we currently stand?

Innovation is the need of the hour to take us ahead

The domestic pharma sector has shown immense growth potential and continues to showcase its manufacturing prowess. With an impetus on

self-reliance, the industry has scaled newer opportunities in recent years, with the introduction of lucrative PLI schemes and scaling up resources, including setting up medical parks and incentivising domestic production.

To further modernise, the Indian pharma space needs to harness the powers of research and innovation. The 2022 fiscal budget has taken a rightful note of the same, with the pharma and healthcare sector ingeminated as the 'sunrise' sector. The slew of investments announced by FM Nirmala Sitharaman has also been highly suggestive of governmental support. The intent to look for newer growth opportunities and prioritised investments isn't an isolated stance. With the introduction of helpful policy reforms, experts have brought in renewed focus to catalyse R&D changes time and again.

The 2022 fiscal budget has taken a rightful note of the same, with the pharma and healthcare sector ingeminated as the 'sunrise' sector. The slew of investments announced by FM Nirmala Sitharaman has also been highly suggestive of governmental support

Genome and biotech can define the next 10 years of pharma growth

The unprecedented challenges in the past two years have functioned as a turning point in the sector's growth trajectory, with new business models, areas of research and drug development coming to the foray. It has also certainly helped companies understand the needs and challenges for innovation, especially since R&D remains to be in the nascent stages of adoption on the domestic front.

When we talk about the 'sunrise' sectors, biotech and genomics are rapidly advancing and stipulated to dominate the sector in the coming years. There is a huge market share worth exploring and a big market player like India can certainly tap into this revenue.

Today, the use of biologics has revolutionised several treatment strategies, including cancer and auto-immune diseases. With eight out of the top 10 talked-about molecule drugs said to go off-patent in this decade, it is strategically the best time for large domestic players as ours to strike the iron when it's hot. Increasing our investment onus in this direction would be an exceptional opportunity to not only maximise the production, but also focus on the development of newer molecules and biosimilars.

Genomics, too, holds enormous potential for improving the state of healthcare and prevention strategies. It has proven to be quite vital in our COVID management plan, especially with tackling the newer variants. However, the genotype-phenotype supportive infrastructure lacks here, which can hinder decision making and genetic disease detection. In a country that houses over 21 per cent of the world's disease burden, it remains crucial that we expand our investments. GoI has also strategised investments into the genome sector, with the launch of programmes like 'Genome India Project' by the Department of Biotechnology (DBT), which aims to collect 10,000 genetic samples across the country to build a reference pool. We need more such projects and targetted investments to tap into the growing sector. Amid expanding our investments, we must also rely on supportive technology to create a fulfilling ecosystem.

Policy support is essential for further growth

The road ahead offers tremendous growth potentials, opportunities as well as unprecedented challenges. While substantial investments to boost local production of core APIs and Drug Intermediates (DIs) have benefitted, Research-Linked Incentives (RLIs) can also act as a helpful gesture for companies to evolve and grow. Innovation bonds and low-cost funds, to promote growth, must also be looked towards, at the government level.

To strengthen the R&D ecosystem, stakeholders also need to work in tandem with the public sector to amass a transformation that benefits the industry financially and qualitatively. We have ample young talent and manpower, and we can channelise them effectively through industry-academia cooperation and national-level policies. We must also have access to modern tech, innovation trends and digitisation, and address any challenges to sustain the momentum and innovation ecosystem.

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INTERVIEW

IPC has become more receptive and open to stakeholders

After having spent more than 20 years in corporate pharma, **Dr Rajeev Singh Raghuvanshi**, PhD, Secretary-cum-Scientific Director, Indian Pharmacopoeia Commission (IPC), Ministry of Health and Family Welfare, was looking for a more impactful role to contribute in activities which can create long-lasting impact on society. His current role at IPC gives him that opportunity. He shares more of his achievements and experiences in an exclusive interaction with **Akanki Sharma**

Take us through your journey in the Indian as well as the global pharma industry.
My journey in the Indian pharma industry started with Ranbaxy Laboratories. After completing my PhD from the National Institute of Immunology, I wanted to be in academics and research. However, life had something else in store for me. I reluctantly joined Ranbaxy, but ended up spending more than 20 years in the industry, of which 12 years were at Ranbaxy and 11 years were at Dr Reddy's Labs. At Ranbaxy, I was one of the few who started the NDDS team and initiated 505b(2) development for the first time in India. Later on, I took internal transfer to conventional generics team.

After 12 years at Ranbaxy, I switched to Dr Reddy's Labs in Hyderabad. The first eight years at Dr Reddy's was with Proprietary Products BU and we were mandated for pharma product innovation. Products were being developed for the US market. In a short time of eight years, the team developed, filed and got approval for seven innovative pharma products through 505b(2) regulatory path, not an easy achievement for a company of our size and resources. All the seven products got approval in the first cycle of review with the US FDA. Later, we also worked on multiple innovative products for India and EM. During this period, I had an opportunity of multiple F2F meetings with global regulatory agencies like the US FDA and MHRA.

While at Dr Reddy's, I also got an opportunity to attend and complete ISB-Kellogg Global Advanced Management Programme and multiple DRL's signature "Annual Leadership Summit" at Boston where we were taught by HBS professors in classroom settings. The later part of my work with DRL was spent in establishing a dedicated R&D team for Emerging and India markets called BRaIN (Branded and Innovation).

Both Ranbaxy and DRL provided me with extensive global exposure. I got opportunity to travel and work with partners and teams in the US, France, the UK, South Korea, China, Russia, Japan, South Africa, Netherlands, Romania and Sweden. This helped me develop global perspective on pharma business.

Experience of Ranbaxy gave me opportunity to build strong technical competence with great execution skills. It taught us to hold the bull by the horn and not run away from problems and looking for long-lasting solutions. Stay and training of DRL helped me become a mature leader with global perspective. I could develop great soft skills, essential for leadership roles.

After having spent more than 10 years with DRL, and more than 20 years in corporate pharma, I was

looking for a more impactful role where you have the opportunity to contribute in activities which can create long-lasting impact on society. The current role as Secretary-cum-Scientific Director of the Indian Pharmacopoeia Commission (IPC) gives me that opportunity. Our interventions help improve and maintain quality of medicines being sold in the country. It directly touches millions of lives on daily basis.

It's been over a year now since you joined IPC. Tell us about all that you have achieved during this stint.
A lot has been achieved in the last one year. First and foremost has been the change in mindset. The organisation has become more receptive and open to stakeholders. Customer-centricity has improved. We created a platform on Telegram - IP Discussion Forum, with current membership of 850 members, mostly from industry and majorly from MSMEs. Members are resolving their issues and doubts instantaneously. The best part is that solutions are coming from members only. IPC is facilitating the discussion on the platform. Accountability has increased at every level, team members are answerable, decision making is data-driven and faster.

On pharmacopoeia side, the inventory of Impurity Reference Standards has grown by 70 per cent, 165 to 277, the highest increase in any single year since IPC's inception. Multiple awareness programmes, some of them in collaboration with organisations like USP, SMPIC on pharma quality are being conducted for customers. On an average, once a month, I am personally speaking on one or the other platform on pharma quality, issues and probable solutions for India. Offtake of IPRS is improving, which is an indicator of increasing quality cautiousness among manufacturers.

IP is on its way to becoming at par with other leading global pharmacopoeias. We are introducing dissolution specifications in the Prolonged Release Formulation monographs which was not there till now. For the first time, we are implementing "Flexible Monograph" policy in IP. There is an increased focus on veterinary part of IP. We have new Veterinary Expert Committee working, that is aligned with IPC's methodology and frameworks. We are initiating development of digital IP. If everything works as per plan, we should be able to launch digital IP during the current year, 2022.

On pharmacovigilance side, we have demonstrated significant growth on all the growth indicators. Number of AMCs have increased from 346 to 530+, the highest increase in any single year since the start of PvPI. The number of adverse event reporting has grown. We initiated celebration of the National Pharmacovigilance Week (17th to 23rd September) for the first time, and it is going to be an annual phenomenon from now onwards. The number of centres for MvPI has grown three times, and so has the adverse event reporting in medical device domain.

There is a new energy in the system. It is just the beginning of IPC phase-II.

What are the major targets that you wish to achieve during your tenure here?
During my tenure, I wish to bring IP at par with leading pharmacopoeias of the world like USP, BP and EP. We want to start few applied educational programmes which will supplement our quality improvement goal. We also want to become source of trained manpower for pharma industry, especially in analytical and quality domains. We want to initiate structured research programmes in

quality and regulatory domain. We would like to start PhD programme in these areas. If you search for an institute which can be identified with their contribution in pharma quality domain, it is difficult to find. Whereas, for other specialisations like dosage form development, pharmacology, medicinal chemistry, phytochemistry, etc, you can easily find researchers and institutes both. We have to fill this gap if we have to address the problem of medicine quality in this country.

On pharmacovigilance/ materiovigilance side, we want to graduate from data collection and regulatory recommending agency to larger healthcare data analytics centre. We want to use the adverse event data for more use and benefit of the society. We want to increase public awareness about pharmacovigilance programme whereby patients and their family members start reporting the adverse events on their own and not get influenced by practitioners. There is lot to be done.

Since you have been a corporate leader for years, and now you are on the other side of the fence as a policymaker. Do you see yourself as a bridge between the pharma industry leaders and the policymakers? Since you might be aware of the challenges faced by both the sides, is it going to help in designing better policies for the pharma sector?

The answer is yes. My experience and exposure is already being used in multiple policy initiatives. My presence in the government system is helping by presenting the customer's perspective.

What have been your key learnings in the past one year? Any change that you wish to bring in IPC as an organisation?

The past one year has validated many management and leadership concepts. Irrespective of corporate or government, these concepts work everywhere. Some of them being: it is important to ask right questions in any system; to work with "keep it simple" approach; delegation; lead by example, if we demonstrate then only we can demand, etc.

At IPC, there was a strong foundation built in the last 10 years. We are trying to build next-level IPC over this strong foundation. The IPC of the future will be more open and collaborative -- a knowledge-generating centre, place to look towards for "quality and regulatory" advisery and a partner in improving pharma quality in this country and beyond.

Apart from the pharma domain, what other areas interest you?

Spirituality, leadership development and organisational building.

What is the one thing that always motivates you to keep following your goals - be it professional or personal?

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ANALYTICAL DEVELOPMENT CONCLAVE 2022

PREPARING FOR AN ERA OF INNOVATION

Experts discuss different aspects of new-age analytical techniques and technology for increased productivity, product efficacy, and regulatory compliance in the pharma sector at the first-ever ADL Conclave

ANALYTICAL DEVELOPMENT CONCLAVE 2022

WELCOME ADDRESS
◆ **Ms Viveka Roychowdhury,** Editor, Express Pharma & Express Healthcare, Indian Express Group.

SPECIAL ADDRESS : Preparing for an Era of Innovation
◆ **SM Mudda,** MD, Misom Labs

PANEL DISCUSSION : Current advances in Pharma Analytical Development : Trends and Technologies
◆ **Ms Viveka Roychowdhury,** Editor, Express Pharma & Express Healthcare, Indian Express Group (Moderator)
◆ **Dr BM Rao,** Head - EMQA, ASAT & CQC, Dr Reddy's Laboratories
◆ **Dr PK Agarwal,** Head: Analytical - Research & Technology, Hikal
◆ **Dr Veena Shetty,** Technical Director - Analytical Development, Reliance Pharmaceuticals
◆ **Dr Vijaya Bharathi,** VP & Head, Analytical Solutions, Aragen Life Sciences

Make your labs future ready and sustainable!
◆ **Vinita Singh,** Sr Product Manager, Lab Water Solutions - India & Singapore, Merck

Optimising analytical functions for accelerated drug development
◆ **Shitalkumar Pathak,** VP - Analytical Research (Formulations), Glenmark Pharmaceuticals

Dealing with challenges in testing and use of Stable Isotopic Labelled Standards
◆ **Mallikharjuna Reddy,** Associate Director - Quality, Clearsynth

PANEL DISCUSSION : Best practices in analytical QbD
◆ **Dr Ranjit Barshikar,** CEO-QbD International; United Nations Adviser - Geneva (Moderator)
◆ **Dr Sujay Rajhans,** President & Head of R&D, JB Chemicals & Pharmaceuticals
◆ **Dr Sandeep Zokande,** VP - Analytical, Indoco Remedies
◆ **Dr Shakil Sait,** Associate VP-Analytical Development (API & Formulation), USV
◆ **Dr Amarnath Chatterjee,** Sr Lead Investigator & Head Analytical Development Biologics, Syngene International Ltd.

Analytical strategies for complex therapeutics
◆ **Dr Sachin Dhondiram Patil,** Associate VP, AR&D, Caplin Steriles

Vote of Thanks / Emcee's Concluding remarks

WELCOME ADDRESS

Express Pharma recently launched the Analytical Development (ADL) Conclave. Held in a virtual format on March 11, 2022, the first-ever edition of ADL Conclave witnessed experts and professionals discuss on different aspects and implementation of analytical development methods and technologies in the pharma sector.Merck and Avantor were the gold partners for the event.

It kickstarted with an address by Viveka Roychowdhury, Editor, Express Pharma & Express Healthcare. Welcoming the eminent speakers and the august attendees, she spoke on the vision and mission behind the launch of the ADL Conclave.

She explained, "The ADL Conclave is the latest addition to a brand that was created 26 years ago in December 1994, when we launched *Express Pharma Pulse*, now rebranded as *Express Pharma*. From 2017, we have launched conferences like Formulation and Development (FDD) Conclave, Pharma Packaging and Labelling (PPL) Conclave, and the Pharma LabNext Conclave. And today we create one more platform - ADL Conclave, under the theme 'Preparing for an era of innovation'."

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She added, "Many of the experts we spoke to as we planned this Conclave said that we were already in an era of innovation and the COVID pandemic became the latest trigger for innovation in the pharma sector. Today's speakers touch on various aspects of analytical development, the new tools and techniques, and their sustainability as the sector strives to increase productivity, product efficacy and regulatory compliance."

Preparing for an Era of Innovation

Mr. SM MUDDA
MD, MISOM LABS

SM Mudda, MD, Misom Labs gave a Special Address at ADL Conclave 2022 on the theme of the event, "Preparing for an era of innovation". He drew from his vast experience as a pharmacy professional with over 40 years experience in leading Indian multinational pharma companies present in India, the EU and the US to share a lot of insights which are relvan to the industry's progress. He underscored the importance of optimising and honing each and every pharma process for continual improvement and enhanced outcomes. He also shared his insights on how India Pharma Inc needs to adapt, innovate and transform to step up and navigate new challenges and opportunities in a rapidly shifting landscape.

He highlighted that the challenges posed by the COVID pandemic has led to several crucial learnings for the pharma industry. He pointed out how the pandemic has accelerated the adoption of digitalisation and automation for improved productivity, quality and compliance. Citing an example, he said that one of the emerging tools in these times is predictive quality analytics tool that forecasts the quality of the products.

He also stated that the advent of emerging technologies likes AI and IoT have the potential to transform every aspect of the pharma industry, be it drug discovery and development, manufacturing, supply chain or monitoring of ADRs.

He concluded that investment in the right strategies and technologies that foster innovation is vital and makes for a compelling business case since progress and success cannot be achieved with yesterday's methods. He urged the industry to build new capabilities and embark on a path of innovation.

Current advances in pharma analytical development: Trends and technologies

As India Pharma Inc strives to transform into a more value-led and innovation-driven industry and accelerate its next phase of its growth, it has to invest and build capabilities which will enable the development of innovative and differentiated pharma products across a range of indications. This, in turn, also necessitates development of strategic analytical capabilities to leverage scientific expertise and meet the needs of evolving regulatory environments across the globe.

Therefore the topic for the first panel discussion at ADL Conclave 2022 was 'Current advances in pharma analytical development: Trends and technologies.' Moderated by Viveka Roychowdhury, Editor, Express Pharma and Express Healthcare, the panel for this discussion comprised Dr BM Rao, Head – EMQA, ASAT & CQC, Dr Reddy's Laboratories; Dr PK Agarwal, Head: Analytical - Research & Technology, Hikal; Dr Veena Shetty, Technical Director – Analytical Development, Reliance Pharmaceuticals; and Dr Vijaya Bharathi, VP & Head, Analytical Solutions, Aragen Life Sciences.

In this panel discussion, steered by the moderator, our expert panel examined current trends in this field, explored proactive approaches for better results and shared insights on the potential of emerging technologies and solutions to transform this sphere.

The panelists spoke on the evolution of this segment with the advances in technology and highlighted how tools like LCMS, scanning electron microscopy, X-ray spectroscopy and Raman spectroscopy with imaging etc are ushering better efficiency across processes to improve outcomes in processes such as impurities profiling and extractables and leachables. They also spoke on how the QbD approach is being adopted rapidly in analytical research and development. Citing examples of how manual methods are being replaced by automated tools, they elaborated on how this has helped to improve traceability, reduce errors and assure quality in the sphere of analytical development.

Discussing opportunities and challenges emerging in this sphere and strategies to tackle them, the experts stressed the importance of choosing and implementing the right technologies. They also emphasised how pivotal it is to invest in continuous skilling and training of analytical development professionals to keep pace with technological advancements. Building capabilities in AR&D activities within the company was one of the recommendations offered by the panelists.

Thus it was an insightful session, with several vital takeaways for the audience.

KEY HIGHLIGHTS

- Digitalisation and robotic process automation tools are improving efficiencies in analytical processes across study design, data analysis and documentation. - **Dr BM Rao,** Head – EMQA, ASAT & CQC, Dr Reddy's Laboratories
- Continuous improvements in analytical development methods and technologies have increased their scope of application. Regulators are also encouraging adoption of new technology to improve quality. - **Dr Vijaya Bharathi,** VP and Head, Analytical Solutions, Aragen Life Sciences
- Companies need to invest in skilling and training to get best results from technological advancements in analytical development. - **Dr P K Agarwal,** Head - Analytical, Research and Technology, HIKAL
- It is better to build a lot of in-house capabilities in AR&D activities to gain valuable experience and best outcomes. - **Dr Veena Shetty,** Technical Director - Analytical Development, Reliance Pharmaceuticals

Make your labs future ready and sustainable

Ms. VINITA SINGH
SENIOR PRODUCT MANAGER,
LAB WATER SOLUTIONS – INDIA AND SINGAPORE,
MERCK

Speaking during the ADL Conclave 2022 about Milli-Q IQ 7000 lab water purification system, Vinita Singh, Senior Product Manager, Lab Water Solutions - India & Singapore, Merck, said that this purification system allows scientists to focus on problem solving, without worrying about the purity of their water. "Its smaller, ergonomic design reduces waste and helps increase productivity and accelerate research for scientists in the lab," she said.

She further mentioned the various roles of water in the laboratory. These include sample preparation (dilution, extraction, QuEChERS); preparation of buffers, reagents, HPLC mobile phases; preparation of microbiology media and solutions; preparation of standards and blanks; feed for washers, autoclaves, stability testing chambers, water baths; and washing, rinsing of sample and reagent containers. She also emphasised that the labs today and in the future need sustainability, result quality, innovation and lab productivity.

Going forward, she highlighted the features of MyMilli-Q, which are 24/7 remote monitoring, addressing of emerging productivity needs in QC, time-saving diagnostics and assistance, rapid planning, tracking of service plans and consumables shipments and streamlining audit preparations with effective data management solutions. Labs of future need innovation like smart HD touchscreen, new Q-POD and E-Pod dispenser, new IPAK purification cartridges, mercury-free UV lamps, aesthetic and compact installations, range of services, and data and connectivity, she concluded.

Optimising analytical functions for accelerated drug development

One must be a partner in development rather than a supporter/service provider, and use scientific acumen to fast track the activities over popular shortcuts, commented Shitalkumar Pathak, VP - Analytical Research (Formulations), Glenmark Pharmaceuticals, while speaking at the ADL Conclave 2022.

He then spoke about the four pillars of analytical development: human resource (right hiring, placing right people for right job, continuous learning/adapting to new technologies); instrumentation (current trends... UPLC Vs HPLC, NIR, Raman); analytical procedures (smart and short methods, single method for multiple tests and QbD-based development) and material selection (columns, excipients and flavours).

Mr. SHITALKUMAR PATHAK
VP - ANALYTICAL RESEARCH (FORMULATIONS)
GLENMARK PHARMACEUTICALS

> One must be a partner in development rather than a supporter/service provider, and use scientific acumen to fast track the activities over popular shortcuts

He also talked about focus areas in F&D that include forced degradation studies: degradation pathways; particle size, shape and morphology, polymorphism, dissolution and reverse engineering. Regarding the overall role of analytical research, he said that it involves method development, process optimisation, stability studies, SPEC finalisation, method validation, analytical tech transfer and specification/STP. Apart from it, there are characterisation activities like nitrosamines, elemental IVRT/residual solvent risk assessment and reverse engineering. IP support, regulatory support and plant support are some other important factors that play a crucial role in analytical research, he concluded.

Dealing with challenges in testing and use of Stable Isotopic Labelled Standards

Mallikharjuna Reddy, Associate Director - Quality, Clearsynth drew from his experience of 20+ years in analytical research and development and expertise in impurity profiling and quantification of GTI by LCMSMS/GCMS, Reference Standards during his session on 'Dealing with challenges in testing and use of Stable Isotopic Labelled Standards' at ADL Conclave 2022.

He began his session by sharing information on Stable Isotopic Labelled Standards and their application in analytical development. He went on to explain that labeled standards are preferred as internal standards (ISTD) for varied reasons. To begin with, they improve the efficiency of bioassay or quantification methods.

Mr. MALLIKHARJUNA REDDY
ASSOCIATE DIRECTOR - QUALITY
CLEARSYNTH

They minimise changes in preparation/extraction/ionization and offer phytochemical properties almost similar to the unlabeled standards. As deuterated and other isotope labelled internal standards have similar extraction recovery, ionisation response and matrix effect they also improve the accuracy of the quantification method. They reduce chromatography time, and make assays more robust by increasing throughput and lowering rejection rates as well.

> As deuterated and other isotope labelled internal standards have similar extraction recovery, ionisation response and matrix effect they also improve the accuracy of the quantification method. They reduce chromatography time, and make assays more robust by increasing throughput and lowering rejection rates as well

He also elaborated on the important aspects of Stable Isotopic Labelled Standards such as isotopic purity, parent mass interference, degree of labeling while selecting an isotopic standard, chemical stability of standards, label position, dealing with internal standards of bioassay etc.

Panel discussion: Best practices in analytical QbD

The ADL Conclave 2022 also saw a panel discussion on the topic "Best practices in analytical QbD." The panellists in the session involved Dr Ranjit Barshikar, CEO, QbD International; United Nations Adviser - Geneva (Moderator); Dr Sujay Rajhans, President and Head - R&D, JB Chemicals and Pharmaceuticals; Dr Sandeep Zokande, VP - Analytical, Indoco Remedies; Dr Amarnath Chatterjee, Sr Lead Investigator and Head - Analytical Development Biologics, Syngene International and Dr Shakil Sait, Associate VP - Analytical Development (API & Formulation), USV.

Dr Barshikar, while beginning the session, said that Quality by Design (QbD) is not new to the world. It is over seven-eight decades ago that this has been introduced, but pharma industry is way behind in implementing this concept. In the last one decade though, things have taken speed in terms of implementation, especially on the product development for the QbD elements' implementation to ensure robust process, product development and minimise the failures and rejections (if any), and to increase the consistency in manufacturing batch after batch. He further mentioned other benefits of QbD, while taking the panel discussion forward.

During the discussion, Dr Rajhans gave information on the USP moving ahead into QbD for the industry purpose. Dr Sait said that there is lack of experience or knowledge on the drug substance and drug product, lack of knowledge in the physicochemical properties, improper screening of different phases through different lot, inadequate screening of mobile phase, etc. "aQbD is a systematic approach where we cover all the issues faced in the traditional approach. There, we define an Analytical Target Profile (ATP), where we design screening method based on scientific knowledge and experience, establishing critical quality

PANELISTS

Dr. SUJAY RAJHANS
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JB CHEMICAL AND PHARMACEUTICALS

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MODERATOR

Dr. RANJIT BARSHIKAR
CEO - QBD INTERNATIONAL
UNITED NATIONS ADVISER - GENEVA

attributes, method optimisation using DoE for multi-variant factors, and then coming to method validation. aQbD helps us to have a robust, rugged and quality analytical method. It takes care of the lifecycle management and gains an ongoing assurance and ensure that the method remains in the state of control during entire routine use."

Dr Chatterjee also shared his views with the audience on USP introducing general notices on analytical QbD, specifically with regard to the biological products.

Dr Zokande informed that the pharmacopoeia standards are designed based on the available information at the time of setting those standards, and are based on the regulatory requirements. "When we apply the pharmacopoeia standards for our generic formulation or generic drugs, those standards may not be suitable as it is. We try to use the pharmacopeia standards, but when those are not suitable, we are designing some type of justification which means that our methodology is superior than pharmacopeial standards. So, aQbD is one such approach which is designed based on the science."

The panellists also talked about recruiting people and training them in the process of aQbD, among several other topics of importance.

KEY HIGHLIGHTS

- Lifecycle approach is important as that is where the regulators are focussing today:
  - **Dr Ranjit Barshikar,** CEO, QbD International; United Nations Adviser - Geneva (Moderator)
- The next decade is going to be a big thing in terms of pharma quality with the help of QbD:
  - **Dr Sujay Rajhans,** President and Head - R&D, JB Chemicals and Pharmaceuticals
- When pharmacopoeia standards are not suitable, companies design a method which is superior to these standards. QbD is such an approach that is designed based on science:
  - **Dr Sandeep Zokande,** VP - Analytical, Indoco Remedies
- It is important to incorporate ATPs and CQAs while designing a method, and that's where QbD becomes important, especially for biologics:
  - **Dr Amarnath Chatterjee,** Sr Lead Investigator and Head - Analytical Development Biologics, Syngene International
- An improper design screening of analytical methods has been creating a lot of method-related issues. Implementation of a QbD will make the life of our developers and QC analysts easier:
  - **Dr Shakil Sait,** Associate VP - Analytical Development (API & Formulation), USV

Analytical strategies for complex therapeutics

Dr. SACHIN DHONDIRAM PATIL
ASSOCIATE VP, AR&D ANALYTICAL
CAPLIN STERILES

Dr Sachin Patil, Associate VP, AR&D, Caplin Steriles addressed a very crucial topic at ADL Conclave 2022. He spoke in detail on analytical strategies for complex therapeutics. Dr Patil shared insights gained from over 18 years of experience in analytical method development in pharma industry and characterisation of different complex drug delivery systems with data interpretation and satisfactory response to regulatory agencies.

His session emphasised on the importance of reliable, robust analytical methods for successful drug development and commercialisation of complex therapeutics. He spoke on the role of method development, qualification, and validation in understanding the critical quality attributes of the molecules of complex drugs and biologics.

He also drew attention to the CMC issues in analytical methodologies that include lack of standardised analytical methodologies for characterisation of complex products in his session. Highlighting that the requirements of FDA mentioned in the product specific guidelines are very extensive, he emphasised that it is important to meet those requirements before submitting the dossier.

He pointed out that novel, more discriminative methodologies developed by the industry are not accepted by the agency since they don't match USP and urged the industry to look closely at regulatory requirements while developing analytical methods for complex therapeutics.

He advised that analytical method development for complex formulations should consider sample viscosity, sample dilution, particle refractive index and sample temperature to get best outcomes.

OPINION

Tackling the rise of antibiotic-resistant infections: The role of antibiotic subscription and pooled procurement

Daniel Berman, Nesta Challenges; **Professor Sabiha Essack**, University of KwaZulu-Natal; and **Professor Sujith J Chandy**, Christian Medical College, Vellore, explain the need for more rational use of the existing antibiotics and diagnostics

To address the dangerous trend of increasing rates of antibiotic resistance, there will need to be dramatic changes to the way people access antibiotics. Part of this change will be to increase the use of diagnostic testing so that the first-line 'access' antibiotics are used in cases when they will still be effective, while the second- and third-line 'watch' and 'reserve' antibiotics are used sparingly and only when absolutely necessary.

There has been a lot written about the broken system of R&D for new antibiotics. For sure, this is a critical issue, but so is the need for more rational use of the existing antibiotics and diagnostics. There is an urgent need for market shaping, which will undoubtedly mean new ways of financing and procuring these products. This market cannot be fixed unless we collectively acknowledge the fact that we want companies to sell as few 'watch' and 'reserve' antibiotics as possible.

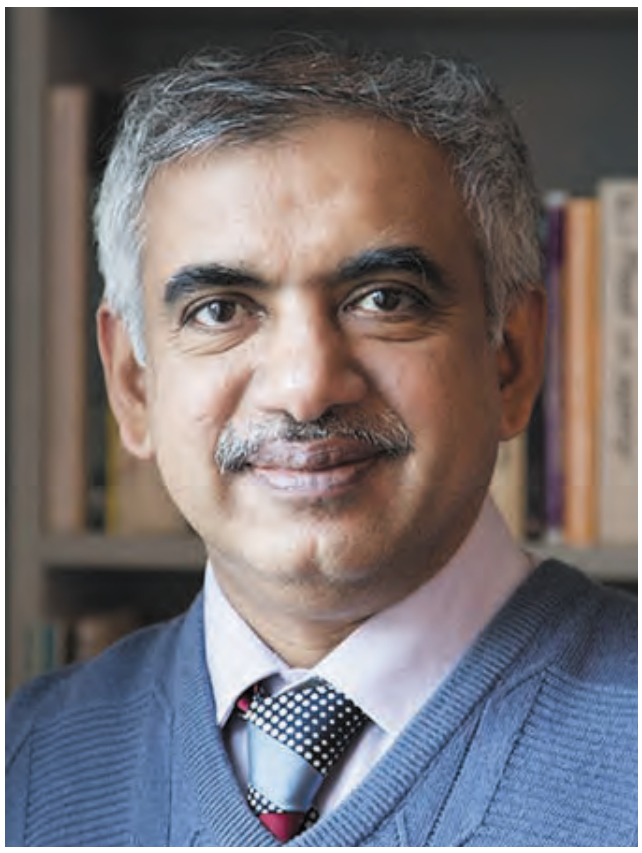
Why would they do this? It's counterintuitive to how the rest of the medicines market works - selling high volumes at low prices and low volumes at high prices. To ensure access to the existing and new antibiotics, there a is need for a new paradigm to engage producers.

If a drug developer's payment is not based on the number of units consumed, but rather their obligation to cover a defined population over a set period of time, a model is created that rewards long-term engagement and disincentivises promotion of antibiotics. This is much like the way Netflix's fee system works. Netflix gets paid the same amount regardless of how many films or shows each household watches. If suppliers of antibiotics and diagnostics were guaranteed fees over a number of years, they may be willing to align their marketing approach to stewardship principles.

When it comes to rapid diagnostic tests for AMR, developers today are focussed on high-income markets because their investors demand that they maximise their return. If, through subscription contracts and pooling of demand, there are more funds allocated to purchasing AMR diagnostics in LMIC markets,

Daniel Berman

Professor Sabiha Essack



Professor Sujith J Chandy

then test developers and sellers will be keen to service this market. The need to reinvent the way antibiotics and diagnostics are deployed is urgent if you consider trends in resistance and antibiotic use in many countries, including India.

Finding a viable solution to our reliance on reserve antibiotics

In our recent paper published in *The Lancet*, we explored the growing reliance of health systems in South Africa and India on 'reserve' antibiotics, as resistance increased to both 'access' and 'watch' drug cohorts in the last decade.

Overall, the rising consumption of antibiotics such as meropenem and tigecycline, along with increasing levels of resistance to carbapenems, colistin, tigecycline and vancomycin, as mentioned in the paper, highlights the worrying trend of escalating resistance to last resort antibiotics. Increased use of these products will raise the selection pressure for resistance, thereby further depleting treatment options in countries where infectious diseases remain among the leading causes of mortality.

Access to and registration of new antibiotics, ideally with new mechanisms of action, is, therefore, imperative. So too is a strong and rewarding market for diagnostic tests that aid the effective stewardship of the drugs we have.

We have, therefore, proposed a novel approach to create a predictable Low- and Middle-Income Country (LMIC) market that ensures access to products that address growing resistance and treatment failure. In *The Lancet*, we described how Antimicrobial Subscription and Pooled Procurement (ASPP) could be implemented as a multi-national or regional mechanism in which countries (or states within a country) leverage their combined purchasing power for a portfolio of newer and future antimicrobials and diagnostic products. In India, in particular, we believe this could work at either a state or national level.

ASPP would be operationalised through multi-year subscription contracts for a portfolio of antimicrobials and diagnostic products that are negotiated for participating states. Diagnostic products would include point-of-care tests, routine laboratory reagents and equipment for pathogen identification and susceptibility testing. Including diagnostics in the portfolio would help to ensure that antimicrobials are prescribed on the basis of diagnostic stewardship.

The portfolio approach sends a clear signal to manufacturers that products will be procured when quality, safety, efficacy and pricing criteria set by procurers are met, and that a market exists in countries that are being too often overlooked.

Tackling AMR head on

The impact of AMR is being felt harder in LMICs such as India. It's likely for this reason that it is also at the vanguard of fighting AMR's rise, thanks to concerted efforts and dedicated funding from the likes of BIRAC. India's world-class network of innovators and diagnostic test developers are creating a new generation of tests that can identify bacterial infections and the correct antibiotics to prescribe, not least those pursuing the £8m Longitude Prize.

ASPP could provide a solution to the market question to secure the stable and affordable supply of antibiotics and diagnostic tests to ensure consistent access. Administering the right antibiotic in the first instance is an important part of the strategy to address AMR, and ASPP will support it by making sure products are there when they are needed.

INSIGHT

Gearing up for an era of innovation

SM Mudda, MD, Misom Labs highlights that we have entered into an era of disruptive innovation and emphasises that those who keep pace with innovation will be the future leaders

A few years ago, the hot topic that was discussed at most of the forums was how to deal with the challenges posed by the VUCA world, not knowing that we will face one such real global disruption in the form of COVID-19 pandemic soon.

"There are decades when nothing happens but there are weeks when decades happen." COVID pandemic was one such brutal disruption the world went through, and has come out much wiser with a lot of learnings that are known as 'New Normal.'

The world has learnt that with the help of innovative technology, it is possible to witness a never-seen-before feat of producing a potential vaccine candidate in mere months for a novel virus.

We realise like never before that we have entered into an era of disruptive innovation and recognise that those who keep pace with innovation will be the future leaders.

Challenges of the VUCA world

Talking about the challenges in the pre-COVID era, there are questions and realisations that:

◆ India is no longer the low-cost centre for the manufacturing of pharmaceuticals?

◆ The price of medicines (patented and generic) will fall in the next five years?

◆ Cost of manufacturing will increase?

◆ Our compliance with regulatory expectations, particularly the US FDA, continued to be a lingering issue and remain an ongoing concern.

◆ Amazon, Google and Apple will have a profound impact in healthcare in the next decade

Balancing three Cs - Customer, Cost and Compliance

The pharma industry is faced with the challenge of balancing overlapping three circles—Customer expectations; Profit and efficiency – Cost control; Legacy and reputation – License to operate; within the constraints of shrinking resources and time.

The pharma industry has been focussing, amongst others, at the latest technologies like complete digitisation of operations, automation at manufacturing units and Big Data and Machine Learning to enhance accuracy, reduce time and efforts, and remain in the state of compliance.

The focus has already shifted to smart innovation that will give

a disproportionate return in terms of improved efficiency. We need to work on the principle of *'Less is More'* which is the new mantra.

Industry 4.0

The tremendous ongoing digital transformation – better known as Industry 4.0 – is profoundly changing manufacturing, processing and production industries. The term Industry 4.0 encapsulates all the rapidly evolving technologies, processes and practices that are currently changing the world of manufacturing.

Advanced technology is undoubtedly becoming the backbone of futuristic quality assurance in the pharma and biotech industry.

Digitisation – A strategic priority in post-COVID era

Post-COVID-19, adoption of digitisation has become a strategic priority for business in the pharma industry. Such benefits will be highlighted in the areas of:

◆ R&D

◆ Manufacturing and Quality

◆ Role of regulators in supporting innovation

Pharma R&D

The advent of new emerging technologies like AI, IoT, digitisation and automation have the potential to revolutionise every element of the pharma industry from drug discovery to production to efficient and secure supply chain to monitoring of ADRs.

Some of the benefits in the area of drug discovery and R&D include use of digital tools in

◆ predicting the behaviour of new chemical compounds in potential drugs

◆ selection of target molecules using high-throughput screening

◆ predicting patient outcomes from Electronic Health Records (EHRs)

◆ Virtual and decentralised clinical trials, etc.

These tools will help in developing new innovative products for patient benefit that include the patient-related quality attributes in the design of the product and make the novel drugs available to the patients on fast track.

Pharma manufacturing

Some of the potential applications of Industry 4.0 are seen in the form of continuous manufacturing technology.

◆ Use of Internet of Things (IoT) for data collection in real time from the networked equipment can help in predictive maintenance of equipment, thus reducing the downtime.

◆ Use of track-and-trace technology for ensuring supply chain integrity, etc.

◆ Predictive quality analytics is a tool used by manufacturers to forecast the quality of the products, components and materials that are already in the production process. It can address the root causes of problems in advance—before any quality issues occur.

Pharma labs

Quality 4.0 is a less-hyped, but quickly emerging concept within Industry 4.0.

Creating a fully integrated lab of the future that adopts modern technologies and

practices, and is data-driven, enables manufacturers to develop, manage and maintain quality standards throughout their supply chains.

As a subset of Industry 4.0, the development of analytical methods alongside the product developments assumes a significant importance, and it is expected that the tools of digitisation are used in developing robust, simplified and validated test methods. These methods have to be transferrable and have to be integrated in the smart lab of the future.

The big pharma companies have adopted these technologies in building digitised and automated labs and have improved operational efficiency in terms of savings up to 40 per cent of the cost. The concept of distributed labs is being used in supporting the continuous manufacturing technologies for providing real-time on-line feedback on key quality parameters.

Role of regulators

The role of the regulators and the government is equally important in providing an ecosystem that encourages and facilitates innovation. During the development of COVID vaccine and related drugs, we have seen the regulators world over adopting flexibilities in the process of:

- approval of new products for emergency use,
- providing GMP flexibilities in terms of accepting remote /virtual inspections,
- extension of validity periods of GMP certificates, etc.

The learnings from this period can be leveraged to introduce simplified regulatory processes by adopting a risk-based approach. The industry and the regulators have to work together to bring such approaches in practice for alleviating the concerns about compromise to patient safety.

Adaptive challenges

The adoption of new innovative technologies of this scale is a transformational change that requires a huge capital investment and a compelling business case. Besides, we need to have a qualified team with the required capabilities for such adoption.

This is an adaptive challenge more than a technical challenge since we have to break the barrier of inherent immunity to change that exists in us and in our systems.

Therefore, it is important that digitalisation initiatives are built within the company's quality system. This requires a leadership team with systems' thinking abilities to appreciate that a modern pharma quality system integrates all five manufacturing systems to operate within and interact with each other.

Improving a part taken separately will not improve the whole system, but, at times, can damage it. Any improvement implemented outside of a QMS will not be scalable and sustainable.

Therefore, we need to focus not only on a small q (QC) but a BIG Q (Quality System).

We cannot do today's work with yesterday's methods and still be hopeful to succeed tomorrow. What brought us here will not take us any further if we do not focus on innovation. Innovation is the key to success for the pharma industry.

Automation and digitalisation will not replace humans, but instead augment the human capability. It is this integration of human capabilities with technology that will lead to beneficial results that neither humans nor technology can alone deliver.

How pharma industry generates entrepreneurship opportunities

Dr D Sreedhar, Associate Professor Senior Scale, Department of Pharmacy Management, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, points out that there are several entrepreneurial opportunities closely associated with the pharma industry and urges budding entrepreneurs to explore and leverage the huge growth potential in this sector

Venkataraman S describes entrepreneurship as a scholarly discipline and defines it as, "seeking to understand how possibilities to bring into existence future goods and services are identified, developed, and exploited, by whom, and with what repercussions."[1] Pharma industry has offered a plethora of entrepreneurial opportunities. Many have explored the opportunities to become successful entrepreneurs. Entrepreneurship, or having an entrepreneurial spirit, is crucial in today's economic climate for generating innovation and establishing a prosperous society.[1,2]

The pharma sector and biomedical research rely heavily on innovation. Every medical

or therapeutic product that is produced and delivered to the market is the result of an intellectual curiosity that necessitates a proof of concept and takes years. The pharma and wellness industries have had a huge impact on Indian society. Moreover, entrepreneurial activity is becoming a key factor of growth and development in every country. According to statistics from the Union Ministry of Health and Family Welfare, there were times when the life expectancy rate was abysmal, at 42 years. The progressive advancements in the medical sector, on the other hand, have aided in the expansion of India's life expectancy rate. This was possible due to the advances in the field of pharmacy and healthcare.

The Indian pharma sector is rapidly adopting new technologies and medical procedures. Because the pharma industry is still in its growth phase with fewer companies in the market today.

By amending FDI restrictions (for the pharma business), the government has made it plain that it wants entrepreneurial excursions into the sector to help it grow. Entrepreneurs should take advantage of this opportunity and start looking into the pharma industry. The industry has a wide range of applications, making it an appealing prospect for private investors. The drug manufacturing firms that can manufacture quality medicines, the dearth of medicinal products, especially with

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respect to rare diseases and lacunae in supply chain can be explored by the interested.

Many entrepreneurs make up the Indian pharma sector. Suppliers, stockists, distributors, retail pharmacists for example, are critical components that run the healthcare system. Entrepreneurship in pharma industry evolved over the years encompassing not only the industry as whole but each of the fields that are associated with it. Two very different areas of the Indian economy have generated immense riches and produced a record number of billionaires in the last decade and a half. The software services business is one of them, and it has been in the spotlight for a long time. The pharma and healthcare sector, on the other hand, is only now starting to get the attention it deserves.

A few who have started their entrepreneurial journey went on to build significant empires and became billionaires. One among them, Dilip Shanghvi became the richest man in the country. A fifth of India's 100 wealthiest families now work in the pharma and healthcare industries. Some of them, like Shanghvi, have become household names; Ajay Piramal, who sold Piramal Healthcare's formulation division to Abbott for $3.7 billion in 2010, the Singh brothers of the Fortis healthcare chain, who sold Ranbaxy to Daichhi Sankyo (the latter has sold it to Shanghvi), the Reddy family of Dr Reddy's Laboratories, Dr Prathap Reddy of Apollo Hospitals, Deshbandhu Gupta of Lupin, Y.K. Hamied of Cipla, Cyrus Poonawala of Serum institute, and Kiran Mazumdar-Shaw of Biocon, to name a few.

There are quite a few entrepreneurial opportunities that are closely associated with the pharma sector, to name a few, 24-hour pharmacies, mobile pharmacy, online pharmacies, medical devices manufacturing, App developers, natural home remedies services, educational and training institutions, publishers, consultancy services, counselling centres. Each of them have the potential to become a successful business enterprise.

The government has acknowledged the importance of entrepreneurship and has developed programmes such as Start-up India and Make in India to encourage people to pursue their dreams. Because these programmes have also opened the doors to innumerable chances for entrepreneurs, now is a better time than ever to start a business in India and to be a successful entrepreneur. Overall, India's startup ecosystem is thriving, yet entrepreneurship remains a major struggle for many creative minds, as there are numerous exceptional challenges that cannot be overlooked. While the government has taken some positive moves, there are several challenges that are making it difficult for startups to grow quickly.

Overall, the Indian pharma sector is flourishing now because of successful entrepreneurs in India who support initiatives like Make in India. They have been working relentlessly, especially during COVID-19, to ensure that there are no drug shortages on the market. Every day, this country's entrepreneurs teach us lessons on perseverance.

Entrepreneurs are wealth generators, and self-created money protects against disasters such as recession. It is past time to understand the importance of allowing entrepreneurship to thrive and to provide an atmosphere that allows it to do so without hindrance.

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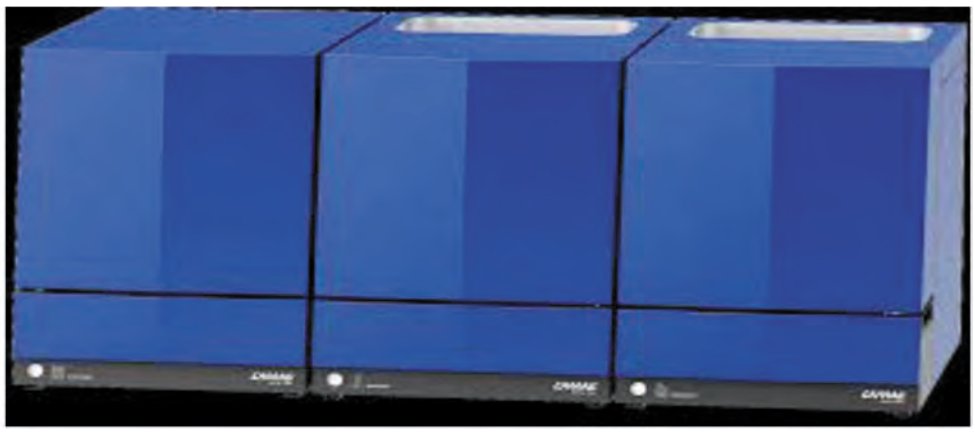
CAMAG HPTLC PRO: The future of HPTLC

Although HPTLC is derived from thin layer chromatography and their principles are same but HPTLC practice is fully instrumental and GLP/USP/EP-compliant

Thin Layer Chromatography (TLC) is by far the most popular chromatography technique for qualitative and semi-quantitative analysis, since the 1960s. However, it does not meet modern regulatory requirements. Traditional TLC is unsuitable for QC because of several reasons such as non-compliance with GLP, non-validated and qualitative/semi-qualitative methods, separation in non-equilibrated conditions, etc. In spite of all these reasons, TLC is used widely, for last many decades because of its utility, low cost and powerful separation ability.

But, now-a-days, modern version of TLC i.e., HPTLC has improved the thin layer chromatographic technique. Although HPTLC is derived from thin layer chromatography and their principles are same but HPTLC practice is fully instrumental and GLP/USP/EP-compliant. HPTLC is now official technique in USP (Chapter 202, 203), EP (2.8.25) since recently.

HPTLC system is further modernised and made completely automated to a robotic CAMAG HPTLC PRO. HPTLC PRO targets customers with a need for low-cost, high-throughput analysis with full automation, under regulatory conditions. HPTLC PRO system is integrated into the latest CAMAG vision CATS HPTLC software. This system is best suited for routine quality control of analytes from complex matrices, providing reproducible and reliable results. It supports analysis of 75 to 125 samples, up to five plates, and three independent developing solvents without intervention with pharmacopeial compliance. The possibility of derivatisation, MS coupling and hyperspectral evaluation modules are soon to be included.



Fully automated sample analysis and evaluation for routine QC modules of CAMAG HPTLC PRO available now

The focus of CAMAG HPTLC PRO system is on automation, high through put and eliminates the limitations of TLC with technology. This system has best application in routine quality control. There are six individual modules for six steps. They are identical from the outside but internally have different roles to play. Due to its design, the PRO system chromatographs a plate autonomously. Automated conveyorised transport of plate between any modules eliminates human intervention.

Standardisation and automation of entire process leads to cGMP compliance of HPTLC PRO system which delivers reproducible and auditable results.

Once five 20 x10 cm HPTLC glass plates are placed in the 'plate storage module,' the sample vials are loaded into the module application, the user can start the fully automated HPTLC process with a single mouse-click in the visionCATS software. The system uses a built-in conveyor to transport plates from one module to the other throughout the entire HPTLC process. After analysis, the plates are moved into the module plate storage. The first three modules, commercially available are described below.

Module 1- Plate Storage: Plate storage module aids in sequential application and development of several plates. It feeds the HPTLC PRO system with clean plates and stores the processed plates during or after analysis. Unlike the present HPTLC system, use of this module minimises the plate handling requirement during analysis steps, resulting in the highest analytical quality and in great handling convenience. The analyst's work is now limited to preparing the samples and required solvents, filling the stacker with clean plates before the start and removing the processed plates at the end of the process.

Plate storage module has two stackers for holding five clean and five processed HPTLC glass plates (20 x 10cm) each. To avoid cross contamination of plates in plate storage module, a fume extraction system is present for the active suction of vapours from the stacker holding the processed plates. This module is integrated in CAMAG HPTLC software visionCATS. The module Plate Storage allows to run a sequence of HPTLC analyses autonomously overnight.

Module 2- Sample Application: The sample application

Image at 366nm after derivatization-Sorbitol on tracks 1-5, maltitol, Iditol and mannitol on tracks 6-10, with increasing RF values (Plate applied and developed in CAMAG HPTLC PRO)

module has been designed for 'touchless analysis' of up to 75-125 samples, on up to five HPTLC glass plates. The possibility of using two complementary rinsing solvents, significantly improves the cleaning efficiency and minimises contamination. The rinsing process creates a precise separation bubble in the application syringe, which prevents contact between the rinsing solvent and the sample solution. The precision of the application is improved by controlling the dosage speed and the distance between the needle and the layer using a laser. For each sample solvent in use, the needle distance is optimised to give the sharpest application zone. Each set of syringe and needle, marked by a serial number, is qualified and tested for accuracy.

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> Standardisation and automation of entire process leads to cGMP compliance of HPTLC PRO system which delivers reproducible and auditable results

Other three modules of HPTLC PRO system are expected to be launched in the near future.

However, the most critical steps in the HPTLC PRO i.e., sample application and chromatogram development are already taken care of. The documentation and evaluation can be done today with a CAMAG image documentation system 'Visualizer' and 'Scanner' both controlled by HPTLC visionCATS software. Adding further modules of PRO will be just plug and play. Any existing CAMAG HPTLC user can upgrade to PRO right now.

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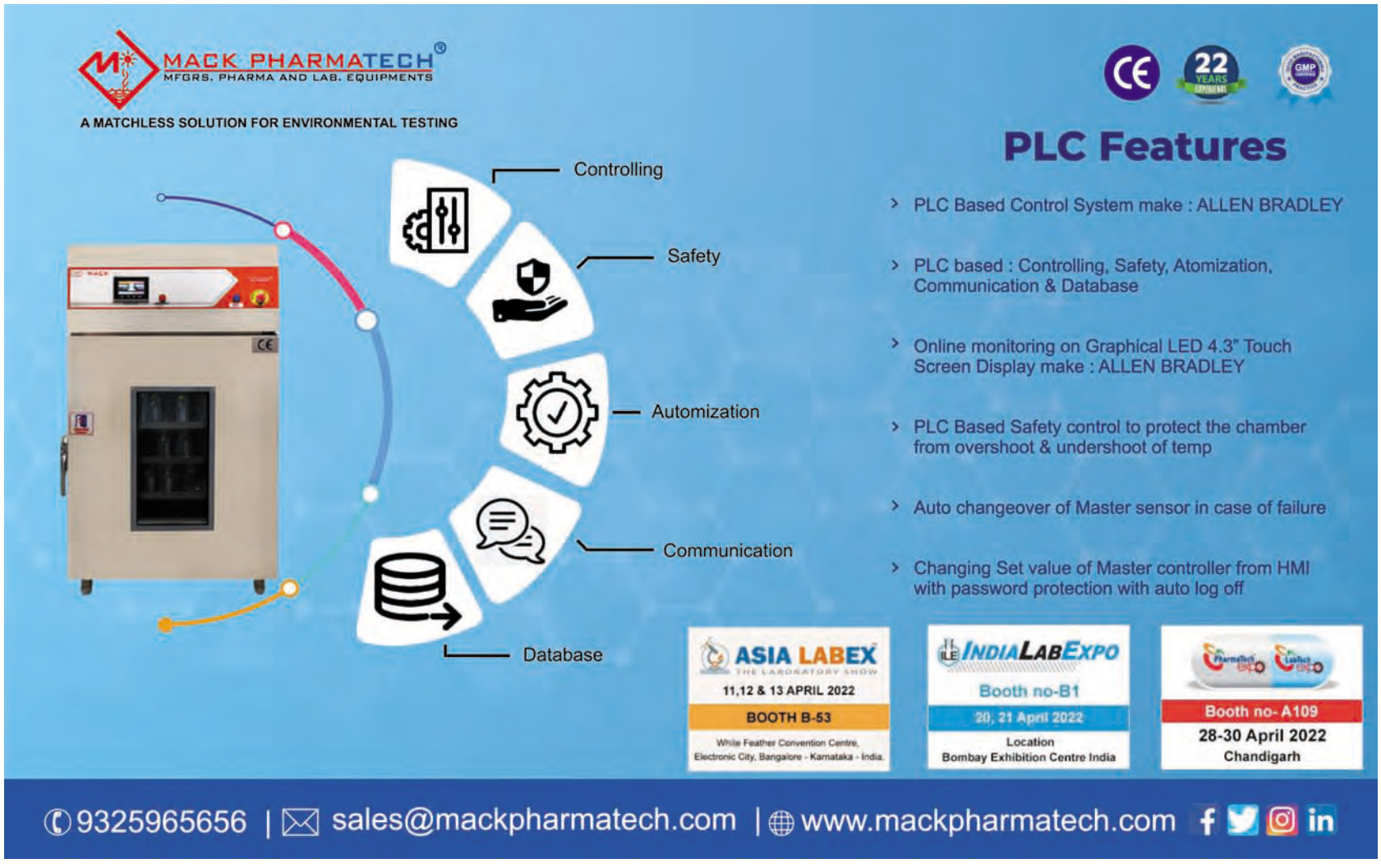
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Reducing errors and increasing throughput in Content Uniformity & Assay Testing

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What is Content Uniformity and Assay testing?

Content uniformity testing of solid dosage forms is a critical quality control test amongst several other tests (appearance, average mass, dissolution, etc.) that needs to be performed during drug development. As per USP chapter <905>, uniformity of dosage units ensures consistency of dosage units, such that each unit in a batch should have drug substance content within a narrow range around the label claim. Content uniformity tests are performed for drug products with label claim less than 25 mg. Another important quality control test - Assay of the drug product is performed to determine the amount of active pharmaceutical ingredient (API) present in the dosage form. In pharmaceutical analysis, the results of drug product assay testing help in making decisions regarding the quality, efficacy, and stability of the drug product. Prior to commercial release, the content of API in the individual dosage unit and in the bulk samples from a batch needs to be tested and should be within the acceptance requirement set by the regulatory bodies globally.

Content uniformity tests are divided into the 2 main parts – sample preparation and sample analysis. Sample preparation is most critical step since it has direct impact on the results and there exist a high scope of variability since it involves multistep processes. The workflow of manual sample preparation process includes sample selection, weighing, trituration and transferring, extraction and filtration. Out of all the steps, trituration, transferring, and extraction steps are the most time consuming and the chances of error introduced are highly attributed to these two steps. Other than these process factors, the formulation variables that influence the uniformity of content in the dosage form are the excipient compositions, blend rates, drying time, and tablet compression forces.

Archana Pokkalath

Aditya Marfatia

Current challenges of the manual procedure for Content Uniformity testing

Inability in following accurate sample preparation practices, maintenance of appropriate documentation, not tracking and investigating OOS and OOT results have been key points in warning letters issued by the FDA to several companies. The number of dosage units that needs to be examined is considerably large in the content uniformity testing. As per USP chapter <905>, Stage I testing requires that a minimum of 10 individual dosage forms be examined for uniformity although this number can increase to a total of 30 units if Stage II testing is required. Additionally, the manpower, reagents, and time needed to carry out this testing become resource intensive and laborious as the units for testing expands. The commonly faced challenges in the manual sample preparation are listed in the Table no. 1. To summarize, the multi-step manual sample preparation workflow is a time-consuming process, is more prone to introduce errors and inter-lab variations which is attributed to both instrument and analyst intervention.

Table No. 1: Challenges in Trituration, Transferring and Extraction Steps in Content Uniformity/Assay testing

Sr. No	Challenges	Outcome
	Trituration	
1.	Hygroscopic API or excipients	Sticking on the wall of the mortar or pestle. Incomplete product recovery.
2.	Unequal forces exerted on the product during extraction is analyst dependent	Introduce variability in results
3.	Serial process of trituration	Time consuming process since one tablet is triturated at one time.
4.	Presence of certain excipients (menthol, camphor, phenol, etc.) in the formulation	Liquefaction of contents on trituration.
	Transferring	
1.	Sample loss during transfer	Inaccurate results
2.	Analyst to analyst variation	Irreproducible results
3.	Serial process	Time consuming
	Extraction	
1.	Time consuming – batch testing	Decreased productivity
2.	Non-standardized apparatus used for extraction	High Inter-lab variation
3.	For temperature sensitive drugs, no temperature monitoring during extraction	May result in product degradation

Importance of automation in sample preparation process for content uniformity and assay testing

The switch to novel, rapid, and resource friendly automated technique for preparation of content uniformity/assay samples automation in sample preparation can overcome the current shortcomings in the manual lengthy and cumbersome processes. In a study performed on automatic sample preparator for content uniformity/assay testing– Xtractr, the entire process was evaluated and compared with the manually extracted samples by sonication method. In the Xtractr apparatus, up to 10 individual units was tested simultaneously. One dosage unit was added in each tube called Xtainer and was fixed into the Xtractr apparatus. The high shear mixing action of the SS blades crushed the tablets and allowed entire extraction to be completed within minutes.

The samples extraction using the Xtractr apparatus was proven to be significantly

Figure 1: Setup for manual extraction (left) and Xtractr (right)

shorter than that required by the manual process, i.e., 5 mins at 2000 RPM vs 1 hr with Xtractr and manual process, respectively. On extrapolating this data to the 10 & 30 samples in Stage I & Stage II levels of content uniformity testing, respectively, significant time can be saved in automatic preparation compared to the manual process. As depicted in the Fig 2 (b), the samples that were prepared using Xtractr aided in reducing RSD (0.903 %) within assay results compared to the samples prepared by the manual process (1.155%). This can be attributed to the minimal analyst intervention occurring when the Xtractr apparatus is used. The automated sample preparation typically requires little user interface for operation and involves lesser chances of error. Additionally, the samples extraction via the automated sample preparator led to 100% drug recovery. By increasing the throughput with simultaneous sample preparation of multiple dosage units, the automated sample preparation in content uniformity and assay testing can be an effective alternative to traditional sample preparation methods.

Key Features of Xtractr:

◆ The automatic sample preparator can prepare 10 samples at one time compared to serial lengthy manual preparation process.

◆ Quick sample extraction from high-shear mixing action of the built-in stainless steel blades helps in analyst save a significant amount of time in testing.

◆ TemSen technology - Contactless temperature monitoring and control by automatic motor on/off within the set temperature range throughout the test. Ideal for temperature control in temperature sensitive APIs and excipients (eutectic mixture, polymers) used in the formulation.

◆ Available with wide volume ranges of sample holder tubes called Xtainers in both clear and amber color (light sensitive products).

◆ The tester routinely prompts audio-visual alerts about the instrument status (D'light technology)

◆ The generated data from the apparatus can be printed via serial printer and documented as part of data management for routine audits.

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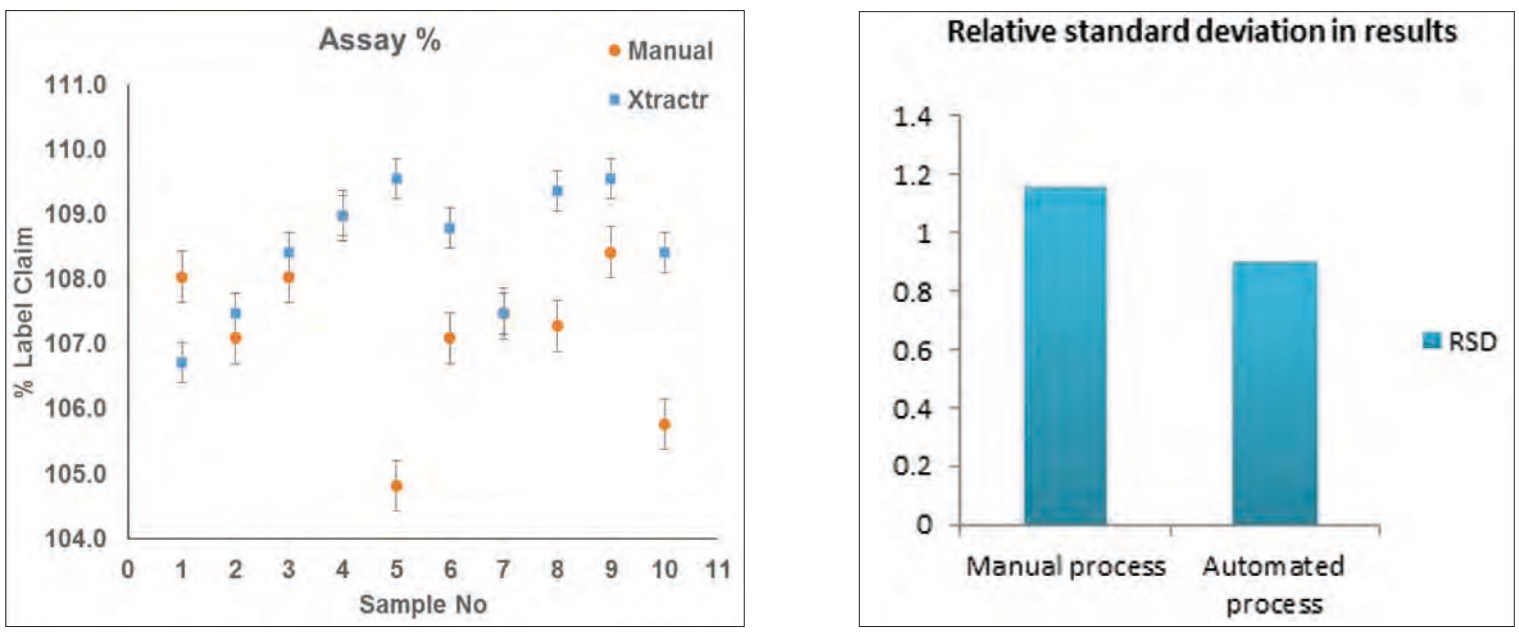

a) b)

Figure 2: a) Individual values plotted for the assay results in content uniformity testing from manual process and using Xtractr apparatus. b) The comparison in RSD in assay results from manual and automatic sample preparation techniques

Better safe than sorry

Observing regulations, putting them into practice and maintaining an awareness of the prevailing physical conditions all play an important part in establishing safety and protection in dangerous working areas

Protection and safety are crucial aspects of industrial manufacturing. They not only protect people's lives and prevent injuries, but also avoid financial loss. We often hear about accidents in production companies causing damage that could easily have been avoided. Time and again, significant injury to persons or damage to property results from a failure to heed safety measures, improper use of machinery or simply carelessness.

As modern industry has developed, machinery and production plants have been designed and constructed to be increasingly safe. Rules and regulations have always played a part in this and continue to do so, as they indicate framework conditions for manufacturers and operators which help to ensure safety and protection in manufacturing. Given the complexity of the industrial landscape and its increasingly international nature, there are a huge number of transnational regulations dealing with safety, which particularly affect companies and manufacturers operating on a global scale. These regulations might have similar principles underpinning them, but they differ in terms of how they are executed. In all cases, however, they have to be observed by every party affected by them.

Flammable substances and potentially explosive atmospheres in production represent a significant source of danger in modern manufacturing facilities. Many branches of industry use flammable substances such as gases, vapours, mists or dust, which can quickly form an explosive mixture when they come into contact with oxygen: this is a problem that affects much more than just the chemical and petrochemical industries. Even in seemingly non-hazardous production facilities, such as those used in food production, there is a risk of explosion. Flour dust, for example, can ignite when making bread. And when you use toiletries or cosmetic products, do you ever stop to think that filling aerosol cans demands particular protective measures for employees and machinery to eliminate the risk of explosions?

In production areas at risk of explosion, 'Better safe than sorry' is a useful maxim to work by. Observing regulations, putting them into practice and maintaining an awareness of the prevailing physical conditions all play an important part in establishing safety and protection in dangerous working areas. Using metal detectors in these hazardous areas requires the manufacturer to have in-depth knowledge of the physical circumstances as well as extensive expertise that enables them to comply with the various international regulations. Meanwhile, operators must be aware of the location and equipment requirements of these regulations and conditions, to make sure they are implemented correctly.

The white paper provides an overview of explosion protection in relation to metal detectors with the aim of ensuring as high a level of safety as possible in manufacturing environments.

After all, it's better to be safe than sorry!

ATEX is an abbreviation for "ATmosphere EXplosible". It the abbreviated name of the European Directive 2014/34/EC concerning the placing on the market of explosion-proof electrical and mechanical equipment, components, and for use in explosive atmospheres. If operating in a potentially explosive atmosphere, GF metal detection systems can be supplied to comply with ATEX regulations. Certain components get changed for ATEX-certified components. (The GF head is also IECEx certified, but not the complete system)

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High Speed Door – Prime Metallic

High Speed Door-Prime Metallic is the unsung hero of the warehousing facilities for any industry

Traditional industry entrances do not provide the necessary protection for today's volatile security landscape. Normal rolling shutters do not mitigate tailgating and piggybacking, even when used in conjunction with access control devices. As a result, High Speed Doors are growing in popularity due to their ability to effectively control access while creating a clear trail, which is ideal for regulated industries.

High Speed Door-Prime Metallic is the unsung hero of the warehousing facilities for any industry. Their top speeds combined with top security protects against unwanted burglars. Prime Metallic Door provides a variety of applications which includes internal use as a partition between two rooms and external use as a secure hall closing door. The door also ensures environmental separation, energy efficiency and time efficiency leading to hastening the logistics process.

Characteristics of High Speed Door – Prime Metallic

Prime Metallic Doors fast opening and closing speeds sharply reduce the potential for tailgating, piggybacking or people on foot sneaking in through the doorway. The door has an inbuilt inverter motion system to adjust different speeds, with progressive control of acceleration and deceleration during braking. High Speed Doors also reduce the potential accident by material handling equipment. It has an opening speed of 2.5 m/s and closing speed of 0.5 m/s.

Prime Metallic door includes double-skinned Aluminum Alloy, Anodised with 40mm Polyurethane Foam Insulation. It is designed to provide sturdiness during the closed condition that also gives better separation between different working areas, characterised by a thermal intensity, or intended for different uses. The door reduces leakage of heat and air, heat preservation. The contactless operation of the door leaf prevents surfaces from being scratched, while the optional transparent vision laths remain transparent even after extensive use. Additional features include the capacity to withstand wind pressure of Class-IV subject to standard EN 12424.

> Prime Metallic Door provides a variety of applications which includes internal use as a partition between two rooms and external use as a secure hall closing door

In high-traffic environments, these doors maintain a smooth flow of material handling equipment in and out of the warehouses while ensuring building security. The doors are designed with minimal maintenance with energy-efficient motors and self-diagnostic controllers – to ensure trouble-free, efficient operation, day in and day out.

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Salts, buffers and stabilisers in pharmaceuticals

Sredstva Regionale Chemie offers inorganic salts and chemistry that comply with regulations and standards for formulations

Pharma salts are acid or base compounds of sufficient purity and quality for use in pharma composition. Buffers are solid or aqueous agents that are used to maintain an adequate PH level of a formulation. Stabilisers are used to help APIs maintain the desirable properties of the product until consumption. Many APIs are plagued with issues such as poor solubility and bio-availablity, thereby affecting the formulation. Hence, a strong need arises to address the problem faced.

Choosing the right one

The past decades have seen revolutionary changes in drug discovery and development. In search of more potent and highly specific drugs, more and more selection of highly insoluble compounds are selected. Hence, salt forms are critical to solve the problem. The selection of an appropriate salt form for a potential drug candidate is an opportunity to modulate its characteristics to improve bioavailability, stability, Manufacturability, and patient compliance. Salt forms must be chosen based on early stages of drug development, aqueous solubility, degree of crystallinity, etc.

Buffering agents such as citrates, phosphate and acetates are commonly used to ensure solubility and stability of formulations such as biotherapeutics. Recognising the importance of pKa is the first step in choosing a buffer that has a value close to middle of the range requirement. Other factors like desired temperature, purity and cost of a buffer are decisive factors as well.

Selecting a stabiliser involves practical considerations; relating to a drug such as solubility of a drug in a stabiliser solution, lipophilicity, etc. Stabiliser-related parameters involve concentration of a stabiliser that affects the adsorption efficiency, hydrophobicity, viscosity, affinity for a drug, and dispersibility, among the most common.

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> "Overcoming formulation challenges is critical to bring a finished dosage into a market"

Conclusion

Developing a stable formulation is a time-consuming and expensive process. Excipient choice has typically been a trial-and-error process involving the preparation of numerous different formulation variations and placing them on accelerated stability. The need for new excipients as well as a better understanding of the existing excipients is highly desirable. Overcoming formulation challenges is critical to bring a finished dosage into a market.

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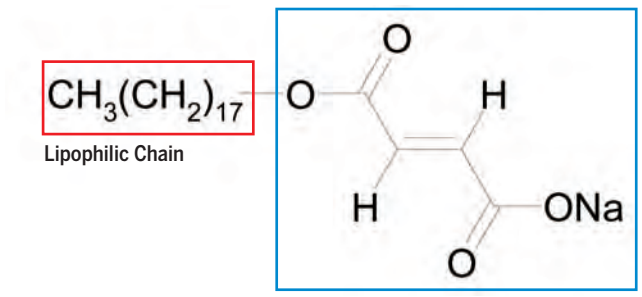
PRUV® -The original Sodium Stearyl Fumarate

JRS Pharma's PRUV® is the original sodium stearyl fumarate (SSF) introduced in the market over 20 years ago

Pharma lubricants are the inactive agents i.e. excipients added into tablet and capsule formulations in a very small quantity (usually 0.25-5.0 % w/w) to improve the processing properties of formulations. They decrease the friction at the interface between tablet's surface and the die wall during the compression and ejection phase of the tableting so that the wear on punches and dies are reduced. They prevent sticking of tablets to punch faces as well as sticking of capsules to dosators and tamping pins. In terms of powder flow, lubricants can improve the flowability of blends and aid unit operations [1].

A good balance between hydrophobic and hydrophilic moieties in PRUV® (Sodium Stearyl Fumarate) makes it an ideal lubricant [2].



Common lubricants used in drug development

Most of the lubricants used in the pharma processes are boundary lubricants. Certainly, metallic salts of fatty acids such as magnesium stearate; stearic acid and sodium salt of fatty acid such as sodium stearyl fumarate are the most common ones.

A. Fatty acid esters: Fatty acid esters, including glyceride esters (glyceryl monostearate, glyceryl tribehenate, and glyceryl dibehenate), sugar esters (sorbitan monostearate and sucrose monopalmitate) and alcohol ester of stearic alcohol with fumaric acid, including sodium stearyl fumarate are often used as lubricants. In particular, sodium stearyl fumarate and glyceryl dibehenate are effective lubricants to replace magnesium stearate when the latter hampers dissolution and has chemical incompatibility issues. Relative to magnesium stearate, sodium stearyl fumarate has similar lubrication efficiency with a higher optimal concentration (around 2%, w/w). In addition, the use of sodium stearyl fumarate does not affect compressibility [1].

B. Metallic salts of fatty acids: Use of the metallic salts of fatty acids as lubricants has a long history in the pharma industry and they are still the most dominant class of lubricants. Magnesium stearate, calcium stearate and zinc stearate are the three common metallic salts of fatty acids used [1].

C. Fatty acids: Fatty acids are also common lubricants used in the pharma industry with stearic acid as the most popular one. Chemically, stearic acid is a straight-chain saturated monobasic acid found in animal fats and in varying degrees in cotton seed, corn and coco. The commercial material of stearic acid has other minor fatty acid constituents such as myristic acid and palmitic acid [1].

D. Inorganic materials and polymers: Inorganic materials and polymers are also used as lubricants when magnesium stearate cannot be used. In terms of inorganic materials, talc (a hydrated magnesium silicate (Mg3Si4O10(OH)2), is often used as a lubricant or as a glidant in formulations. Talc provides some essential lubricity for pharma operations because of its hydrophobicity and weakly bonded sheet structure [1][6].

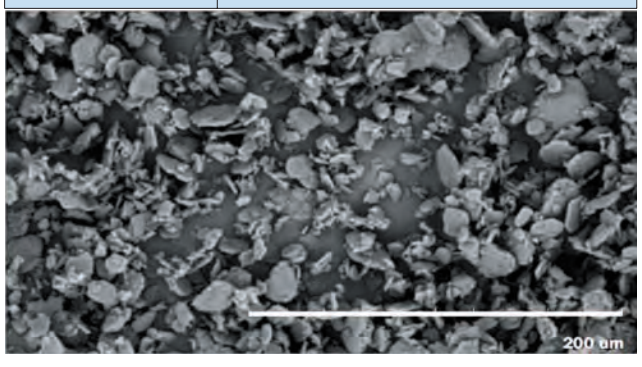
Mechanism of lubrication:

There are four lubrication mechanisms: [1]

1. Hydrodynamic lubrication,
2. Elasto-hydrodynamic lubrication,
3. Mixed lubrication, and
4. Boundary lubrication.

As their names imply, the first three mechanisms are related to the usage of liquid lubricants to some extent. In the pharma industry, boundary lubrication is the most common mechanism functioning in unit operations.

Typical properties of PRUV®: [5]	
pH	About 8.5 (10% aqueous solution at 90°C)
Saponification value	142.2-146.0
Moisture	<5.0%
Solubility	0.5mg/100 ml at 25°C/
	10 g/100 ml at 80°C
	20 g/100 ml at 90°C
Melting point	224-245°C



SEM Picture of PRUV®

For boundary lubrication, a lubricant typically forms layers/film between surfaces or at interfaces to reduce friction, where the penetration of the lubricant into surface asperities occurs. Structurally, the lubricants commonly used for boundary lubrication are long chain molecules with active end-groups. The typical end-groups include:

1. –OH (long chain alcohol);
2. –NH2 (long chain amine);
3. –COOH (long chain fatty acids); and
4. Metal ions such as Mg2+.

Considerations for selecting a lubricant

There are many factors to be considered for selecting an appropriate lubricant for preparing solid dosage forms, including low shear strength, being able to form a durable layer covering the surface/particles, non-toxic, chemically compatible with APIs and other components in the formulation, low batch-to-batch variability, and having minimum adverse effects on the performance of the finished dosage forms. [1][3]

In addition, the optimal concentration and mixing time are also needed to be taken into consideration when selecting a lubricant because both of these two parameters greatly affect the performance of pharma products and processes. [1][6].

After understanding what are lubricants, commonly used lubricants in pharma formulation, mechanism of lubricants and considerations for selecting the best lubricant, let's focus on more detail regarding PRUV® (Sodium Stearyl Fumarate) lubricant from JRS Pharma.

PRUV® (Sodium Stearyl Fumarate) characteristics:

◆ Highly efficient lubricant and anti-adherant
◆ More water-soluble than Magnesium stearate
◆ Well-defined particle size and specific surface area
◆ High melting point (230°C)
◆ Lamellar structure
◆ High purity and batch-to-batch consistency

How PRUV® works?

◆ **PRUV®** reduces inter-particulate friction during tablet manufacturing while acting as a boundary lubricant in the formulation.
◆ **PRUV®** facilitates lubrication during blending through shearing.
◆ **PRUV®** is more hydrophilic, dissolution is not compromised wherever facing dissolution issue with magnesium stearate.
◆ **PRUV®** goes beyond lubrication and it also accelerates dissolution.

Applications of PRUV®

PRUV® can be used in dry granulation as well as wet granulation technology to avoid sticking of intra-granular blend to roller or RMG wall. PRUV® can also be used in capsule dosage by reducing friction between the particles. PRUV® is a perfect lubricant for high-speed tableting/continuous manufacturing because it is less sensitive to heat. PRUV® can also be used in hot melt

extrusion due to its higher melting point (224-245°C).

Following are the case studies of PRUV® to evaluate the effect on physio-chemical properties on tablet dosage form [4].

In this study, the effect of different lubricants on Acetaminophen formulation was studied. Acetaminophen API blended with PROSOLV SMCC HD 90 for 15 min and afterwards blended with sieved lubricants for three minutes. Different lubricants like PRUV, Magnesium stearate, stearic acid and sodium stearate are used. Tablets were compressed to 800 mg weight. tablet.

Magnesium stearate is the most widely used lubricant in the pharma industry. Hence, PRUV® is compared with Magnesium stearate in the following section:

PRUV® helps to avoid API incompatibilities and enhances API stability. With a few exceptions, PRUV® can be applied to any formulation for lubrication, particularly those in which API stability or tablet taste is compromised due to magnesium stearate. Magnesium cation (Mg2+) is electrophilic, it interacts with the free electrons of an API and forms insoluble salts. This is one of the many causes of API incompatibility with magnesium stearate. [4]

Electrostatic Properties: Magnesium stearate shows higher voltage and retention time than PRUV®. Low electric charge and retention improve lubricant dispersion during blending. As a result, PRUV® due to its low voltage and retention can be considered a superior lubricant with improved lubricant uniformity.

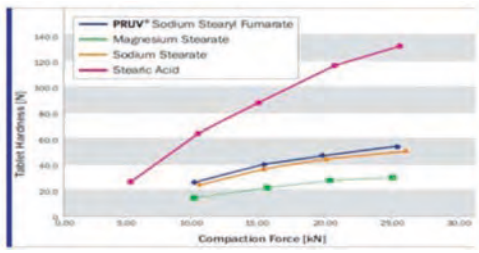
PRUV® was carefully designed to consistently deliver the following functional characteristics:

Ingredients	Quantity (%)	Quantity (mg/unit)
Acetaminophen	62.5%	500 mg
PROSOLV® SMCC HD 90	35.5%	248 mg
Lubricant	2.0%	16 mg
Total	**100.0%**	**800 mg**

LUBRICANTS: PRUV® (SODIUM STEARYL FUMARATE), MAGNESIUM STEARATE, STEARIC ACID, SODIUM STEARATE)

Tablet Hardness/Compactability

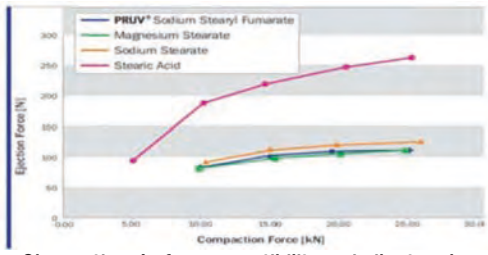
In this study, the effect of different lubricant on tablet hardness was evaluated



Observation: The kind of lubricant used had a significant influence on the hardness of the tablets. While tablet lubricated with stearic acid resulted in the highest tablet hardness, those made from magnesium stearate exhibited the lowest hardness. Tablets made from PRUV show intermediate hardness.

Lubrication efficiency

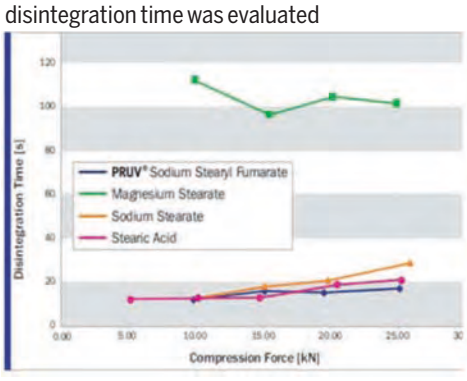
In this study, the effect of lubrication efficiency of different lubricants was evaluated



Observation: As for compactibility, a similar trend observed in the ejection forces. The tablets lubricated with stearic acid showed the highest ejection forces, while magnesium stearate was found on the lower end of the ejection force spectrum. Tablets made with PRUV exhibited the same low ejection forces as compared to magnesium stearate.

Disintegration time

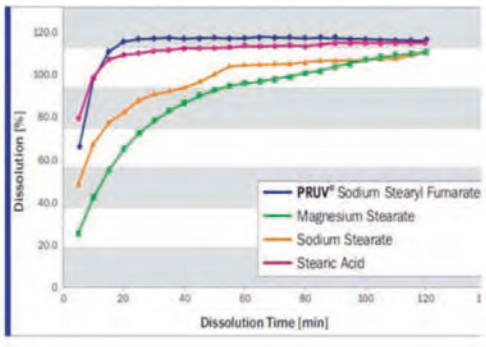
In this study, the effect of different lubricant on disintegration time was evaluated



Observation: Tablets lubricated with magnesium stearate needed by far the longest time for disintegration. All other tablets were found to have disintegration times in the same range

Dissolution behaviour

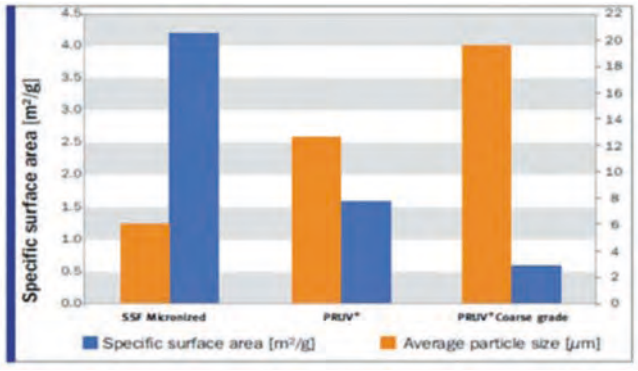
In this study, the effect of different lubricants on dissolution behaviour was evaluated



Observation: Tablets containing magnesium stearate showed by far the slowest dissolution rates. Sodium stearate and stearic acid-lubricated tablets released the API much faster. The faster drug release was observed for tablets lubricated with PRUV®

Grade	D(50)	BET
SSF Micronized	7.6	4.2 m^2/g
PRUV®	13.6	1.6 m^2/g
PRUV® CG (Coarse Grade)	20.4	0.6 m^2/g

PARTICLE SIZE AND SPECIFIC SURFACE AREA FOR DIFFERENT GRADES OF SSF[4]



◆ Tight particle size distribution
◆ Well-defined specific surface area
◆ Reproducible particle morphology

The outstanding performance of PRUV® is based on its well-controlled particle size and shape. Following studies show the effect of deviating from the ideal values.

Conclusion:

Beyond tablet lubrication properties of PRUV®:
It shows:

◆ Improved API stability
◆ Superior blending properties
◆ Faster disintegration
◆ Faster dissolution times

The choice of lubricant can influence the quality of the tablets as well as the dissolution rates. Since APIs tend to be less water-soluble and difficult to compress, choosing the right lubricants continues to become an even more important task.

Most commonly available lubricants are very hydrophobic and thus increase dissolution times significantly. In such cases, a less hydrophobic lubricant can help to decrease the dissolution times as well as increase the API release.

PRUV® Sodium Stearyl Fumarate complies with Ph.Eur., NF and JPE. It has the ideal particle size and specific surface area to offer a perfect balance between all functionality aspects. It is the preferred choice over magnesium stearate in terms of improving disintegration time and dissolution.

Furthermore, different particle sizes are available, which help to fine tune tablet formulation resulting in the desired dissolution profiles.

Regulatory status of PRUV®:

◆ Ph.Eur., NF, JPE, GRAS status
◆ C-DMF is available for PRUV®
◆ Non-animal origin
◆ BSE/TSE-free
◆ GMO-free
◆ OVI-free (USP<467>) and conforms to the residual solvents requirement of Ph.Eur.(5.4) and USP <467>
◆ QBD dossier available
◆ Elemental impurity statement available

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QR Code:
Scan the QR code for more details regarding PRUV® from JRS Pharma.

PRUV®
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Mr Prashant Bhangdiya
Technical Manager, Pharma Business unit, Rettenmaier India
Prashant Bhangdiya, Technical Manager, Pharma Business Unit, Rettenmaier India, is responsible for the JRS Pharma's Excipients Business in South India, East India and Bangladesh, including but not limited to, supporting the business development team, customer service and logistics team.
He completed M Pharmacy from Poona College of Pharmacy, Pune (Bharati vidyapeeth). He has also completed Diploma in Intellectual Property (IP) rights from Symbiosis International, Pune.
He has over 10 years of experience in the field of formulation development and pharma excipients.

PharmaEdge from B&R India: SCADA for pharma

This system supports FDA compliance and 21 CFR Part 11, and is aligned with the needs of Industry 4.0

The pharma industry is one of the world's most consistently growing industries. Pharma companies are bound by a multitude of regulations and standards. Implementing innovation in this fast-growing industry faces numerous challenges every day in terms of safety, traceability and data availability. Today's pharma companies face significant manufacturing challenges, including standards compliance and traceability to detect errors immediately. To meet these requirements, many pharma companies rely on a well-established approach: SCADA systems.

Today, a new generation of requirements have pharma companies looking for new solutions. Data acquisition is no longer enough, and factories are demanding faster and more accurate solutions with capabilities for energy monitoring, condition-based predictive maintenance, MES/ERP connectivity, reporting and advanced analytics. In today's fast-growing industry, large corporations are looking for a single-source solution and an integrated approach to leverage the existing capabilities and be ready for the future.

> In today's fast-growing industry, large corporations are looking for a single-source solution and an integrated approach to leverage the existing capabilities and be ready for the future

Data-driven SCADA system

Data is the new science. The world is now awash in data, which helps consumer needs be identified more accurately. Industries are looking for techniques and solutions to analyse the data easily, quickly and securely. To do this, they need a system that combines all the little data into one process. Futuristic manufacturing techniques are the hallmark of an excellent pharma facility. The pharma industry thrives on integrating such systems and techniques into its operations. SCADA represents one of the most significant advancements of the past and has helped shape today's manufacturing industry.

The pharma industry, in particular, has realised the importance of this system that allows them to analyse, implement and identify errors, if they find any. Pharma companies spend a large portion of their revenue on protecting their data. Despite the market being flooded with various SCADA systems, they are looking for a secure network system. B&R India, a leading manufacturer of industrial products and a reliable partner, has recognised the security gap in the pharma industry. That's why they have packaged important innovations for the pharma industry in a solution called PharmaEdge. This system supports FDA compliance and 21 CFR Part 11, and is aligned with the needs of Industry 4.0.

SCADA built just for pharma

To meet the demands of the pharma industry, B&R has developed an integrated single-PC solution for monitoring and controlling the entire operational process that also meets the increasing requirements of FDA compliance, one of the fundamental benchmarks for pharma manufacturers. PharmaEdge offers all the benefits of SCADA and a robust control system in one device. In short, it is a one-stop solution with the ability to add energy monitoring, condition-based predictive maintenance and MES/ERP connectivity. It also enables the implementation of smart machines for the future of the industry. The integrated PharmaEdge solution helps users optimise the performance of their automation systems while improving cost and energy efficiency. Instead of using separate control systems for process control, SCADA, energy monitoring and condition monitoring, users get all these functions in a single integrated system with built-in cybersecurity. With this innovative one-box solution, users in factories can monitor and control their entire operation with a single system.

The unique PharmaEdge solution consists of a B&R industrial PC running a hypervisor solution with Linux and B&R's real-time operating system, providing easy access to machine and process automation libraries for easy configuration. There are no restrictions on internal tags and no incremental costs for additional tags. The PharmaEdge solution's built-in features support easy reporting and historical data retrieval. Several additional features such as access protection, protected data archiving and retrieval, electronic signature, easy batch reporting, user-friendly audit trail and change management, to name a few, make this solution even more trustworthy. The PharmaEdge solution is OPC-enabled with seamless connectivity to MES/ERP/ EBMR and easy cloud connectivity via MQTT. It also has simplified dashboards for easy data analysis. It is compatible with standard browsers or mobile devices and consists of iOS and Android apps that provide access to dashboards and reports. This solution is user-friendly and easy to use, and is designed primarily for the challenges faced by pharma companies.

Complete pharma solution - testo Saveris Pharma

Testo provides the best-in-class solution for comprehensive data monitoring and management for equipment as well as environmental parameters in pharma industry called the testo Saveris Pharma

A sector like pharma, which is governed by strict norms and regulations, must operate with utmost efficiency. Testo provides the best-in-class solution for comprehensive data monitoring and management for equipment as well as environmental parameters in pharma industry called the testo Saveris Pharma. It is an automated system that is integrated in the facility and constitutes wireless or Ethernet probes installed at different locations that are connected to one base station to document and monitor all measurement data of its own. The monitoring process is uninterrupted, and the system provides number of alarm options in case the measurement values violate the defined limit values. Some advantages of testo Saveris Pharma for environment and equipment monitoring system include:

- Holistic system comprising sensors, software and services
- In accordance with 21 CFR Part 11 and GAMP compliance
- Provides seamless recording, automated tamper-proof documentation
- Secure triple-layer storage of the measurement data of all audit-relevant parameters
- The data is stored in the probes, so even if software connectivity is lost, the data is safe and can be downloaded once the software is logged in
- Real-time alarm facility to highlight unexpected results

Testo Saveris Pharma system consists of testo Saveris base V 3.0 which is the core component of the system. It manages and evaluates data from all over the facility from 3,000 channels. The four testo 150 data logger modules can be flexibly combined with the three communication modules (WLAN, LAN, testo Ultra-Range) making it very convenient and user-friendly system, along with the web-based, intuitive cockpit to detect alarms, initiate corrective measures and to acknowledge them, whenever necessary.

Testo Saveris Pharma system consists of testo Saveris base V 3.0 which is the core component of the system. It manages and evaluates data from all over the facility from 3,000 channels

Application areas

- Manufacturing/ production area
- Research and QC labs
- Cleanrooms and data centres
- Warehouses and packaging
- Deep freezers, refrigerators, cold rooms
- Incubators, stability test and walk-in chambers
- Blood and tissue banks
- Autoclaves and nitrogen tanks
- Sterilisers and many more.....

Testo's specially trained service team supports its clients throughout the process in a very systematic way - from planning, documentation, system qualification and software validation through to service and support. Testo also has a NABL-accredited service and calibration LAB that takes care of the after-sales support locally from Pune.

For more details, login to *www.testo.com or write back to info@testo.in*

Coronavirus, fear or not?

Dr SK Chauhan, Centre for Food Technology, University of Allahabad; **Dr Krishna Kumar Ojha**, Department of Bioinformatics Central University of South Bihar; and **Dr Naseem Khan**, Head INDIA - Drug Delivery and Excipients Sredstva Regionale Chemie, explain details about bacteria and viruses, while also shedding light on the fears around corona virus

Bacteria are single-celled prokaryotic microorganisms, that means they do not have a true nucleus, mitochondria, or any other membrane-bound organelle like eukaryotes whose cells have a nucleus enclosed within membranes (and other membrane-bound organelles, e.g. mitochondria, Golgi apparatus).

The number of bacteria on Earth exceed the number of all plants and animals, with an approximately 5×1030. In one gram of soil, there are 40 million bacterial cells, and one million in a millilitre of fresh water.

In humans, there are ~39 trillion bacteria, with 30 per cent more than the number of human cells (in case of a 70 kg, 170 cm tall person.) Most of them live in the gut flora and on the skin[1] and are harmless, some of them are beneficial, especially those in the gut flora.

Several bacteria are pathogenic and cause infectious diseases, like the black plague caused by Yersinia pestis, Lyme-disease by Borelia burgdorferi or cholera by Vibrio cholerae.

Anti-bacterial drugs are used for the treatment of bacterial infections. This class of drug is considered as one of the biggest successes of medicinal chemistry. Penicillin saved countless lives in world war II. The first patient for septicemia was successfully cured on 14th March, 1942. For D-day, 2.3 million of penicillin doses were prepared.

Dr S K Chauhan

Dr Krishna Kumar Ojha

Dr Naseem Khan

However, nowadays, we easily fall into exaggeration with the excessive use of antibiotics, that implies antibiotic resistance for several kinds of bacteria.

Viruses, on the other hand, are self-reproducing chemical entities on the edge of living and lifeless. They are free forms of DNA or RNA that can't reproduce on their own, they lack the enzyme systems needed for the genetic material reproduction. "They make more copies of themselves by hijacking the machinery of cells to replicate themselves"[4]. Their number is more than sum of the living organisms on Earth. Viruses can infect all types of life forms. They contain one type of single or double-stranded DNA or RNA, one of their classifications is based on the type of their genetic material.

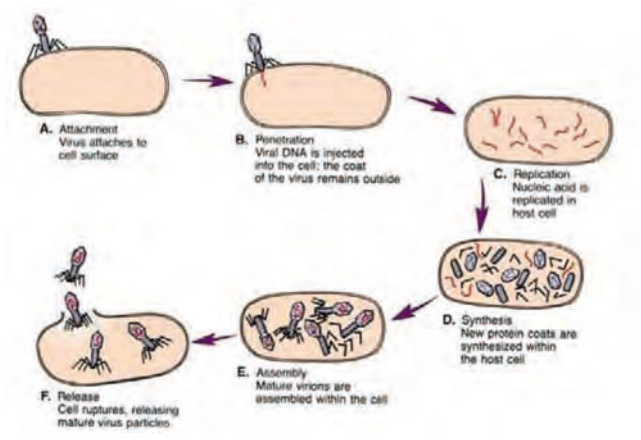

Figure 2: Stages of viral replication

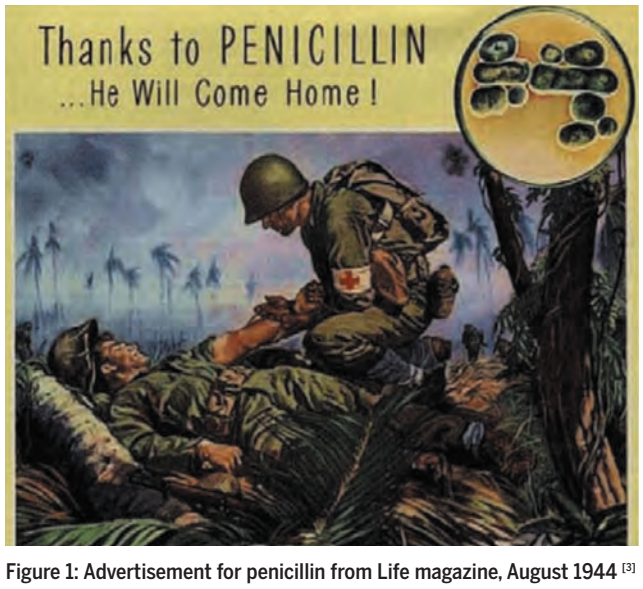

Figure 1: Advertisement for penicillin from Life magazine, August 1944 [3]

The scheme of viral replication can be seen in Figure 2. However, the processes are different in the case of DNA and RNA viruses (DNA viruses have to enter the nucleus for replication, RNA viruses can replicate in the cytoplasm).

Vaccines are mainly for immunisation, thus for the prevention. Antivirals can interfere in several points of the viral replication. One major problem with the vaccines and the drugs is the high mutation rate of the viruses (especially of the RNA viruses, up to a million times higher than their hosts. [5]).

Now a few words about today's the most feared virus: Coronavirus (Figure 3).

Coronaviruses contain a positive single-stranded RNA genome and a nucleocapsid (protein outer shell) with helical symmetry. The electron microscopic image of the virus looks like the virions have a halo or a crown, that is where their name comes from.

This is not the first case in history that coronaviruses cause epidemic. For example, in 2003, the Severe Acute Respiratory Syndrome (SARS) or the Middle East Respiratory Syndrome (MERS).

The novel coronavirus (2019-nCoV, SARS-CoV-2) infection is also a zoonosis, like the uppermentioned diseases (spreading from animals to humans). The epicentre of the viral infection is in Wuhan (Hubei province) in China. The origin of the virus is still unknown. Some articles say that it has originated from bats, others from snakes. It is well-known that bats are the reservoir of several coronaviruses. So, it is possible that the evolutional leap of the novel virus may have

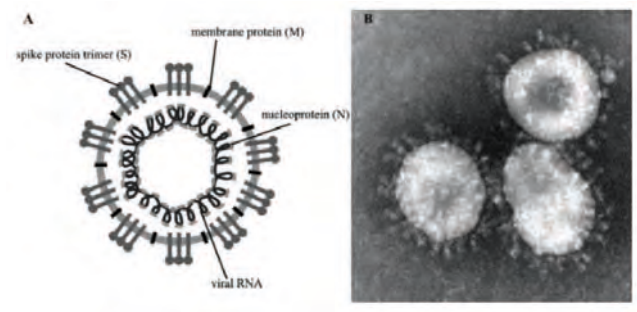

Figure 3: Structure and electron microscopic image of the corona virus particles

started from them.

Should we fear the SARS-CoV-2 ?

On 8th February, WHO announced that the disease caused by the novel coroanvirus will be referred to as COVID-19 ('co' and 'vi' stands for coroanvirus, 'd' for disease, and 19 indicated the year when it was first discovered).

Let's compare it with the flu: According to the data from the CDC, the flu this season caused approximately 19 million illnesses with 180,000 hospitalisations and 10,000 deaths. The fear of the novel coronavirus comes from several points, one of them is that we know very little (including the death rate, however, it seems higher than that of the flu's) of the SARS-CoV-2 because it is very new, compared to the flu. We know a lot about the flu, because scientists have been studying it for decades. So, we know what to expect. Moreover, the population learned to live with it.

Thanks to the Chinese scientists and authority, the full genome of the SARS-Cov-2 virus is reported [6]. Thus, several research groups have started developing a possible cure or vaccine.

Even cyclodextrins are involved in the fight against viruses. This blog reported several articles about cyclodextrins as antivirals. Also, a few cyclodextrins can be as adjuvants for some anti-viral drugs. For example, as solubility enhancers, e.g. Gilead uses Sulfobutyl-ether-beta-cyclodextrin-enabled remdesivir. The company supplied remdesivir for 500 patients in China. Also, two clinical trials have been started in patients with moderate and severe corona virus infections [7].

What do you think, should we fear it?

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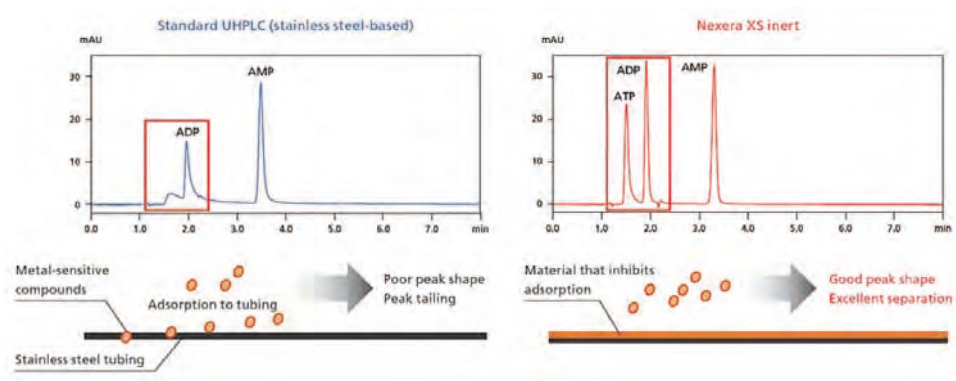
Better bioanalysis using Nexera XS inert UHPLC

Shimadzu offers the ideal solution for the separation of biomolecules by combining the elevated pressure tolerance of a UHPLC system with complete inertness of the sample flow path, ensured by the absence of wetted metal surfaces and offering ultra-high resistance to corrosion, explains **Ashutosh Shelar**, Domain Expert - Biopharma, Shimadzu Analytical (India)

The pharma industry pipelines and portfolios have changed significantly in recent years, with the small drug molecules that used to dominate increasingly giving way to biologics. Biologics include a wide group of drugs such as monoclonal antibodies, vaccines, enzymes, cytokines, nucleic acid (DNA, RNA), etc. The analysis of biopharma is decisive throughout the production steps and definite methods are requested to the qualitatively and quantitatively analyse. The High-Performance Liquid Chromatography (HPLC) is the widely used and accepted analytical tool in the biopharma industry.

The complex surface chemistry and amphoteric nature of biologics leads to the adsorption onto the surfaces they meet by multiple affinity mechanisms. Non-specific adherence of biomolecules onto surfaces can occur due to the complexity of such analytes. Each bio molecule usually has numerous positive and negative charges as well as numerous hydrophobic moieties. Hence, there is the potential for numerous points of interaction that result in sticking to surfaces. In addition to carryover and instrument problems, this can negatively impact your chromatography. Slow secondary ionic interactions between the biomolecules and the column can cause problematic peak tailing. The potential adsorption of an analyte onto wetted surfaces of HPLC instruments poses some critical challenges when analysing biomolecules. While elevated pressure tolerance is required to achieve optimal chromatographic separation when using small particle size columns, the inertness of the wetted surfaces is also of the utmost importance, as is resistance to corrosion due to the use of mobile phases with high salt concentrations and extreme pH values. The Nexera XS inert UHPLC system from Shimadzu offers the ideal solution for the separation of biomolecules by combining the elevated pressure tolerance of a UHPLC system with complete inertness of the sample flow path, ensured by the absence of wetted metal surfaces and offering ultra-high resistance to corrosion.



The Nexera XS inert uses a non-metallic material in the flow path where the injected sample comes into contact, reducing the adsorption of molecules to the LC system (bioinert). In addition, highly corrosion-resistant titanium alloy and nickel alloy are used in the flow path of the liquid feed pump to realise stable liquid feed even in the mobile phase of high salt concentration used for biomolecule analysis (biocompatible).

The pump from Nexera XS inert inherits the robustness while changing the flow path components from stainless steel to titanium alloy, nickel alloy, etc with high corrosion resistance. This makes it possible to use stably for a long period of time even in analyses using a high-salt mobile phase especially used during biomolecules analysis.

The autosampler from Nexera XS inert inherits the excellent basic performance, including the world's highest level of ultra-low carryover and multi-rinse capability, while adopting non-metallic materials such as PEEK and ceramics in the sample flow path to suppress adsorption of biomolecules with metal adsorption to the system. This improves the shape of the peak, and is expected to improve separation, peak intensity (sensitivity) and repeatability. In addition, the system pressure tolerance of 105 MPa enables the use of long columns and fine particle columns, supporting a wide range of applications.

In Size Exclusion Chromatography (SEC) and ion exchange chromatography used for the analysis of antibody drugs and other biomolecules, the pH of the mobile phase has a significant effect on the separation. pHM-40 measures the pH of the mobile phase online and records it in the LabSolutions software data file, helping to ensure data traceability.

The Nexera XS inert provides the same high resolution, high sensitivity separations with the flexibility and ruggedness to run all the different modes of chromatography like ion exchange (IEX), size exclusion (SEC), hydrophobic interaction (HIC) and hydrophilic interaction (HILIC) or reverse phase required in biomolecules analysis.

Tired of tedious manual plasmid DNA preparations?

Biotage has developed an automated process that simplifies the mass-scale plasmid purification process, offering high-quality and consistent results every time

Plasmids are one of the cornerstones of modern biology, providing the foundation for several areas of important research, including DNA vaccines, mRNA vaccines, viral vectors and monoclonal antibodies. This small, circular DNA is found in bacterial cells, and is used widely as a vector for specific DNA fragments across multiple fields, including molecular biology, biochemistry, biotechnology and cell biology. Plasmid purification, therefore, has a wide range of applications and its importance is reflected in recent scientific triumphs, including the development of COVID-19 vaccines and advancements in gene and cell therapies.

Plasmids that are used in a lab setting have been designed to introduce a DNA fragment into another cell via the use of cloning methods. They are attractive tools for scientists as they are easy to modify and can self-replicate within a cell. As a result, plasmid purification is a fundamental technique used every day in labs all around the world.

One of the most widely used applications of plasmids is in transient transfection, which results in the mass production of proteins and viral vectors. Through this technique, plasmids enable mammalian cells to express the protein that is coded by the gene they carry. Plasmids produced for transfection studies also need to be of very high quality and relatively pure for successful transfections to take place, which can also be time-consuming. While there have been numerous advances in other aspects of the production of mammalian proteins, plasmid purification technology has remained unchanged for over 40 years, but all this is about to change with the introduction of Biotage's PhyPrep plasmid purification system, which can simplify and streamline the plasmid purification process, saving both time and money and providing better quality results.

Plasmid purification challenges

Before diving into Biotage's PhyPrep plasmid purification system, one might be wondering what the issue is with the techniques currently in use in lab settings across the globe, especially if these techniques have not been changed in over 40 years. Well, to start, large-scale plasmid purification is a long, drawn-out process that can take days in the lab or weeks, if it is outsourced. There are also several challenges that we can highlight that are associated with developing and purifying plasmids for scientific studies, especially when the amount of plasmid required is in the maxi-, mega-, or giga-scale.

Firstly, plasmid purification is not only a labour-intensive process that involves multiple steps such as centrifugation, lysis of cells and chromatography, but, it also involves a lot of time spent at the bench carrying out repetitive and monotonous tasks. This highly laborious process involves the addition of multiple reagents which leaves a wide margin for human error. Secondly, the purification step has additional challenges, including removing contaminants such as RNA, host cell DNA and endotoxins as well as cell debris. Plasmids typically represent less than one per cent of the dry cell mass. So, there are a lot of potential contaminants that are structurally similar to plasmid DNA that need to be removed. In addition, when producing plasmids on a large scale, there is also a large cell pellet which can be difficult to resuspend. Looking at all this together, it's clear that plasmid purification is a long and tedious process with multiple steps that leave room for several errors to be made, potentially compromising the quality of the plasmids produced. With all this in mind, Biotage has developed an automated process that simplifies the mass-scale plasmid purification process, offering high-quality and consistent results every time. The PhyPrep plasmid purification process can address all mass protein production needs as it is purely for maxi-, mega- and giga-scale plasmid purification. It is transfection grade and endotoxin-free and is straightforward to use. So, let's look at how it works.

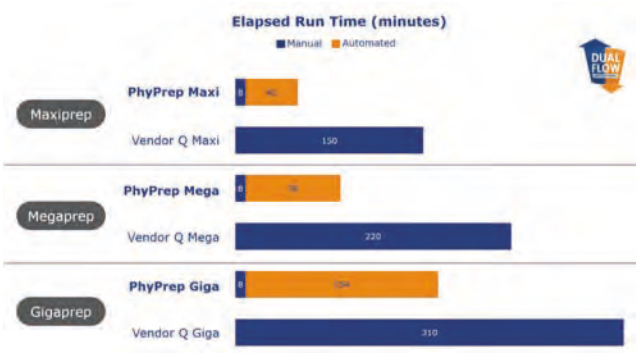


Fig- Automated vs manual plasmid purification

Introducing PhyPrep

Biotage introduces the PhyPrep system, the only automated plasmid purifier capable of operating on the maxi-, mega- and giga-plasmid preparation scales. The result is highly pure, endotoxin-free*, supercoiled plasmid DNA – the optimal starting point for downstream applications, such as transient transfection. PhyPrep comes with everything needed to generate highly pure plasmids, from a simple sample preparation step to a fully automated walkaway solution, freeing up one's time to get on with the really important work – scientific research.

Automated plasmid purification

The PhyPrep instrument is both simple and robust, and requires less than eight minutes of one's time for sample preparation, but how exactly does it work?

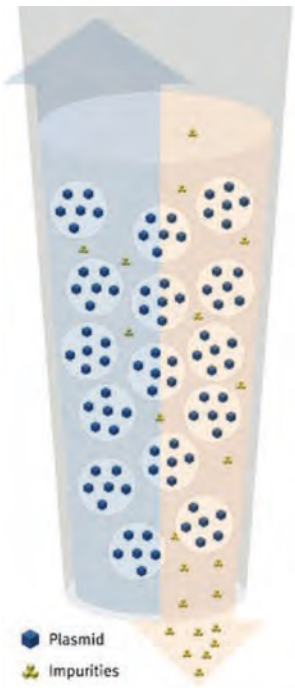
This system makes use of dual-flow chromatography technology which is highly reproducible and easy to automate. Dual-flow chromatography involves using a pipette tip column that is packed with resin. The sample is loaded and flows back-and-forth in a slow and highly-controlled manner.

High reproducible yields of up to 1 mg for MaxiPrep, 5 mg for MegaPrep and 10 mg for GigaPrep can be achieved. Purification performance and transfection efficiency is comparable to the leading manual plasmid preparation alternatives available in the market.

The automated plasmid purification allows the user to spend their time on other activities and return once the plasmid purification has been completed. The resulting plasmids are pure, endotoxin-free and supercoiled, which is an important criterion for transfection efficiency.

Why choose PhyPrep?

The PhyPrep instrument is a fast and efficient machine that enables researchers to produce plasmids using an automated system that results in high-quality plasmids the very same day. Our instrument produces quality plasmids consistently and removes the need for long and laborious days in the lab. The workflow, kit and software are easy to use, enabling a user to devote less time to monotonous plasmid purification and more time to those tasks that the user often struggles to fit into his/her day. In addition, it is cost-effective, reliable and allows the user to have complete control over the whole process.



Therefore, manual plasmid purification can be a tedious, repetitive and time-consuming process. Automating this workflow enables the user to make more effective use of his/her valuable time. Biotage® PhyPrep system increases the productivity and efficiency of one's laboratory, vastly simplifying plasmid purification with results better than ever.

Read more at
www.biotage.com ;
https://www.biotage.com/phyprep

For any queries, mail at
india@biotage.com

How to control water activity in pharmaceutical packaging

In terms of the pharmaceutical industry, water activity is an important metric as it tells us how much moisture is available in a pharmaceutical product for reacting with other substances

Numerous studies are carried out at Cilicant to understand the processes behind the challenges faced by formulators and manufacturers when it comes to pharmaceutical packaging. It's only by doing so that we can develop products that tackle issues causing the degradation of pharmaceutical products successfully.

One area in which we have invested considerably is in studies related to water activity, or equilibrium relative humidity (ERH), as it is more commonly known. As a result, we have discovered that the use of relative humidity regulators is the best desiccant choice where water activity must be maintained within a narrow range.

To understand why, we need to look at the science behind it.

Defining and determining water activity

Water activity is defined as the ratio of the vapour pressure of water in a given sample (P) to the vapour pressure of pure water (P0) at the same temperature. The formula used is:

$$a_w = \frac{p}{p_0}$$

Pure water has a water activity of 1.0, while other substances fall along a sliding scale from this upper limit towards a water activity value of 0.0, indicating complete dryness. When it comes to packaged pharmaceuticals, it's more convenient to express water activity in terms of the ERH of the sealed system. The ERH expresses the water activity as a function of the packaging environment and the relationship between the two is represented by the following equation:

$$ERH(\%) = a_w \times 100$$

Next, it is important to understand the difference between 'water activity' and 'water content,' as these are different concepts. Water (or moisture) content of a pharmaceutical is typically used to refer to percentage of water molecules in a

product, while water activity is a measure of how reactive those water molecules are.

Although there is no direct formulaic approach to plot the relationship between water content and water activity, the changes in the relationship between water content and water activity is known as a 'moisture sorption isotherm' and can be determined for each pharmaceutical product. As the composition of the product changes, so too will the moisture sorption isotherm.

There are several ways to determine the water activity of pharmaceuticals. The dew point or chilled mirror method is the gold standard. Here, specialised instruments measure the temperature at which air (at moisture equilibrium) condenses on a polished, chilled mirror exposed to a test sample of the product. This temperature is referred to as the dew point and determines the estimated relative humidity of the sample. Other approaches involve the use of capacitance hygrometer sensors or resistance hygrometer sensors.

Water activity and protecting pharmaceuticals

In terms of the pharmaceutical industry, water activity is an important metric as it tells us how much moisture is available in a pharmaceutical product for reacting with other substances. Unlike moisture content, water activity accounts for the energy levels of this water, which will impact the shelf-life of pharmaceutical products.

Since pharmaceuticals have different water activity values, by measuring the water activity, we can evaluate how resistant a pharmaceutical product will be to microbial contaminants. After that, we can assess the best ways to pack the product in order to maintain a water activity range that is optimal against microbial growth.

Of course, pharmaceuticals come in a combination of formats, such as gel capsules and powder, depending on the most effective delivery mechanism to induce the effects of the medication on human body. The key is the difference in water activity between the two materials. As moisture moves from a region of high water activity towards one of low water activity, the disparity can lead to issues, such as the cracking of gel capsules or an increase of water activity in the powder.

Many pharmaceutical packaging solutions incorporate the use of one or more desiccants to regulate moisture levels. Together, these aim to bring about low water activity to protect products against microbial proliferation and other degradation issues due to moisture build-up. However, where the ERH of the packaging environment must be maintained within a specific range, these 'standard' desiccants may cause over-desiccation.

Introducing ACCUFLIP: A better way to regulate water activity

Cilicant has addressed this issue by creating a new range of products- ACCUFLIP. These moisture-regulating sorbents, or humidity regulators, are a new type of desiccant designed to maintain a stable ERH within packaging. Unlike traditional standard desiccants that can be too aggressive when reducing moisture, moisture-regulating sorbents maintain the ERH of the packaging at an optimum level, allowing for an optimal shelf-life. Furthermore, these moisture-regulating sorbents can be adjusted to meet the requirements of specified ERH levels, making these highly versatile and ideal for a wide range of pharmaceutical packaging scenarios.

Applications

Since humidity regulators can regulate water activity in all forms of pharmaceuticals, the application potential is huge.

For instance, in gel capsules, the water activity of the exterior coating needs to be maintained at a level that prevents the coating becoming brittle as a result of very low ERH, or becoming sticky as a result of high ERH. Since moisture-regulating sorbents take up and release moisture as required to maintain a constant ERH, the gel capsules are protected from both high and low ERHs. A standard desiccant would be ineffective in this instance as it would aggressively remove moisture from the environment, potentially leading to a very low ERH and low water activity, resulting in capsule brittleness.

Another application can be seen with dry powder inhalers, widely used for delivering of drug doses to the lungs. It's essential that these devices are packed in an environment with a stable ERH as moisture fluctuations have negative effects on the stability of the product, detrimentally impacting efficacy for end-users. A high ERH here would result in powder particles clumping together making efficient drug delivery to the lungs problematic. Here, moisture-regulating sorbents prevent moisture levels becoming too high or too low, where standard desiccants would over-desiccate and create electrostatic charges, potentially lowering the dose available to lung tissue.

ACCUFLIP - a new tool in pharmaceutical packaging

Clearly, the importance of a well-regulated water activity in the stability of many pharmaceutical dosage forms cannot be overemphasised. While traditional and standard desiccants can lower water activity in packaging environments and extend the shelf-life of pharmaceuticals, these can also lead to over-desiccation. In these scenarios, moisture-regulating sorbents, such as ACCUFLIP, provide an effective alternative that helps to keep the ERH of packaged pharmaceuticals at an optimal level for longer shelf stability. Cilicant always looks at new and innovative ways of solving problems for its clients in the pharmaceutical industries and believes that these desiccants will play a vital role in the pharmaceutical packaging industry as more products requiring strict ERH levels come to market.

To see the full white paper related to this article, visit www.cilicant.com.

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Waters introduces faster, reliable and automated solution for mass and purity analysis of biomolecules

New Intact Mass software application on waters_connect enables simplified and significantly faster analysis of biomolecules for mass and purity

Waters Corporation introduced new software and analytical columns to aid biomolecule drug discovery and development. The new Waters™ Intact Mass app on waters_connect™ allows scientists using the BioAccord™ LC-MS System to confirm the mass of biomolecules and impurities made by synthetic or recombinant processes nearly twice as fast as other commercially available options. (i)

"Acquiring mass and purity data of biomolecules is time-consuming. Skilled analysis of complex mass spectrometry data is required, typically in remote specialist analytical laboratories," said Jon Pratt, Waters Division Senior Vice President, Waters Corporation. "The new Waters Intact Mass App enables bioengineers and biochemists to accelerate drug discovery and development with simplified technology to generate mass confirmation data on their own in minutes/hours instead of days/weeks."

Intact mass analysis is routinely performed during all stages of the development of biological drugs including proteins, peptides, oligonucleotide therapies and conjugates. In early stages of drug discovery, biochemists must analyse hundreds or even thousands of different samples per week. To help speed this process, the Waters Intact Mass app provides a fast, reliable and automated solution to facilitate mass confirmation and purity determination of novel biotherapeutics. The application features intelligent automated deconvolution to process sample results within minutes of their capture, with minimal user input.

System gives bioprocess engineers key information about drug and process quality within minutes

> Intact mass analysis is routinely performed during all stages of the development of biological drugs including proteins, peptides, oligonucleotide therapies and conjugates

Introducing Waters MaxPeak Premier Protein BEH C4 300Å Columns for intact and subunit protein analyses

Complementing the introduction of the Intact Mass app is a new line of analytical columns that are essential for analysing intact biomolecules and their subunits. The ACQUITY™ Premier and XBridge™ Premier Protein BEH C4 300Å Columns for the BioAccord LC-MS System feature MaxPeak High Performance Surfaces (HPS) technology that prevents the loss of sample analytes due to adsorption of phosphorylated and carboxylated molecules between the sample and metal surfaces of both the LC system and column. This enables up to 3X greater sensitivity for low-level intact mass analysis and 2X greater sensitivity for the intact mass analysis of phosphorylated proteins and low-level subunits of monoclonal antibodies. (ii)

The Intact Mass App on waters_connect is available for new BioAccord LC-MS Systems and as an upgrade to previously installed systems. MaxPeak Premier Protein BEH C4 300Å Columns are now available from Waters worldwide.

Additional resources

Read the blog post: Automating Intact Mass Deconvolution: It's About Time
See application note: Intact Mass - A Versatile waters_connect Application for Rapid Mass Confirmation and Purity Assessment of Biotherapeutics
Follow and connect with Waters via LinkedIn, Twitter, and Facebook

About Waters Corporation (www.waters.com)
Waters Corporation (NYSE:WAT), a global leader in analytical instruments and software, has pioneered chromatography, mass spectrometry and thermal analysis innovations serving the life, materials and food sciences for more than 60 years. With more than 7,800 employees worldwide, Waters operates directly in more than 35 countries, including 14 manufacturing facilities, and with products available in more than 100 countries. Waters, BioAccord, ACQUITY, Premier, UPLC, XBridge, MaxPeak, and waters_connect are trademarks of Waters Corporation.

(i) Estimate based on obtaining the results for 96 samples using a Waters BioAccord System and Intact Mass parallel acquisition and processing approach as compared to the "acquire then process" workflow of commercially available offerings.

(ii) Based on a comparison of MaxPeak Premier Protein BEH C4 300Å Columns with stainless steel ACQUITY Protein 300Å Columns

Application of Single-Use Technologies (SUT) in Biosimilar Development

Single-use technologies offer savings in cleaning expense, especially purified water and WFI usage and have demonstrated greater safety without endangering environmental efforts compared to stainless-steel systems

The current processing paradigm of large manufacturing facilities dedicated to single-product production is no longer an effective approach for the best manufacturing practices. Additionally, in recent years, patents on several blockbuster biologics have expired, which means leading pharma companies can no longer charge a premium for these products.

The subsequent launch of biosimilar drugs, which can be sold at a lower cost, has put pressure on manufacturers to lower production spending in order to stay competitive.

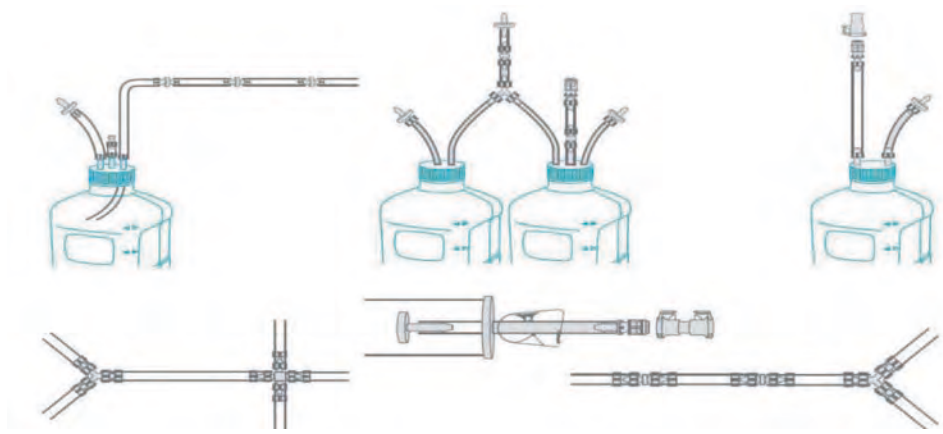
Single-use systems are ideal for multi-product manufacturing facilities, especially where process steps may differ. They eliminate contamination crossover, change out time, and downtime for cleaning and sterilisation between batches and products. Therapeutic developers are increasing their use of single-use systems for clinical batches, and many will continue at production scale as batch sizes become smaller.

Benefit: Single-use system

Primary savings benefit of single-use systems for biosimilar development is the reduced cost for process development and clinical trials. By changing out pre-sterilised single-use bags between product batches, manufacturers can eliminate the risk of inter-batch contamination from more difficult to manage in-house sterilisation processes. Single-use systems also have applications in formulating and filling operations, moving purified biosimilar drug substances to the formation container.

Single-use technologies offer savings in cleaning expense, especially purified water and WFI usage and have demonstrated greater safety without endangering environmental efforts compared to stainless-steel systems. By implementing single-use systems, manufacturers can avoid issues related to cross contamination between batches and products. Cross contamination is a risk with all bioprocessing equipment that is reused, including piping, tanks, mixers and bioreactors. Cleaning validation for such equipment is expensive and time-consuming.

Single-use systems reduce costs associated with cleaning, maintenance and assembly, minimise operator exposure and free facility resources for other activities. Eliminating user-managed cleaning and sterilisation reduces the need for a utility system and piping within a facility, leading to faster facility build time and lower capital cost. Establishing a single-use-enhanced facility takes about half-to-a-quarter of the time that it takes to install a stainless-steel facility.



SINGLE-USE SYSTEM: PROS AND CONS		
Technical	**Traditional Stainless Steel Technology**	**Single Use Technology**
Product change over time	Slower	Faster
Flexibility to change	Painful	Easy
Campaign turnaround times	Slower	Faster
Water usage/waste water	High	Low
Solid waste disposal	Less	More
Leachable/extractable validation	Small	High
Facility size	Large	Smaller
CIP	Complex	Simpler
SIP	Complex	Simpler
Sustainability	Low	High

A solution toward single-use assemblies

Ami polymer offers wide range of gamma-irradiated single-use assemblies for various critical applications in biopharmaceuticals. These range from simple tubing with connector to complex manifold with several joints/connections. All the assemblies are manufactured and packed in Class 7 certified clean room. The company covers the whole upstream and downstream bioprocess, ranging from laboratory scale and pilot plant scale to production scale. Few applications of upstream and downstream production in biopharma industry where Ami polymer is supplying assemblies are listed below:

- Buffer and media transfer (feeds, the addition of base/acid, antifoam, growth medium, and other liquids),
- Collecting samples with zero risk of contamination assemblies,
- Media filtration assemblies,
- Inoculation assemblies,
- Removal of liquids from bioprocess assemblies,
- Carboy/bottle assemblies for cell culture,
- Product filtration assemblies,
- Filter manifold assemblies and
- Peristaltic pump tube manifold assemblies.

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REGD.WITH RNI NO. MAHENG/2005/21398, POSTAL REGD. NO. MCS/164/2022 – 24, PUBLISHED ON 5TH EVERY MONTH,
POSTED ON 9TH, 10TH, AND 11TH EVERY MONTH POSTED AT MUMBAI PATRIKA CHANNEL SORTING OFFICE, MUMBAI – 400001