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EXPRESS PHARMA

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

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EXPRESS PHARMA

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

Interviews

ANAND NARASIMHAN
MD, Merck Specialties

Dr RUPALI PARANJAPE
Implementer, Auditor, Trainer and Consultant for Regulatory Compliance for pharma companies

WHAT'S NEXT IN DRUG DELIVERY?

Experts share insights on the advancements in drug delivery to enable sustained drug delivery, facilitate drug protection, encourage drug adherence and improve patient-centricity

Aerodynamic Particle Sizer® Spectrometer Rapid Tool For Accelerated Inhaler Development

TSI Instruments India Private Limited
Bengaluru, India

Dr. Ramakrishna Ramisetty (Rama.ramisetty@tsi.com),
Nishant Mittal (nishant.mittal@tsi.com)

Website: www.tsi.com
#Aerodynamic Particle Size Spectrometer , Model 3321

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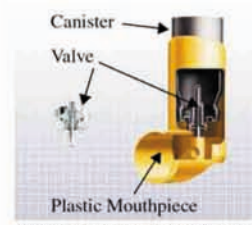
01 Looking for Faster Product Development?



MDI illustration courtesy of Stephen Stein, 3M™ Drug Delivery systems

The aerodynamic diameter of a pharmaceutical aerosol determines where and how efficiently the drug will deposit in a patient's lung, and is thus an important parameter affecting performance of inhalation devices.

Aerodynamic size distribution tests are widely used during the development of these devices and are a mandatory test prescribed by the regulatory agencies. Inertial size-separation by cascade impactors has been used as the "gold standard" to aerodynamically size-analyze inhaler-derived aerosols for many years. This method involves collection of aerosol sample on substrates with subsequent chemical analysis of the collected material. Unfortunately, the cascade impactor tests are extremely time consuming (approximately 2 to 4 hours for the preparation and analysis of a test). Furthermore, due to the nature of chemical analysis, the results are usually not available until at least a day after the test is conducted, and the entire process is labor intensive. During the development of inhalation devices, typically hundreds of formulations are screened before the final product is developed. Alternative fast and more convenient tools are desired to speed up the product development process.

02 The Aerodynamic Particle Sizer Spectrometer is the Solution

The Model 3321 Aerodynamic Particle Sizer® (APS™) spectrometer is an attractive alternative to cascade impactors or impingers for rapid screening of particle size distributions of inhaler-generated aerosols. The APS operates effectively in the range of greatest interest for inhaler testing (0.5 to 20 m aerodynamic diameter) and requires just a few seconds for a complete on-line measurement. Using patented time-of-flight technology*, the APS provides significantly higher size resolution (32 size channels per decade) to the cascade impactors (typically 6 size channels per decade), and is highly sensitive in detecting small changes in particle size distributions. This is particularly important when studying the effect of subtle changes in formulations on the inhaler output.

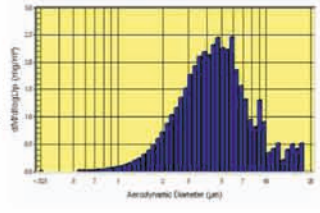
The APS measures number-weighted size distributions which are converted to mass- weighted size distributions (Figure 1) by the data management software supplied with the instrument. The software provides statistics for each measurement, including mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD).. The instrument is compatible with TSI's Model 390069 data merge software with advanced curve fitting options. When desired the Model 3306 Impactor Inlet with a USP throat can be used in conjunction with the APS (Figure 2) to collect respirable or fine particle fraction (FPF) of the drug on a filter for subsequent chemical analysis.


Figure 2. Model 3321 APS spectrometer shown with Model 3306 Impactor Inlet.

03 Comparison Results with Cascade Impactors

During the last decade or so, a number of inhaler product development efforts have utilized the APS spectrometer. Many of these studies have reported excellent correlations with traditional cascade impactor results. Inertial impactors are the "only" method currently written into the US and European pharmacopeias. Consequently, size analysis reports for the final product submitted to the regulatory agencies must be based on impactor tests. It is therefore important for any alternative method used for convenience and speed during the drug development process to correlate well with the cumbersome cascade impactors. The APS has been successfully utilized for inhaler characterization for both MDI and DPI devices. (Ex1. Graph)

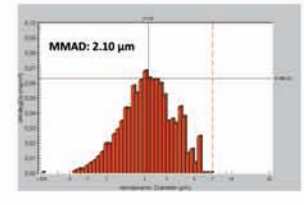
Exaample 1: MDI Output Measured By APS 3321



04 Dry Powder Inhalers

DPI characterization is an emerging application where APS is finding increased use. M. Svensson from AstraZeneca has developed a method for analyzing doses from DPIs at optional flows utilizing the APS (Svensson et al., 2006). Their tests confirmed good correlation between the APS 3321 and impactor measurements at various flow rates. The authors note that the APS demonstrated a significant speed advantage (25x faster) over conventional impactor tests. (Ex2. Graph)

Example 2: DPI A (one active drug + one excipient)



Svensson, M. 2006, "High throughput inhaler testing III-Modified APS for DPIs," Proceedings of Respiratory Drug Delivery X, 2, 475–478

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* Responsible for selection of news under the PRB Act.

Taking India beyond 'Pharmacy of the World'

Even as US revenues contract due to continued high single digit to low teens price erosion in the US generics market, pharma companies are keeping an eye on the evolving situation in a couple of geographies which are on the boil: Ukraine-Russia and Sri Lanka, to name just two hotspots.

ICRA's recent report puts India's pharma exports to Russia at 2.5-3 per cent while Ukraine's is much lower at less than 1 per cent. While not making too much of an impact on the export revenues of India based pharma companies, emerging markets are an important hedge, to prevent over dependence on a few big markets. But the other side is balancing the humanitarian angle of sending life saving medicines when most required, putting lives over revenues.

ICRA predicts that the Indian pharma industry will grow by 8-10 per cent in FY2022 and growth momentum is likely to moderate in FY2023, thanks to contraction in margins due to pricing pressures and rising raw material costs.

The ICICI-direct report based on their pharma universe also has muted expectations, citing logistical delays and high freight cost due to the Russia-Ukraine conflict and closure of China's port cities amid its ongoing COVID wave, leading to inflationary input costs of solvents, KSM, API cost.

How can India's pharma sector combat these headwinds? The launch of the AYUSH Export Promotion Council and special AYUSH visas at the recent groundbreaking ceremony of the WHO Global Centre for Traditional Medicine (GCTM) in Jamnagar, Gujarat and the convening of the Global Ayush Investment and Innovation Summit (GAIIS) could be seen as a strategy to add more diversity to India's exports basket, to balance the headwinds to traditional pharma exports.

Regulators in India are aware that India cannot rest on her past laurels. In fact, Dr Mansukh Mandaviya, Union Minister for Chemicals & Fertilizers, & Health and Family Welfare, Government of India emphasised that the main intention behind the recently concluded 7th India Pharma & Indian Medical Device 2022 was to "decide the roadmap of Indian Pharma and Indian Medical devices sector for the next 25 years to take India beyond 'Pharmacy of the World'."

A policy to incentivise pharma R&D is crucial as there are already signs that pharma R&D dives when revenues dip

A key milestone in India Pharma Inc's Vision 2047 roadmap would be reducing India's dependency on imports for pharma and medical devices, and stressing not just on scaling up manufacturing of generics but putting as much focus, if not more, on innovation and research. Dr Mandaviya indicated that the government is soon to announce a policy aimed at bringing more innovation and research into the country.

A policy to incentivise investments in pharma R&D will be crucial as there are already signs that companies are cutting down on R&D expenses due to thinning margins. The R&D expenses for leading seven companies moderated from a high of 9.0 per cent in FY2017 to 7.3 per cent in FY2021 and 7.2 per cent in 9m FY2022, according to ICRA's Q3FY2022 report. Clearly, pharma R&D dives when revenues dip.

Thus it is imperative that a policy push towards pharma innovation and research needs to pick up pace, if India wants to become a natural choice in the China Plus One strategy. Let us hope that India's pharma sector is a focus area of the Prime Minister's Office's blueprint for 'India@2047', an ambitous plan to targetting to make the country one of the world's top three economies by the 100th year of its independence. Reports claim that there will be an an official announcement with finer details per sector around August 15, India's 75th Independence Day.

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INTERVIEW

COVID-19 pandemic has shed light on healthcare gap

Anand Narasimhan, Managing Director, Merck Specialties (healthcare arm of Merck KgaA), interacts with **Akanki Sharma** to explain about the various business opportunities for the company in India, the impact of COVID-19, future plans and much more....

Since its operations began in India, what business opportunities has Merck Healthcare created for itself? At present, how huge is the Indian market for it to expand its business further here?

At Merck, we are guided by our purpose 'As One for Patients' to address the healthcare challenges of APAC, with the aim to improve the health of nine million patients per year by 2025. We aim to improve treatment management and medical outcomes through our specialised therapies and indications, innovative drug delivery devices and digital technologies. Merck India's ambition to be a global specialty innovator is driven by four core specialties of oncology, fertility, Cardiometabolic Care & Endocrinology (CM&E) and Neurology &

Immunology (N&I).

We are quite optimistic about the areas in which we operate. In 2022, we continue to take a consolidated view across our therapy areas for core and launch assets. Our focus stays sharpened across our TAs

- **CM&E:** Maintain market leadership and grow key brands
- **Fertility:** Cement Merck position as innovator and partner for fertility
- **Oncology:** Expand and establish new growth opportunities
- **N&I:** Drive growth and market share.

What impact did COVID-19 have on your healthcare business? What challenges and opportunities (if any) did it bring?

The pandemic highlighted the significance of research infrastructure and funding for public health emergencies and the importance of being prepared for any disasters and resiliency. COVID-19 had limited impact on sales in the healthcare business sector in the second quarter of 2021. One of the best things that happened due to the pandemic is digital innovation, which has helped to accelerate development in India to a different level. Our teams leveraged the acceleration of digital tools during COVID-19 as a safe, but effective means to engage with high-risk individuals across a range of disease areas.

Internally, we have taken the opportunity to embrace new collaborative tools to enable more efficient ways of working while building digital capabilities amongst our workforce to ensure that noone is left behind. The COVID crisis has demonstrated science and technology's importance in tackling global problems. In the pharma industry, innovation has had a crucial role since it affects the quality of life. In our pharma world, science and innovation have indeed been refocussed, notably with the introduction of the COVID vaccine.

Any lessons learned?

The COVID-19 pandemic has shed light on the healthcare gap, and has given us a reality check on the urgent need to build a robust healthcare system. We need to be highly proactive in planning for emergencies and also ensure to keep the organisation agile and curious to see how quickly we can adapt and adopt to changing market conditions. To deliver on our ambition to be a global specialty innovator, and after a tumultuous year with the COVID-19 pandemic, we decided on a strategy to sharpen the focus of our teams and to drive sustainable growth across our franchises.

Our refreshed approach is underpinned by four global strategic priorities: growing our core business, maximising launches, leveraging digital to drive growth and harnessing the power of our people and culture.

The effects of COVID-19 on healthcare are immense. The pharma industry has been actively involved in the fight against the virus, wherein innovation played a crucial role in providing treatment strategies and managing the supply chain during the crisis. As a result, the pharma sector was forced to refocus its resources on dealing with the pandemic.

Tell us about the ongoing developments at your company with respect to the COVID-19 treatment.

We have collaborated with other healthcare and lifesciences companies and the Bill & Melinda Gates Foundation to accelerate the development, manufacturing and delivery of vaccines, diagnostics and treatments for COVID-19 and enhance access for everyone around the world. We are also part of the European CARE (Corona Accelerated R&D in Europe) consortium, which aims to accelerate the discovery and development of urgently needed medicines to treat COVID-19.

Our lifescience products and services support pharma and biotech companies in developing COVID-19 vaccines and treatments, including more than 50 potential COVID-19 vaccines, more than 35 solutions for testing, and more than 20 monoclonal antibodies, plasma products and anti-viral drugs.

In February 2021, we announced the expansion of our strategic partnership with BioNTech and will increase our supply volume of lipids needed for the Pfizer-BioNTech vaccine.

What are the current major trends that you are witnessing in the various segments of the pharma industry? Also, if you could tell us about the possible future trends.

The trends to look out for in the pharma market are:

Artificial Intelligence (AI): Adopting AI can improve the success rates of new drugs and create more affordable medicines and therapies. The use of AI in the pharma industry has different roles expected to expand, such as reviving drug discovery and development.

Precision medicine: Personalised or precision medicine is assembled depending on a specific patient diagnosis. Its primary aim is to make sure that the drug is customised for optimal efficacy and patient outcomes.

Digital processes: As the digital processes are significantly being used, manual processes are ending, which has enhanced operational efficiency and facilitated compliance with greater ease. It also improves transparency and can mitigate the loss of data.

Blockchain: Amongst the upcoming trend is blockchain, which can be used to track the path of raw materials, ingredients and components. This is helpful for pharma companies to keep a clear record of supplies and demand.

Rise in e-medicine and telemedicine: With everything becoming digitalised, the rise of e-medicine is only natural. E-medicine makes it easy to deliver drugs to remote locations and increases mass reach. With that, there is also a focus on telemedicine, which also promotes providing quality healthcare to the masses.

Is there anything in the pipeline, specifically with respect to increasing the company's business growth in India?

When we see a need for certain kind of therapy or treatment in India, and this can be addressed through our existing products globally, it would make a great fit. The specialty innovator portfolio is an area where we see great synergies in the need-availability cycle, and we are more than happy to bring global brands to India, serving patients who need them the most.

We are able to significantly leverage Merck KgaA's global portfolio. Over the years, we have been able to bring in few of our key international brands to the Indian market. We have fast paced the launch of certain brands from our global portfolio. Last year was a great example of this as we brought in Bavencio to India in collaboration with Pfizer.

Given our play in certain segments and how we lead the market, we always look for opportunities to bring brands from the global basket to India as seen relevant.

What are your expansion plans for the next five years?

At Merck, we are pursuing a clear ambition with our "Mobilise for Growth" strategy. We want to become the global 21st-century science and technology pioneer. Our approach is about unlocking our full potential to take the company to the next level. Thanks to our three diverse and distinct sectors, our set-up is unique, with leading positions in the fastest-growing science and technology markets. By creating superior value for our customers, patients, colleagues and society, we are set to shape some of the most critical growth and technology trends of the 21st century. We want to continue accelerating our leading role in science and technology. Therefore, we aim to increase the group sales to approximately €25 billion by 2025.

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Vizag Pharma Summit 2022 to highlight the port city's role in India Pharma Inc's progress

The event will also witness experts and veterans examine and explore development strategies to embrace the challenges in this transitory environment and turn them into competitive advantages for India Pharma Inc

Post a hiatus caused by the pandemic, *Express Pharma*, is back with its series of "Pharma Summits." As a partner and facilitator of progress for India Pharma Inc, we plan to organise these summits in different pharma hubs across the country to help optimise their potential and tap into the various opportunities they offer. The overarching theme for this year is 'Sustaining and spearheading growth: Through pandemic and beyond.'

The first one in this series is the Vizag Pharma Summit 2022.

The key objective of Vizag Pharma Summit 2022 is to facilitate this port city's transformation into a pharma centre of excellence, so it will also focus on the strengths and advantages that Vizag brings to the table, as India Pharma Inc charts its blueprint for progress. To be held on May 27, 2022, at the Gateway Hotel, Vishakhapatnam; the event will also witness experts and veterans examine and explore development strategies to embrace the challenges in this transitory environment and turn them into competitive advantages for India Pharma Inc.

They will address key issues such as key imperatives for the pharma industry to sustain its leadership position such as steps to build a culture of quality and compliance across the sector, capability building, leveraging data and tech advancements to foolproof key processes and improve performance, etc.

Key topics for discussion will include:

- Emerging opportunities and growth drivers
- Building secure, resilient, next-gen supply chains
- Strategies to make and innovate in India
- Leaders of tomorrow: Traits and tickets to play
- Balancing profitability with sustainability
- Sustaining cost-leadership with product excellence
- PLI Scheme and its impact: A progress report

For speaker and partnership opportunities, contact Rajesh Bhatkal (Marketing) at +91 9821313017, rajesh.bhatkal@expressindia.com

Coming this June: FDD Conclave 2022

In its fifth edition, looking at the need for a more holistic approach towards health and wellness, FDD Conclave 2022 will deep dive into advancements in the existing drug delivery systems, and examine their potential to keep pace with innovations in formulations and new therapeutic areas. It will expand its focus to include and serve the scientific community involved in FR&D of nutraceuticals and functional foods as well

The corona virus pandemic has served as a wakeup call for the lifesciences sector and continues to impart key lessons to improve the way we treat diseases. Back as a physical event after a hiatus of over two years, Formulation Development and Drug Delivery (FDD) Conclave 2022 intends to reflect on

these learnings and create a blueprint for further progress.

Bridging gaps in disease management

Now, in its fifth edition, looking at the need for more a holistic approach towards health and wellness, FDD Conclave 2022 will expand its focus to include and serve the scientific community involved in FR&D of nutraceuticals and functional foods as well.

This June, under the theme, "Bridging gaps in disease management", FDD Conclave 2022 will bring together leaders, experts and veterans across pharma, nutra and food to discuss trends and transformations in these spheres, share experiences and pain points; and gain practical solutions to future-proof their growth strategies through FR&D.

This year's edition will deep dive into advancements in the existing drug delivery systems and examine their potential to keep pace with innovations in formulations and new therapeutic areas. They will also explore how novel drug delivery systems can enable sustained drug delivery, facilitate drug protection, encourage drug adherence and improve patient-centricity.

The event will showcase how innovations in excipients and ingredients as well as emerging processing and manufacturing technologies are transforming formulation development as well. Attendees will have the opportunity to gain insights from experts in regulatory affairs on compliance to global regulations related to pharma, nutra and food. Moreover, they can gain actionable insights from case studies presented by early adopters of disruptive technologies.

Thought leaders from these segments will also deliberate on the strategic shifts and measures needed to reinforce India's inherent strengths and build new capabilities in formulation development and delivery of drugs, nutraceuticals and functional foods.

Formulation Development & Drug Delivery (FDD) Conclave

Organised by *Express Pharma*, FDD Conclave is 'the' platform for leaders, experts and veterans of formulation R&D to come together, confer and converse on the current and future trends in the industry, their growth drivers and the challenges to tackle them as well as form meaningful alliances to fast-track progress. The FDD Conclave, since its inception in 2017, has been an ideal platform to initiate discussions on key issues in drug formulation and drug delivery as well as drive innovation in this rapidly evolving segment.

Stay tuned for more details.

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WHAT'S NEXT IN DRUG DELIVERY?

Experts share insights on the advancements in drug delivery to enable sustained drug delivery, facilitate drug protection, encourage drug adherence and improve patient-centricity

The healthcare research landscape is evolving constantly to improve treatment outcomes and patient-centricity. As a result, the life sciences industry, be it pharmaceuticals, nutraceuticals, functional foods or cosmoceuticals, is witnessing various innovations in the field of drug delivery as well.

Scientists working in FR&D and drug delivery are on a continuous quest for more targeted and controlled drug delivery methods which can optimise the potential of new therapeutic approaches and mitigate risks and side effects associated with them. A white paper shared by CAS, a division of The American Chemical Society explains, "Targeted drug delivery systems, designed to maximise the therapeutic impact of drugs on a localised area, have been the focus of significant research attention for decades. However, as developers increasingly look to reduce the harmful side effects associated with potent active ingredients, recent years have seen a substantial increase in research output for these technologies."

> The life sciences industry, be it pharmaceuticals, nutraceuticals, functional foods or cosmoceuticals, is witnessing various innovations in the field of drug delivery as well

The same white paper also highlights, "New drug formulations are being continually developed to enhance the stability and efficacy of medicines, improve patient compliance with treatment regimen, and comply with changing regulatory requirements. Furthermore, the trend towards more personalised medicine and greater patient choice has led to active pharmaceutical ingredients being formulated using multiple drug delivery systems and dosage forms to customise offerings for the needs of different patient populations. The continued expansion in IP reflects ongoing innovation in this area."

The India story

In India too, changing demographics, increasing prevalence of chronic diseases, demand for better healthcare facilities, changing consumer behavior, emerging therapeutic areas and technological advancements have led to significant progress in the field of drug delivery for quite some time. The COVID-19 pandemic and the subsequent fears about a scarcity of essential life-saving drugs and devices and to curb the spread of this pandemic as well as for the treatment of other ailments is likely to spur growth over the coming years as well.

Market reports predict substantial growth in India's drug delivery devices market. For instance, a report by *ResearchAndMarkets.com* enlightens that the Indian Drug Delivery Devices Market was valued at around $564 million in FY2020 and is expected to grow at a steady CAGR of 8.05 per cent by FY2026 driven by "growing use of drug delivery systems in healthcare facilities". It further informs, "Growing awareness regarding drug metabolism is expected to propel the market growth through FY2026. In addition to this,

increasing pervasiveness of chronic infections among the population is further anticipated to bolster the growth of the Indian drug delivery devices market in a positive way."

FICCI and KPMG India recently released a report titled, *'Impact of the pharma industry on the Indian economy in the post-COVID era'*. A foreword by Vijay Chawla, Partner and Head - Risk advisory Head - Life Sciences KPMG in India, states, "The coming decade is extremely critical for the Indian pharma sector. India has shown incredible resilience in meeting not only the domestic demand but also catering to the global pharma needs, ensuring accessibility of critical medications. However, with its disruptions, the pandemic has also shed light on the emerging opportunities that lie ahead for the sector. The paper talks about the creation of an integrated ecosystem that focuses on accelerating research & innovation, strengthening manufacturing and supply chains and improving access to medicines. R&D and technology have been key catalysts driving industry-academia collaborations, which are expected to foster innovation and benefit the sector through transformation across the value chain."

It points out, "New chemical entities (NCEs) and New biological entities (NBEs) offer an opportunity for the Indian pharma sector to build expertise in drug discovery. These products have been receiving a significant attention from the leading multinational pharma players. For the Indian pharma industry to be future secured and sustainable, it must leverage its expertise in chemistry and biologics and put concerted efforts into new drug discovery."

All these will also open up avenues for growth and innovation in drug delivery. Likewise, evolving regulations, developments in active ingredients, etc are also instrumental for advancements in drug delivery.

Therefore, Express Pharma's *FDD Conclave 2022*, coming this June, will deep dive into advancements in existing drug delivery systems and examine their potential to keep pace with innovations in formulations and new therapeutic areas. They will also explore how novel drug delivery systems can enable sustained drug delivery, facilitate drug protection, encourage drug adherence and improve patient-centricity.

In the lead up to the event, a few stakeholders and experts from the industry share their insights on the trends in drug delivery and the approaches that are gaining popularity and prominence in this field, especially after the onset of the COVID-19 pandemic.

Read on to know more...

Nano-based drug delivery systems will gain more traction

Amongst all the disruption, confinement and loss caused by COVID-19, there have been some unexpected positive effects on human life. One big positive has been the rapid strides that pharma and biotechnology companies worldwide made in the rapid development of vaccines and advanced device-based drug delivery systems.

Patients and caregivers are now more eagerly looking for advanced devices such as self-administered devices, smart wearables, and connected devices.

For examples

(a) Nanomaterial chemistry has enabled the development of smart stimuli-responsive drug delivery systems that can ensure spatial or temporal, on-demand drug delivery to a targeted site

(b) Connected drug delivery devices provide new capabilities that are never seen on the market like remote control of the drug delivery including programmable delays at the start, managing complex dose rates and dosing regimens from more than one drug container, or even more than one delivery device and connection with diagnostics.

DR SAJEEV CHANDRAN

Director - Advanced Drug Delivery Research & IVIVC/ Biopharmaceutics , Pharma R&D, Lupin

> The nano-based drug delivery systems can increase the cellular uptake of drugs because of the surface charge and they can increase the stability and water solubility of drugs

The nano-based drug delivery systems will gain more traction in the drug delivery devices market due to their ability to offer multiple benefits in treating chronic human diseases by site-specific and target-oriented delivery of precise medicines. These systems can increase the cellular uptake of drugs because of the surface charge and they can increase the stability and water solubility of drugs.

There are several path-breaking applications of nanomedicine (chemotherapeutic agents, biological agents, and immunotherapeutic agents) in the treatment of various diseases on the horizon.

Leveraging our expertise and resources to tackle the worst public health crisis was the biggest learning and victory

Agile ways of working has been one of the biggest lessons learnt from the pandemic. This was amply demonstrated with the fast track development and approval of safe and effective COVID-19 vaccines. Leveraging our expertise and resources to tackle the worst public health crisis was the biggest learning and victory.

We also witnessed a rush to repurpose existing drugs for the treatment of COVID-19. These learnings need to be taken forward to identify novel clinical use to explore treatment options for newer indications. There is a solid knowledge base and safety data of existing molecules and this can help to considerably reduce the drug development process, cost and the time.

DR SANDHYA SHENOY

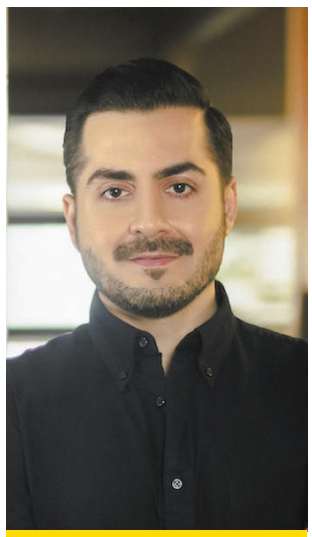
Associate VP, FDC

COVID-19 has led to significant geo-economic and geopolitical shifts. There is a major thrust on self-sufficiency in all the major economies of the world. There needs to be renewed focus on developing capabilities in the API manufacture, complex generics, biosimilars, gene and cell therapies. This will reduce our dependence on other countries and help us address larger global markets.

The pandemic has compelled organisations to think more creatively to overcome bottlenecks. The extraordinary circumstances has undoubtedly hastened the digital disruption and forced to think outside the box. Many organisations have partnered with AI startups to look for drug candidates for a range of diseases. AI is also put to use to build more robust processes to avoid human errors and increase manufacturing output.

Our time is now. The industry needs to invest for the future, without losing focuson quality, speed to market, easy access and affordable healthcare for all.

Sublingual route of administration ensures that supplements are easily dissolved without swallowing or chewing



AVNISH CHHABRIA

Founder, Wellbeing Nutrition

If there's one thing that we have all realised the importance of, courtesy of the pandemic, it is health.

At Wellbeing Nutrition, we use new-age technology and the purest all-natural ingredients to ensure that we only deliver the best to our customers. Our recent tech innovations, including Sublingual Delivery and Delayed-Release Capsules, are our efforts to improve health across the populace.

Sublingual delivery: Sublingual refers to the pharmacological route of supplements/drug administration by which substances get easily dissolved into the bloodstream instead of being broken down during digestion. Our melts range of oral thin strips embodies the sublingual route of administration, which ensures that the supplements are easily dissolved without swallowing or chewing. This ensures quicker absorption and more bioavailability as compared to the traditional formats that are

Continued on Page 22

COVID has accelerated research in inhaled drug delivery

It is time to have a look at the fallout of COVID-19 on drug therapy. The incredible power of vaccines and monoclonal antibodies are among the most striking features. The vaccines protect not just against COVID-19 but shingles, hepatitis, and many other preventable diseases. Vaccines don't save lives, vaccinations do. The mega vaccination drive against covid worldwide has vindicated this.

Among different platforms employed for vaccine development, mRNA technology offers the greatest promise. The technology, though not new, burst onto the global scene to take on COVID-19, and this in turn, encouraged researchers to harness technology to tackle the three deadliest infectious diseases - tuberculosis, malaria and HIV.

DR J B DAVE

Adjunct Professor- LMCP,
President- IPA Gujarat State Branch

WHO holds that technology can also be used for non-communicable diseases like diabetes and cancer.

The advantages include ease of development, adaptability to variants, scalability, stability, etc, particularly with advancements in the synthetic production of mRNA. Diversifying mRNA vaccine manufacturing capacity in different countries should be a global health priority.

COVID has accelerated research in inhaled drug delivery where lung biology interfaces with an inhaler that allows optimum delivery of drugs for specific disease management.

The potential utilisation of nanocarriers for biomimicry and/or targeted delivery of bioactives to cells is being explored to improve therapeutic outcomes.

Scientists at MIT recently have developed a capsule that can deliver 150 mcg of RNA more than mRNA used in the COVID vaccine in the stomach of pigs raising hopes of delivering RNA and DNA therapeutics orally and enhancing patient acceptance.

Lipid-based delivery should be harnessed to treat NCDs

The COVID-19 pandemic disrupted lives bringing the world to a standstill. However, it also made healthcare a priority for everyone. For the pharma companies, it led to a worldwide consensus that drug delivery strategies needed to be changed significantly. Manufacturers and policymakers realised that innovations in drug delivery technologies have to be effective, affordable, accessible and available on a global scale. One of the lessons from the pandemic was how ingredients like lipids played a crucial role in vaccine delivery systems and therefore the need to focus on such technologies to ensure a robust vaccine supply chain.

TANVI GAVANKAR

Manager Scientific, VAV Life Sciences

Lipid-based delivery is one of the powerful, sustainable tools and should be harnessed to treat different non-communicable diseases. Drug delivery strategies and technologies developed during the pandemic can be applied to new therapeutic modalities that can be adapted to improve the delivery of older therapeutics. Industry and government should use the lessons f rom the pandemic to work together to advance healthcare.

Last but the most important lesson we learnt is to respect, care, help, support, protect, value and appreciate life.

Sublingual route...

Continued from Page 21

consumed orally, which go first to the liver for metabolism and then to the bloodstream.

Delayed-release capsules: Slow, a range of time-conscious supplements that help keep up with our fast-paced life and help us sustain it for longer. These capsules contain plant-based ingredient beadlets to give the body sustained nutrition over a longer period. They embody the delayed-release technology that is designed to dissolve slowly over eight hours, protecting the nutrients from the stomach acid and ensuring their proper and most effective absorption. The two-in-one capsule i.e. the capsule in capsule formula ensures a powerful dose of all nutrients, minerals and compounds with the effective absorption benefits of fast-acting oils and slow-release beadlets.

OPINION

Data Protection in lifesciences and healthcare

Atulya Sharma, Partner, and **Sanal Anand**, Senior Associate, Lumiere Law Partners, explain why lifesciences organisations must develop and maintain proactive and thoughtful data protection regimes that not only address the existing data privacy regulations, but also consider future state, national and international legislation on the horizon

The fast-moving digital era has not only challenged the current privacy laws and regulations, but has also impacted public trust vis-à-vis data usage and data protection. Reports of misuse, misinterpretation and breach of data can also threaten an organisation's image of competence and trustworthiness. With the rapid phase of modernisation, developing countries, including India, are on the cusp of digital revolution. Interacting with personal information in the age of regulated data privacy is a gamut of risk, and most organisations

are not just carefully weighing the risk, but are also willing to shoulder against the business value they seek.

While digital health technologies have the potential to advance the medical field, devices that monitor, measure, and analyse various aspects of health and provide ready access to this information are raising questions on data privacy. Properly addressing these concerns might require lifesciences organisations and the healthcare industry to understand the regulations surrounding these tools, their accountability under these regulations and how to address their legal requirements. However, it is important to balance societal benefits of efficient and effective health solutions with an individual's right to privacy, guaranteed as a fundamental right to the citizens under Article 21 of the Indian Constitution.

As part of its attempt to build a secure Digital India, the Indian government recognises the issue of cyber security and the need for robust laws to protect digital data. In India, the provisions in the Information Technology Act, 2000, governs e-health protection, along with the Information Technology (Reasonable Security Practices and Procedures and Sensitive Personal Data or Information) Rules, 2011 ("IT Rules"), which offers some degree of protection to the collection, disclosure and transfer of sensitive personal data, which covers within its ambit medical records and history. Furthermore, important steps in this direction include proposed detailed and comprehensive Digital Information Security in Healthcare Act ("DISHA"), which seeks to provide for electronic health data privacy; confidentiality, security and standardisation; and establishment of National Digital Health Authority and Health Information Exchanges as well as general laws on data privacy like Personal Data Protection Bill, 2019 ("PDP Bill").

According to Section 3 (e) of the proposed DISHA, 'Digital Health Data' means an electronic record of health-related information about an individual, and includes a wide palette of sensitive and personal health-related information of an individual. As the amount of sensitive data pertaining to the healthcare industry grows, so do the privacy and security concerns. These concerns go beyond mere compliance, as threats to the confidentiality, and integrity not only impact privacy rights, but may also impact patients' health, if compromised.

Atulya Sharma

Sanal Anand

The rapid advancement of healthcare strategies may not be possible without the development of new and innovative technologies to support it. Newly-developed medical mobile applications provide clinicians with the ability to remotely collect and access patient data at any time, including physical activity levels, glucose levels, heart rate and medical images. However, this enhanced flow of data to clinicians can come at a cost, still not all products meet privacy standards, giving rise to liability for privacy breaches, insecure data storage and failure to obtain patient consent. Moreover, the use of Artificial Intelligence (AI) also presents a host of new legal and ethical concerns.

Industry regulations, pharmacovigilance efforts and government reporting requirements all complicate the speedy disposal of data, making accountability for this data's protection and governance a long-term relationship. Section 28 of the proposed DISHA lays down provision for 'Rights of the Data Owner' and extends the availability of the data subjective of the individual's consent. Moreover, Chapter V of the proposed act lays down serious penalties for breach or offences committed with respect to the data protection and personal liberty of an individual.

Under the Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations 2002, physicians are obliged to protect the confidentiality of patients during all stages of procedures, including information relating to their personal lives unless there is a serious identifiable risk to a specific person or community of a notifiable disease that the law mandates otherwise. Moreover, the IT Rules require entities holding users' sensitive personal information to maintain certain specified security standards. The proposed legislations and various other steps being taken by the Indian government will change the shape of data protection (personal or health data) in India making it more in tune with global standards.

According to the Section 7 of the PDP Bill, every data fiduciary shall give to the data principal a notice at the time of collection of the personal data containing information such as purpose, nature and details of data fiduciary. It is an obligation of data fiduciary to provide the right of the data principal to withdraw his consent, and the procedure for such withdrawal, if the personal data is processed on the basis of consent. Moreover, Section 11 clearly stipulates that the personal data shall not be processed, except on the consent given by the data principal at the commencement of its processing, which is capable of being withdrawn by data principal. The consent, even though given earlier by a patient, can still be withdrawn at any time, creating necessary infrastructure to enable the return of patient data and prevent it from being used further.

'Anonymisation,' as per the PDP Bill in relation to personal data, is defined as 'such irreversible process of transforming or converting personal data to a form in which a data principal cannot be identified, which meets the standard of irreversibility specified by the Authority.' However, using a patient's health data is relevant in secondary purposes only, i.e., purposes not related to providing patient care. Therefore, anonymised data can help achieve research, public health, certification or accreditation, and marketing, without having to compromise with one's privacy. However, ethics committee (under the Drugs and Cosmetics Rules) approval is nonetheless obtained even for such anonymised patient data.

Thus, Indian law is constantly evolving and increasingly catching up with the stringency of international legislations like the EU General Data Protection Regulation 2016/679. Modern technology for collecting, transferring, and processing data poses both, an opportunity and a threat to organisations in the lifesciences industry. When creating business strategies, leaders from lifesciences companies should not just consider opportunity derived from the data they use, but also the risks and requirements that can prevail to inherent to those strategies. Lifesciences organisations must develop and maintain proactive and thoughtful data protection regimes that not only address the existing data privacy regulations, but also consider future state, national and international legislation on the horizon.

INTERVIEW

"Act as if every day is an audit"

Dr Rupali Paranjape, Implementer, Auditor, Trainer and Consultant for Regulatory Compliance for pharma companies, and author of the book "Blue Ocean of Compliance," speaks to ***Express Pharma*** about her book and her journey in the pharma industry. She also explains why her book is a 'must read' for anyone who is a part of the industry

Dr Paranjape, as a veteran in the pharma sector, what are the main challenges faced by pharma companies in India which prevent them from achieving compliance with global norms?

It is not a matter of Indian or global compliance. Quality and compliance are ethics, duty and social responsibilities. Non-compliances are harmful to the health of any patient or consumer of the drug whether he/she is Indian or global.

The challenges faced by pharma companies are of different types. For start-ups, it

might be different, like financial, availability of the funds, getting talented, knowledgeable people with the right mindset in the range of the salary they want to provide, retention of talent, making their facilities cGMP compliant within their budget constraints, availability of the resources, getting business, generating revenue to sustain all the expenses required to comply the cGMP, 21 CFR guidance and many others.

For established firms, they may be different. In established firms or companies, there is knowledge, talented people, facilities and resources, but the challenge is to maintain the standard of zero 483s or compliance with the guidance 21CFR or other regulatory standards. Maintaining consistency in compliance is a challenge. Maintaining the standard obtained during the inspection is a challenge.

When a product is launched in the market, handling market complaints and product recall are the challenges. The complaints may be related to quality, adverse events, retailer complaints and many more.

Identifying the accurate root cause to minimise challenges, performing risk assessment for critical cases, or, as per guidance, is necessary.

I have discussed the reasons for non-compliance in the third chapter of my book "Blue Ocean of Compliance." These are the reasons applicable all around the globe.

In chapter four, I have discussed the actions to be taken for non-compliances discussed in chapter three. I would recommend reading the book multiple times to stop non-compliances on one's site.

> This book is written by an analyst, a regulatory person, who prepared and submitted the DMF, dossiers, MAA; a compliance person, who has seen closely the manufacturing sites, and has worked with blue-collar employees

What inspired you to write "Blue Ocean of Compliance", and how does it try to address these challenges?

When I look back at the audits I have experienced, I think to myself: instead of operating out of fear or a scared mindset, why don't we operate with a winning attitude and confidence? I think we should change our thinking patterns and work to win, instead of "not to lose." We have to win; we have to work for the outcome of the audit with "no observation." We have to prepare for the audit every day, we must act as if there will be an audit every day instead of preparing when the time comes.

While these thoughts of pain and gain were going on, the idea of this concept came into my mind, to help pharma industries develop a winning strategy to face the audit.

The concept behind writing this book is to give a new angle to look at the regulatory inspections, and to help solve the problem of non-compliances on the site.

How is it different from previous books on this subject?

This book is written by an analyst, a regulatory person who has prepared and submitted DMF, dossiers and MAA; a compliance person, who has closely seen the manufacturing sites, and worked with blue-collar employees.

In other words, a doer who has worked on the shop floor and experienced the pain/challenges of people working on the shop floor. She has also worked with the management and now wants to help the global pharma community to overcome the challenges of non-compliances, and share her learnings with the pharma world so that they become successful and grow in their business and job with less effort and cost.

I never referred to any book available in the market on this subject to write this book. This comes from my heart, and I am going to share it with the global pharma community to make them successful.

Who is the target audience for the book?

If you are working in the pharma industry in the cGMP environment, if you are working in quality assurance, or quality control or, production department, if you are part of the team that is responsible for audits, then this book is for you.

If you face customer audits, then this book is for you.

If you worry about audits and are looking for a better and more efficient approach, then this book is for you. If you are in R&D, then this book is also for you to expand the dimension of your thought process to support the cGMP department.

If you are a fresher who doesn't know anything about audits, why audits happen, and how to prepare for audits, this book is for you.

If you are a CEO, President, Vice President, General Manager, Manager of any pharma company, and want to ensure that your organisation passes regulatory audits with no observation, this book is for you.

If you are a CEO or founder of a pharma company, and you want a brand that everyone trusts, this book is for you.

If you are any of these, and you want to know what are the practices that one should and shouldn't follow, then this book is for you.

In this book, I have covered many of the wrong practices which led international pharma companies on the path of getting enforcement actions,

warning letters and 483s.

This book has been written to help all the people working in the pharma industry, those who are a part of regulatory inspections, business owners of pharma organisations, founders and CEOs, as well as people working in the cGMP areas.

Regulatory inspections, disrupted due to the pandemic, have re-started recently. How do pharma companies gear up to avoid disruptions like warning letters, closures, etc?

If you look at warning letters, you will find there are several reasons why the investigator has issued a warning letter to the firm/s. They include issues like breach in integrity, falsification of data, alteration of data, misleading or false information, misrepresentation of facts, untruthful sentences, deceit, forgery, submission of false or inaccurate information to gain benefits or with intention to deceive, data manipulation, questionable information, misreporting or selective reporting, poor manufacturing practices, false product claims, or incorrect directions for use.

Once you read it, you may conclude that the warning letter has nothing to do with the pandemic. The agency's policy is that warning letters are issued for violations that have regulatory significance. If adequate corrective actions aren't taken promptly, enforcement actions are taken by the regulator.

To avoid any enforcement action, one has to follow cGxP and strictly say no to non-compliances and loss of data integrity.

Chapter two of the book is "Types of Regulatory Enforcement Actions and Regulatory Actions on Non-Compliances and Devastating effects for the Pharmaceutical Industry due to Non-compliance."

I have discussed most of the types of enforcement actions taken by the US FDA regulatory authorities, why these are taken and many other facts and insights. A few of them are warning letters, injunction, prosecution, seizure, recall and field correction, alerting the public, effectiveness checks, recall

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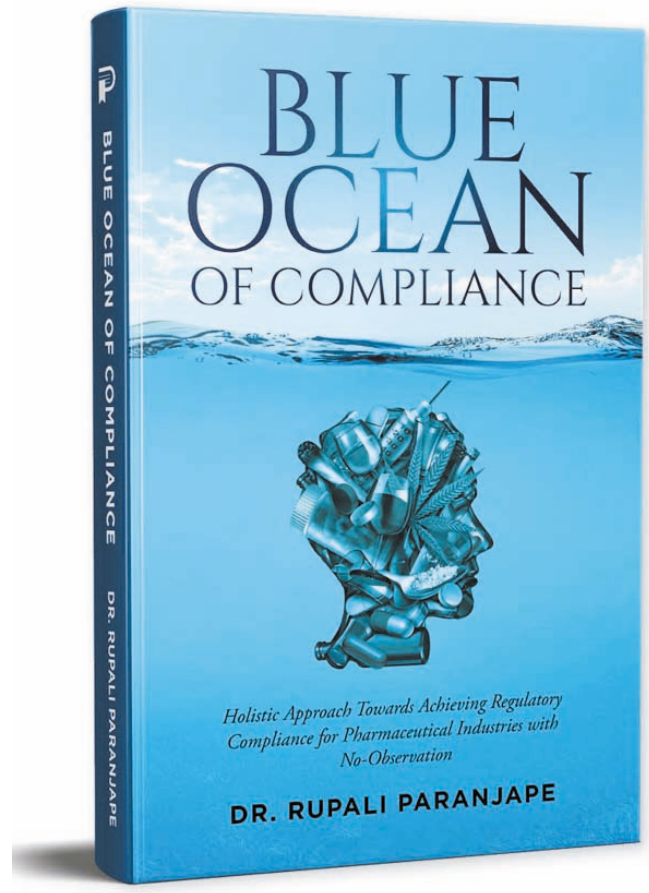

OPINION

Drug regulation in India: A roller coaster

Dr Shoibal Mukherjee, MD, DM Sr Consultant, Clinical Pharmacology and Drug Development, explains why the goal of making India a well-regulated drug market remains distant

In the early decades after independence, the Indian pharma sector was dominated by transnational corporates. However, the situation changed with the India Patents Act of 1970 which did away with product patents. New medicines discovered by transnational corporations became immediately available to the domestic industry to reverse-engineer and market for profits. The situation changed once more in 1995 when India signed the TRIPS agreement overturning the 1970 Patents Act and agreeing to provide patent protection to innovative pharma products. Having grown in size and muscle at home under the earlier patent regime, the domestic industry was now forced to swim into the ocean of international generics markets and did so with remarkable success.

An era of globalisation was underway for the research services sector too. Following the 1990's harmonisation of pharma development guidelines across much of the developed world, research conducted anywhere in the world could be included for regulatory submissions to support marketing authorisation in these markets. Transnational companies began to include India in their clinical research plans, leading to the growth of a vibrant clinical trials sector in the country. Some companies also initiated drug discovery and pre-clinical research in India by setting up research centres of their own, or by outsourcing to Indian research companies.

In this scenario, it was only the regulatory sector that seemed to lag. A parliamentary standing committee in 2012 flagged up woeful understaffing of the pharma regulatory services and inadequate regulatory

mechanisms that did not meet the requirements of the rapidly growing sector. A writ petition filed by activists against the central government led the Supreme Court to comment on the inadequacy of rules concerning clinical trials. The public interest litigation, which is still pending, resulted in the framing of new rules for clinical trials and approval of new medicines that came into effect on 19th March, 2019.

The "New Drugs and Clinical Trials Rules 2019," generally referred to as NDCT 2019, are an enormous improvement on the previous regulations. Some path-breaking initiatives have been introduced, such as a provision for patients to continue to receive the investigational product after the end of a trial, and the institutionalisation of the mechanism for payment of compensation to patients for trial-related injuries. Other welcome provisions include accelerated approval for various categories of drugs, a waiver from a repetition of clinical trials already completed elsewhere in the world, provision for pre-and post-submission meetings to facilitate the application and review process, and an emphasis on time-bound review of applications - an often-overlooked virtue. The issuance of the NDCT 2019 is undoubtedly a landmark in Indian drug regulation. The public, in general, and the pharma and research communities, in particular, owe a round of applause to the individuals and teams that drafted these rules.

All that said, problems persist. Despite its general comprehensiveness, NDCT 2019 remains incomplete without the implementation of enabling steps. Most of all, at this juncture in its development, what the Indian pharma sector needs is greater alignment with the rest of the world - particularly with the developed western countries that are the largest export markets for Indian companies, and the peer group of BRICS nations that are at a somewhat similar level of development and regulatory competency. These countries have achieved a higher degree of harmonisation by adapting their rules and regulations to guidelines developed by the International Conference on Harmonisation (ICH) which aims to find a way to reduce global drug development time and costs while enhancing patient safety and quicker access to new medicines. These guidelines have set scientifically valid standards, and a system of harmonised norms has evolved that eliminates duplication and allows mutual acceptance of data generated in each other's countries.

The interesting thing to note here is that the goal is mutual recognition of each other's data and not each other's evaluation of that data or the approval of a product per se. NDCT 2019 refers to the ICH guidelines in the context of "similar biologics" and recognises ICH guidelines for animal toxicology studies. Unfortunately, NDCT 2019 does not mention ICH guidelines in the context of clinical trials, as trials that do not follow those guidelines, or fail an audit for compliance to those guidelines, will not be accepted elsewhere in the world. This can only be to the detriment of pharma innovation in India, and the disadvantage of Indian science in general.

Further, trials completed in other countries following ICH guidelines should be recognised in India without the need to repeat them here, provided ethnic differences in drug effects can be ruled out. NDCT 2019 acknowledges this with reasoned provisions for the clinical trial waiver in Rules 75 and 80. However, it is a notification of a list of countries under Rule 101 that's holding things up. This rule requires the government to specify the list of countries for implementing Rules 75(7)(i) and 80(7)(i). We have seen three winters go by without this list being notified. The ICH E5 guideline that outlines ethnic factors to be evaluated for acceptance of foreign clinical data has been implemented by a host of other countries, including Brazil, China, Korea and Singapore, besides the ICH countries of the EU, the US and Japan. When those agencies are ready to accept clinical data from India within the parameters of ICH E5, including bioequivalence studies conducted here, Indian hesitation in providing the same degree of reciprocity is inexplicable.

There are other quirks in NDCT 2019 that would merit re-evaluation. These include the need for dual registration of hospital ethics committees, exclusion of non-government hospitals and their patients from access to unapproved new drugs for life-threatening ailments and unmet needs, and a stunted vision of the role of pre-submission meetings in the drug development process. While the roller coaster of Indian drug regulation appears to have come full circle with NDCT 2019, the goal of making India a "well-regulated" market remains distant, an inexplicable hesitancy in embracing global standards coming in the way of the country joining that league.

"Act as if every...

Continued from Page 27

classification, drug product debarments and notations, among many others.

What are the common risk-mitigation steps to avoid/prevent repeat non-compliances?

If non-compliances are repetitive, this means they are not properly investigated, and the actual root cause of deviations or Out of Specifications (OOS) was not identified. Hence, Corrective and Preventive Action (CAPA) is not effective. The result is that even after taking CAPA, non-compliances are repeated.

To prevent any non-compliances, deviations or OOS, they must be properly investigated so that the CAPA is effective and prevents the occurrence of the same problem. Quality Target Product Profile (QTPP), Critical Quality Attributes (CQA), Critical Material Attributes (CMAs) and Critical Process Parameters (CPPs) need to be studied in depth. OOS should be investigated properly. It's like, any disease will be cured only when we get the medicine that cures the root cause, and not just the symptoms.

Compliance must be 24x7x365, and not only for the sake of audit. Compliance is required for every human being, and not just for any particular country. For example, people often respond during audits that since their product is not for the US market/XYZ market, they are not complying with the guidance. However, patients across the globe have the right to be healthy and free of any health risks.

In my book, many such elements are presented, which you will not find in risk assessment and cGMP guidelines.

If non-compliances are repetitive, this means they are not properly investigated, and the actual root cause of deviations or Out of Specifications (OOS) was not identified. Hence, Corrective and Preventive Action (CAPA) is not effective. The result is that even after taking CAPA, non-compliances are repeated

What would be your three top tips as pharma companies prepare and invest to create a compliance culture in a post-COVID world?

1. Act as if every day is an audit.
2. Work to win, and not for survival. You should target no-observation or zero 483, and not just cross your fingers to pass the inspection.
3. Read my book, Blue Ocean of Compliance.

REPORT

Ministry of AYUSH and WHO establish world's first Global Centre for Traditional Medicine in Gujarat

The primary objective of the centre is to harness the potential of traditional medicine from across the world through modern science and technology, and improve the overall health of the communities world over

Kalyani Sharma

The foundation stone of the world's first WHO Global Centre for Traditional Medicine (GCTM) was laid in Jamnagar, Gujarat, by Prime Minister Narendra Modi on 19th April, 2022 in the presence of Dr Tedros Ghebreyesus, Director-General, World Health Organization (WHO) and Pravind Kumar Jugnauth, Prime Minister, Mauritius. The ceremony was attended by Dr Mansukh Mandaviya, Minister of Health and Family Welfare and Chemicals and Fertilizers; Sarbananda Sonowal, Union Minister of Ayurveda, Naturopathy, Unani, Siddha and Homeopathy (AYUSH); Bhupendra Patel, Chief Minister, Gujarat; Dr Munjpara Mahendrabhai Kalubhai, Minister of State, Ministry of AYUSH, and other senior officials of the Ministry of AYUSH and the government of Gujarat.

The primary objective of the WHO GCTM is to harness the potential of traditional medicine from across the world through modern science and technology and improve the overall health of the communities world over. The centre will highlight the potential of traditional medicine and utilise technological advancements to promote its safe and effective use.

The WHO GCTM in India at Jamnagar, Gujarat, will have its interim office at the Institute of Training and Research in Ayurveda (ITRA) in Gujarat. This centre will be supported by an investment of about $250 million from the government of India.

Speaking during the ceremony, PM Modi said, "The WHO Global Centre for Traditional Medicine is recognition of India's contribution and potential in this field. India's traditional medicine system is not limited only to treatment. It is a holistic science of life. India takes this partnership as a huge responsibility for serving the entire humanity."

Adding to it, Dr Ghebreyesus said, "Traditional medicine products are abound globally and the centre will go a long way in bringing the promise of the traditional medicine to fruition. The new centre will focus on data, innovation and sustainability, and will optimise the use of traditional medicine."

He noted that WHO GCTM is a truly global project. "Through this centre, India will be able to take its knowledge of traditional medicine to the world and similarly world will come to India," he added.

Jugnauth also said, "Mauritius and India share the same traditional medicine values. In Mauritius, the practice of AYUSH's medicinal systems is popular and fully recognised. We have recognised that traditional medicine complements scientific medicine and represents healthy living and promotion of good health. With the Global AYUSH Investment & Innovation Summit, I wish for the interactive themes on yoga, ayurveda and traditional medicine to broaden the scope of AYUSH medicine in the region at large."

Sonowal emphasised on the history of traditional medicine in his address.

"India has been proven pioneers in the field of traditional medicine since time immemorial. The knowledge sharing and cooperation has been documented in history and in continuation of the same, focussed efforts have been relentlessly undertaken by the ministry of AYUSH. The establishing of the global centre is an effort to bring synergy, and cooperation

in this domain would benefit all the member states," he said.

Apart from it, the first Global AYUSH Investment & Innovation Summit 2022 (GAIIS) was also inaugurated in Gujarat, Gandhinagar by PM Modi, which was held from 20th to 22nd April, 2022. The summit was organised in line with the Sustainable Development Goal Number 3 of promoting "Good Health and Well-being."

The summit saw participation from industry leaders, academicians and scholars, who highlighted the ways to promote traditional medicines and systems. In addition, as part of the summit, an AYUSH Startup Challenge was also organised, along with an exhibition, wherein startups, incubators and entrepreneurs working in this field displayed their work. The AYUSH sector witnessed Letter of Intents (LoIs) of over Rs 9,000 crores in three days. The investments come across major categories like FMCG, Medical Value Travel (MVT) and services, pharmaceuticals, technology and diagnostics, and farmers and agriculture. During the summit, more than 70 Memoranda of Understanding (MoUs) were signed between countries, research institutes, the farmers groups and industry.

The three days were wrapped up with a total of five plenary sessions, eight round-tables, six workshops and two symposiums, all packed into a short time span of three days. The summit witnessed the presence of 90 eminent speakers and 100 exhibitors.

MAJOR INITIATIVES ANNOUNCED BY PM MODI IN THE AYUSH SECTOR ARE AS FOLLOWS

- AYUSH mark for AYUSH products: This aims to give people all over the world the confidence of quality AYUSH products.
- Government will develop a network of AYUSH parks to encourage the promotion, research and manufacturing of AYUSH products across the country.
- A new category named AYUSH Aahar was announced which will facilitate the producers of herbal nutritional supplements.
- A major initiative for foreign nationals who want to come to India to take advantage of AYUSH therapy was announced. India will soon introduce a special AYUSH visa category.
- Launch of AYUSH Export Promotion Council and four AYUSH ICT initiatives which include AYUSH Information Hub, AyuSoft, AYUSH Next and AYUSH GIS.

Way forward

Traditional medicine is a key pillar of healthcare delivery systems and plays a crucial role in maintaining good health and well-being not only in India, but across the world. In recent year, traditional medicine therapies have also seen a major transformation as the usage of Artificial Intelligence (AI) and various technological innovations have made it more accessible to masses.

Hopefully, the collaboration between the government of India and WHO will help in developing an enabling framework to attract investments, providing strategic support to policies, and will give boost to the AYUSH sector globally.

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INTERVIEW

Avantor provides innovative biopharma products and services that help streamline processes

Amit Sehgal, Managing Director, Avantor India, shares with ***Express Pharma*** the initiatives taken to fight the COVID-19 pandemic, new opportunities and future plans

Could you elaborate on the initiatives undertaken by Avantor to support India in its effort to overcome the challenge of COVID-19?
Avantor provides products and services to the lifesciences and advanced technologies and applied materials industries, with solutions supporting research and process development to commercial scale-up and production. Our mission of setting science in motion to create a better world has never been more important, and we are proud to manufacture and deliver solutions that are essential to address industry challenges during the COVID-19 pandemic.

In vaccine manufacturing, specifically, our understanding of how various chemistries perform in cell culture systems, combined with our portfolio of production chemicals, single-use systems, process chromatography media and final-fill products, helps sustain the integrity and activity of COVID-19 vaccines from upstream production or cell-free synthesis to downstream purification process steps, through final fill.

Our technical and commercial teams collaborated with customers on solutions for therapies being produced. Additionally, the support from our operations and supply chain teams has been equally as important to expand capacity and meet the needs of our customers in India.

It is worthwhile to mention that one of our biggest vaccine customers has highlighted our team as partners because of the on-time development and delivery of materials needed for their COVID- 19 vaccine development, despite lockdowns and other challenges during the pandemic.

> We are proud to play a critical role in key breakthroughs and life-changing therapies for patients. Our deep knowledge in bioprocessing ranges from driving breakthroughs in research and development, to enabling efficiencies in the end scale-up and commercial production of new therapies

In addition to our focus on delivering high-quality products and services to our customers, Avantor was, and remains focussed on associate safety and well-being as a top priority. We introduced several initiatives and programmes for our associates and their families in the country during the pandemic. We maintained focus on helping keep our associates safe and leveraging guidance from creditable health agencies to establish safety protocols. We also launched an Employee Well-being & Assistance Program (EWAP) that continues to offer support and address any personal or work-related challenges that may affect the associate's well-being and work performance. We conducted a vaccination drive for our associates and their immediate families at Avantor locations.

As part of our commitment to foster community engagement in support of our communities, Avantor donated 30,000 N95 masks, 600 infrared thermometers and 600 pulse oximeters, valued at approximately $30,000 to the Indian Red Cross Society state branches in Maharashtra and Uttarakhand to support COVID-19 relief work. This was in addition to a $30,000 donation from the Avantor Foundation, the philanthropic arm of Avantor, to Project HOPE to aid COVID-19 relief work in India. The Avantor Foundation donation to Project HOPE will focus on three programme areas, including distribution of medical equipment and supplies, COVID-19 training for frontline healthcare workers and vaccine, and public awareness campaigns in India.

Avantor also donated 300 infrared thermometers and 90,000 surgical and N95 masks to help protect students of over 250 government schools across Delhi/NCR, Mumbai and Jammu through the American India Foundation.

The coronavirus pandemic has made it clear that we need to reboot healthcare to beef up our defence against the current and emerging diseases. This is expected to increase investments in the lifesciences sector. What kind of new opportunities will it open up for Avantor?
We are proud to play a critical role in key breakthroughs and life-changing therapies for patients. Our deep knowledge in bioprocessing ranges from driving breakthroughs in research and development, to enabling efficiencies in the end scale-up and commercial production of new therapies.

Avantor provides innovative biopharma products and services that help streamline processes and we will continue to actively invest in biopharma production capacity, supporting our core business.

India is a diverse market for pharma manufacturing. Pharma companies in India are servicing almost 200 countries, and Avantor plays an important part in collaborating with these companies. In recent years, the Indian government has demonstrated strong initiative to promote the pharma sector, including a $1.3 billion fund to encourage companies to manufacture pharma ingredients domestically by 2023. The Indian pharma market is unique in many ways: branded generics represent more than 70 per cent of the retail market, and local players have enjoyed a

dominant position driven by formulation development capabilities and early investments. Today, India is one of the leading manufacturers of similar biologics, and there is a thriving domestic market with 93 total products approved through 2019; low cost of research and development has promoted the increased development of similar biologics in the country.

Avantor is well-positioned to continue to be part of this growth and continue to work closely with the biotechnology and pharma companies developing and manufacturing a wide variety of life-altering therapies that will improve patient health.

New product introductions are also a priority for Avantor. We will continue to introduce products in workflow solutions and invest in training team members. We remain committed to advancing the lifesciences industry and our customers in India.

How have you expanded your capabilities for the lifesciences sectors since the onset of the pandemic? What is the competitive edge you offer to your customers through your solutions?

The relevance and criticality of the lifesciences industry has been emphasised by the COVID-19 pandemic, and Avantor is well-positioned to support the life-changing work of our customers globally.

> We will continue to introduce products in workflow solutions and invest in training team members. We remain committed to advancing the lifesciences industry and our customers in India

Avantor focusses on the things that matter the most to our customers, providing exceptional convenience, collaboration and customisation to ensure the success of our customers all over the world. Our offerings range from personal protective equipment, such as masks and gloves, to cGMP production materials and single-use technologies.

The competitive edge we bring to our customers is as follows:

◆ Our local presence combined with our global infrastructure connects us to more than 225,000 customer locations in over 180 countries.

◆ We deploy a customer-centric innovation model that enables us to provide solutions for some of the most demanding applications, from breakthrough discovery to agile delivery of life-saving therapies and vaccines to patients around the world.

◆ The highest performance in health, safety, environmental compliance and quality, and providing excellence to our customers.

◆ Products made under the same quality system at every facility, leading to the same customer experience across the globe. Customers, ranging from small to very large labs, are all showing a preference for quality products and services at competitive prices.

◆ Work performed in the most cost-effective manner possible with a continuous drive toward higher productivity.

Additionally, we have advanced research and applications facilities in India, South Korea and China. Our research and applications specialists are collaborating with our customers to develop solutions that advance their business goals and drive innovation. Research and innovation, especially in the healthcare sector, are progressively adopting digital and Artificial Intelligence (AI) to accelerate innovation and convenience for business transactions with their suppliers or customers.

Where does India fit into the company's global strategy for the future? What are the revenue targets, growth targets for Avantor's lifesciences business in India over the next three to five years, and what are the strategies?

Avantor is well-positioned with the capabilities and expertise to be a key solutions provider for lifesciences customers globally. Our manufacturing, R&D and distribution footprint enables us to serve nearly 225,000 customer locations around the world, and our offering of more than six million products and services, a combination of our own proprietary products plus those of our suppliers, deeply embed us in our customer workflows.

India is an important market for us, and we continue to enable the life-saving work of biologics and vaccine manufacturers in the region. We also support small molecule manufacturing and testing, research and academics, and in-vitro diagnostics. We will continue to focus on India as one of our key markets, and to support the Indian government's initiative of "Make in India" by expanding our local manufacturing capacities, increasing our associate base, and bringing in unique solutions that meet the needs of our customers in the region.

Our manufacturing facilities in Panoli (Gujarat) and Dehradun (Uttarakhand) are providing world-class pharma excipients and diagnostics products to customers in India and abroad. We are rapidly expanding our capacity at these facilities to meet the existing and future market needs. In 2022, we will continue to build on our commercial, field service, application and technical support offerings to our customers.

Our recent acquisitions of RIM Bio and Masterflex strengthen Avantor's end-to-end fluid management solution when combined with the company's existing portfolio of high-purity chemicals and consumables. We have already begun the process to align our global systems, processes and capabilities to offer world-class solutions to customers working on all bioproduction platforms, including monoclonal antibodies (mAbs), cell and gene therapies and mRNA. We also support both therapy and vaccine manufacturing, including for COVID-19 in India locally.

KILITCH HEALTHCARE INDIA LTD.

Accrediations

9001:2015

14001:2015

WHO

Manufacturing Sections

Small Volume Ampoule

Small Volume Vial

Three Piece Ophthalmic Vial

Two Piece Preservative Free Ophthalmic Vial

Prefilled Syringes in Blister pack

Sterile medicated Swab Sticks

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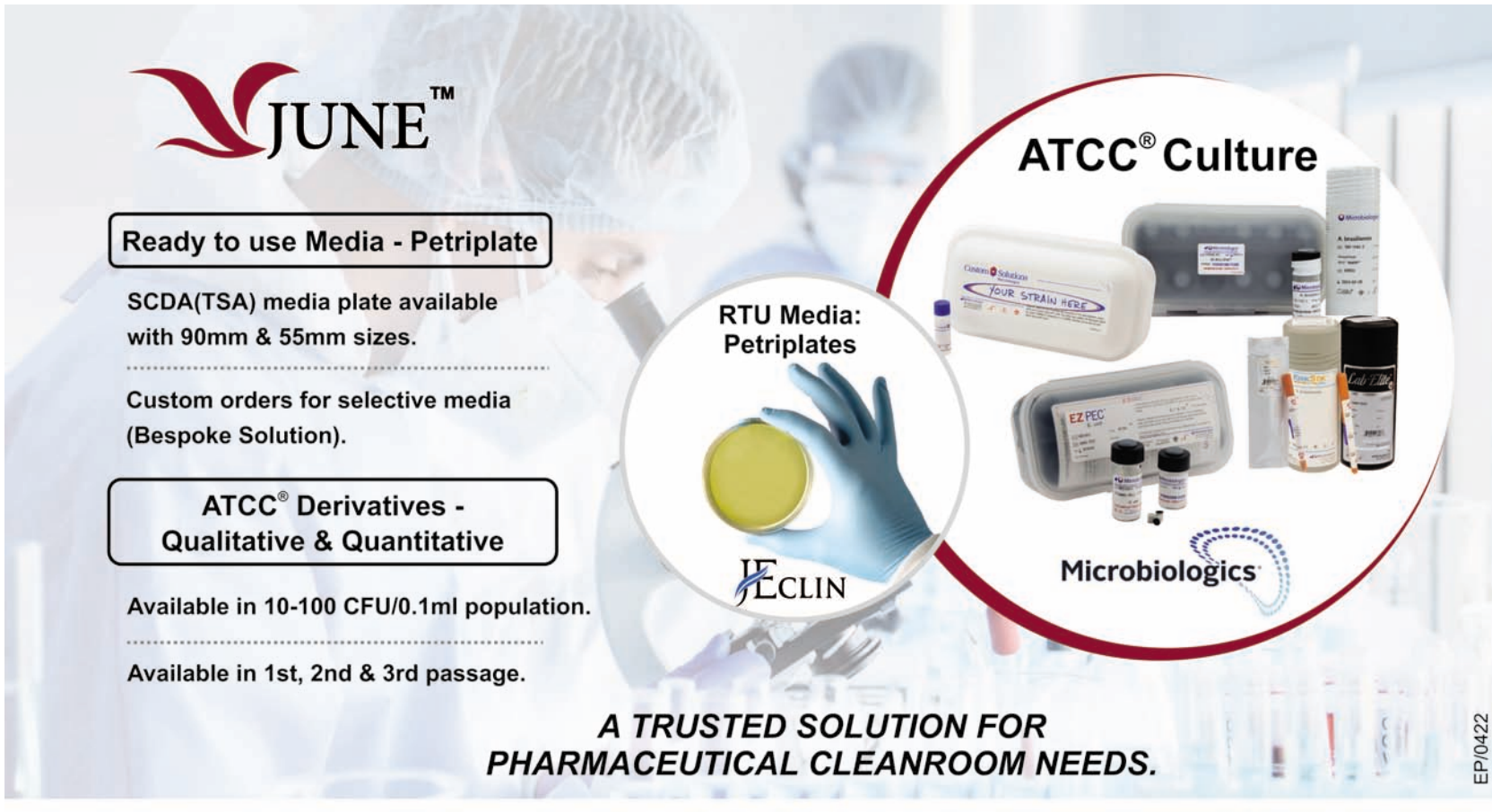

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Virosil Pharma: A revolutionary, eco-friendly fumigant

Virosil Pharma has proved to be effective in controlling aerial bacteria and fungus present in sterile rooms. The area becomes completely sterile within 60 minutes of spraying without causing any irritation to the eyes, nose and skin - unlike conventionally used formulations

ABSTRACT

In the past years, the pharma and healthcare industry has witnessed tremendous growth and there have been tie-ups with a number of multinationals for production and R&D facilities to be nurtured in India. Organisations are applying for ISO standards and upgrading themselves to the latest norms related to health and hygiene.

Microbial contamination and pollution play a significant role in the pharmaceutical industries. Control of microbes has always been the biggest challenge to these industries. A load of microbes are present in areas such as production, storage/packaging, R&D, Q.A/Q.C., filling etc. They are present everywhere in the air, surface, water, instruments, linens etc.

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

ABOUT US

Sanosil Biotech, a Mumbai-based company, has launched a range of multipurpose disinfectants which are eco-friendly, chlorine-free and completely biodegradable and have applications in the pharma and healthcare industry as well as in the food processing industry. It is manufactured in India in technical collaboration with SANOSIL AG of Switzerland. SANOSIL AG in Switzerland is the patent holder and has joint venture agreements in more than 15 countries such as France, Italy, Spain, Holland, Norway, South Africa, Australia, Saudi Arabia, Oman, the UAE, etc. The product is being used in various countries by reputed institutions and has been thoroughly tested under strict regulations imposed by European Health bodies.

PRODUCT DISCRIPTION

Virosil Pharma is a multicomponent fumigant and disinfectant. The oxidizing agent used is hydrogen peroxide, which is bonded with stabilizing agents to form a complex solution. A long-lasting effect is ensured by the addition of silver, which acts as a catalyst in trace amounts. The bactericidal effect of silver is based on the fact that the monovalent silver ion Ag+ binds very firmly to bacterial proteins by a covalent or co-ordinate bond, and thus inactivates or precipitates these.

◆ Its effectiveness against bacteria, viruses, amoebae, fungi and algae; i.e. its extremely wide range of application makes it easy to handle for the end user; i.e. only one product is needed, where so far 2, 3 or various products were necessary.

◆ Owing to the good stability of the product, a long storage time can be guaranteed. As the product remains stable at high water/air temperatures, and as its effectiveness is even increased at high temperatures.

◆ Due to its long-term effectiveness and pronounced characteristics to prevent recontamination, this product is perfectly suited for disinfection of drinking water and wells.

◆ Virosil Pharma is ecologically harmless. Its principal constituent - hydrogen peroxide - does not pollute waste water, because it breaks down into water and oxygen (H2O and O2), i.e. it produces no noxious by-products.

◆ The two basic substances (H2O2 and Ag) enhance their advantages (*synergism). The bactericidal effect comes into action quicker and more intensively than if either substance was used on its own.

USFDA DRAFT GUIDELINES

Clean Area Classification	Microbial limit Cfu / 10 cu.ft.	Microbial limit Cfu / 10 cu.m.
100	< 1a	< 3a
1000	< 2	< 7
10,000	< 5	< 18
100,000	<25	<88

a = samples from class 100 environments should normally yield no microbiological contaminants

WHO 2002 MICROBIAL LIMITS

Grade	Max. no. of microorganisms permitted / m3
A	Less than 1
B	5
C	100
D	500

EU GMP 2002

Grade	Air sample cfu / cu.m.	Settle plates (90mm) cfu / 4 hours	Contact plate 55mm cfu / plate	Glove print Cfu/glove
A	<1	<1	<1	<1
B	10	5	5	5
C	100	50	25	-
D	200	100	50	-

ADVANTAGES

Eco- friendly - It is totally biodegradable since (H2O2) breaks down into water & oxygen
Chlorine free
Non-toxic (no irritation to skin or eyes
No effect on pH
Non carcinogenic and non mutagenic
Excellently rinseable with no remains

PROPERTIES

Can easily be dosed
Does not foam
Decomposes into water and oxygen
It is excellently rinseable with no remains
Treats any other material with consideration

Fumigation with Virosil Pharma, the perfect Salternative to Formalin

Fumigation is one of the most

important factors associated with pharma industries, it plays a vital role in maintaining the sterility of areas and is directly related to production.

Sanosil Biotech is the first company to pioneer the novel concept of eco-friendly fumigation. The company has great respect for human health and the environment. The CEO, Dev Gupta, an MBA from the Bentley Graduate School of Business, Boston, has been actively marketing the brand nationally. According to Gupta, "Virosil Pharma has simplified the lives of so many people who work in the pharmaceutical industry as they are guaranteed sterility with the minimum risk exposure". As there was a high risk to the staff involved in the use of Formaldehyde/Glutraldehyde for sterilization and disinfection.

Owing to the stringent integrated micro contamination control and biosafety requirements, it is desirable to have micro-contamination control procedures and methods that could be monitored, evaluated and assessed periodically, which are convenient, cost-effective and safe.

A glimpse at the standards put down by various would monitoring agencies would help an individual or an organization help decide on choosing the most appropriate control procedure/methods. The important microbial limits which have been prescribed by various agencies is as follows:

To meet those requirements aerial disinfection (fumigation) with formaldehyde was the most convenient method. With the regulatory having restricted the use of formaldehyde and also putting into place the monitoring levels of formaldehyde after fumigation makes it a procedure with its own limitations.

Formaldehyde is a known carcinogen (IARC & NTP). Formalin is toxic by inhalation, toxic if swallowed, may be fatal if swallowed, causes eye burns, may cause blindness, strong sensitizer, causes irritation to skin, eyes, and respiratory tract. Repeated or prolonged exposure increases the cancer risk.

COMPARISON	
VIROSIL PHARMA	**FORMALIN**
Eco-friendly, Non-toxic	Highly toxic
Room gets sterilized within 1 hour after fumigation	Requires overnight fumigation
Requires no de-fumigation	Requires de-fumigation
Person can be present during fumigation	Causes skin, eye irritation even after next day of fumigation
Time Saving	Time consuming
Multiple Applications	Application restricted

Virosil Pharma has been a direct alternative to Formalin Fumigation. Virosil Pharma has proved to be effective in controlling aerial bacteria and fungus present in sterile rooms. The area becomes completely sterile within 60 minutes of spraying without causing any irritation to the eyes, nose and skin - unlike conventionally used formulations. Virosil Pharma can even be successfully used in AHU which are responsible for optimal and steady air exchange in production facility, of which the ducts, air shafts, humidificator, filters, etc. are often contaminated with loads of bacterial and bio-films.

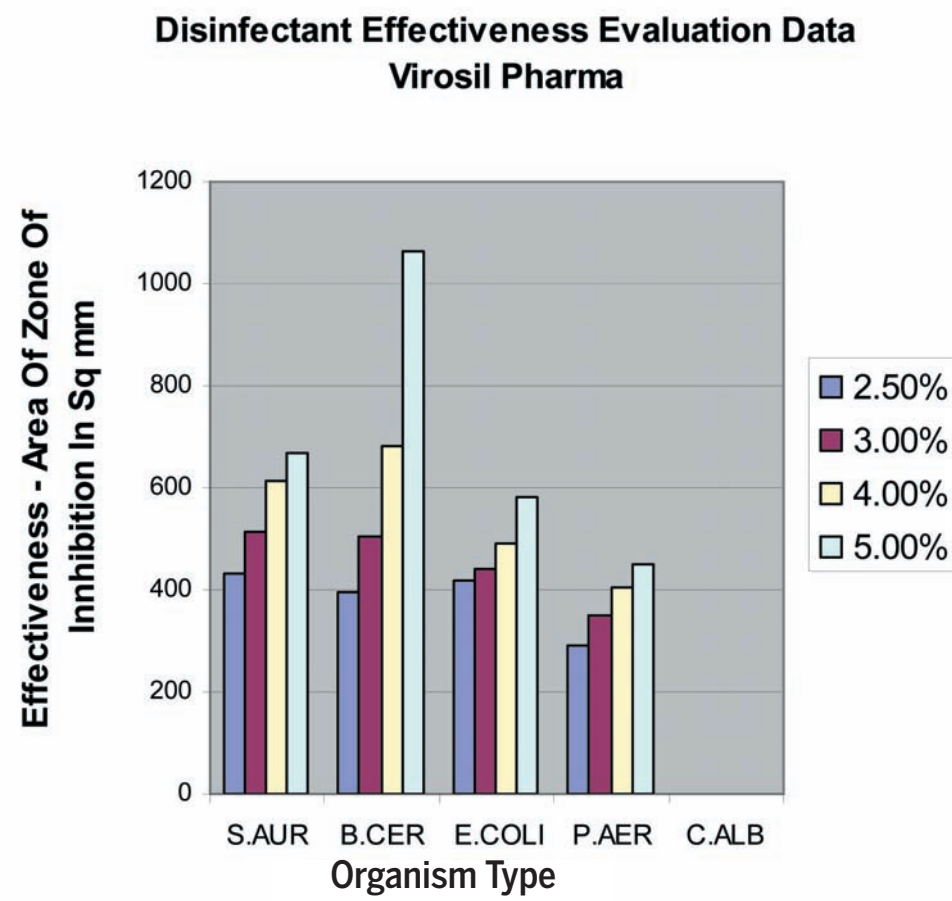
The main aim of Virosil Pharma is to increase productivity by cutting down disinfection time while at the same time providing a totally microbe-free environment.

Virosil Pharma is also very effective in disinfection of all critical surfaces that come in contact with pharma products. There is no requirement to re-wash equipment and surfaces disinfected with Virosil Pharma since it is H2O2 based and decomposes into water and oxygen.

Virosil Pharma has been tested by several reputed and renowned institutions in India with respect to its disinfection and fumigation applications in Pharmaceutical Industry

Because of all these factors, Virosil Pharma has attained maximum satisfaction of the customers in controlling the microbial contamination in their respective applications. The introduction of an eco-friendly, non-carcinogenic and totally biodegradable versatile product, like Virosil Pharma, has not only brought an end to the era of conventional biocides but has completely solved the disinfection requirements which these healthcare industries were prone to.

A GRAPHICAL VIEW ON DISINFECTANT EVALUATION DATA - VIROSIL PHARMA



	S.AUR	B.CER	E.COLI	P.AER	C.ALB
2.50%	429.83	397.4	418.15	289.38	0
3.00%	514.44	502.4	440.92	349.48	0
4.00%	615.44	683.14	490.625	404.5	0
5.00%	669.32	1063.07	580.77	452.16	0

Targets

Sanosil Biotech is marketing this disinfectant under the 'Virosil Pharma' brand name and is targeting the entire industrial belt of India. The company has already set up a distribution and infrastructure network having establishments in Maharashtra, M.P., Hyderabad, Chennai and Delhi.

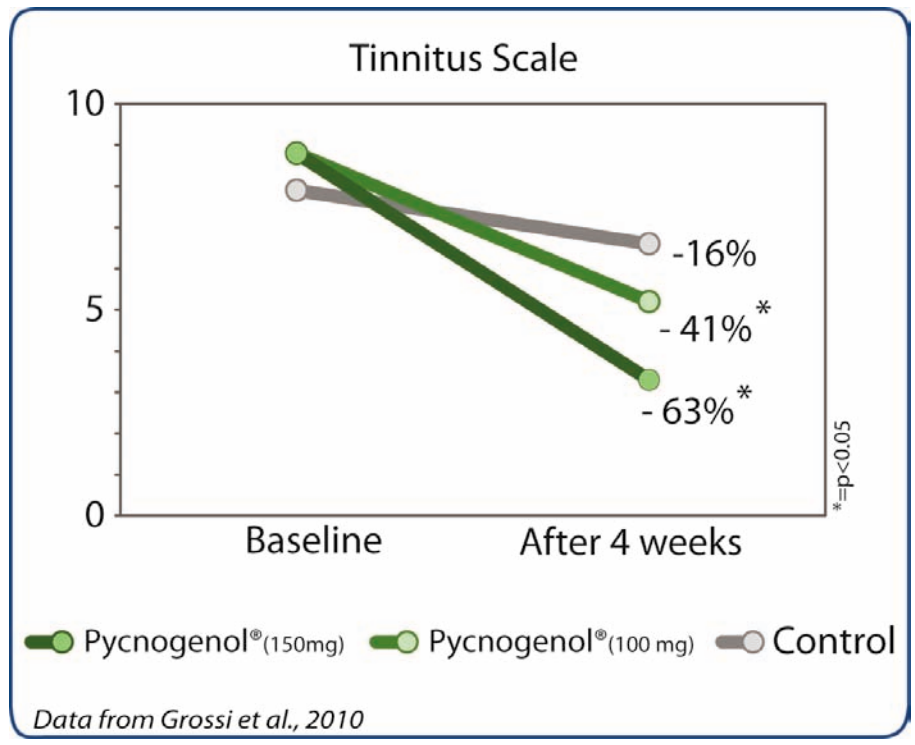
Pycnogenol® effective in relieving tinnitus symptoms

No medication is currently officially approved to treat tinnitus, but several medications are in use, such as anaesthetics, antidepressants, antihistamines, anxiolytics, vasodilators or calcium channel blockers. **Dr Franziska Weichmann**, Manager, Scientific Communications and Product Development, Horphag Research, explains more

Subjective tinnitus is the perception of sound without any external acoustic noise. This sound is mostly described as ringing, sometimes as a buzzing, roaring, whistling or hissing sensation (1). Several people with tinnitus suffer from an associated hearing loss, at least on one ear (1). With a prevalence of 10 to 20 per cent of the population worldwide, tinnitus is one of the most common and distressing ear-related problems in the world (2). In many cases, it affects the quality of life and can be accompanied by anxiety, depression, insomnia or increased sensitivity to noises (hyperacusis) (2).

No medication is currently officially approved to treat tinnitus, but several medications are in use, such as anaesthetics, antidepressants, antihistamines, anxiolytics, vasodilators or calcium channel blockers (3). Many of those medications come with serious risks for side effects.

The natural extract from French maritime pine bark Pycnogenol® was shown to be efficacious in relieving symptoms of tinnitus (4, 5). By improving microcirculation (4-8), normalising hypertension (9-12), enhancing endothelial health (11-17) and reducing inflammation (18-20), Pycnogenol® positively affects mechanisms that are associated with the development of tinnitus.

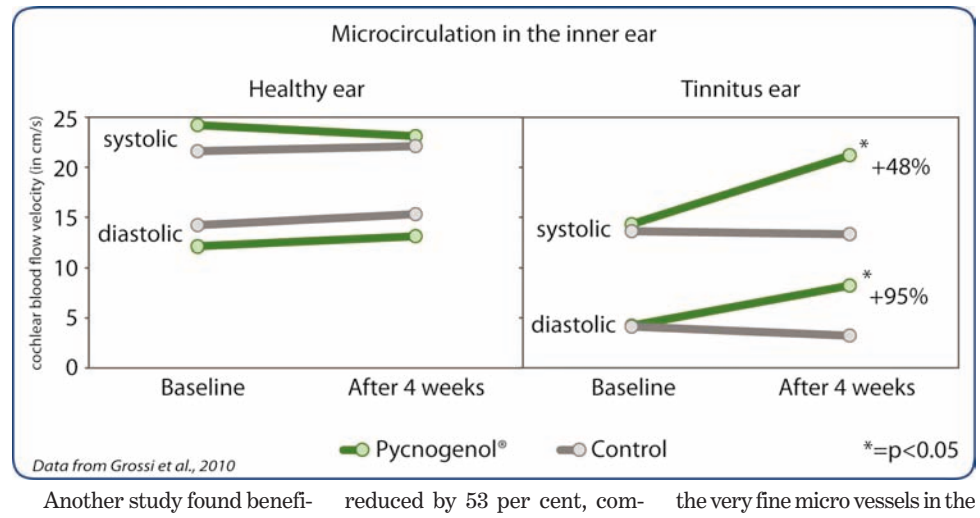


Pycnogenol®'s efficacy against tinnitus

Two studies could show that supplementation with Pycnogenol® ameliorates the symptoms of tinnitus (4, 5).

In the first clinical study with 82 patients, Pycnogenol® supplementation for four weeks had an impressive influence on the tinnitus scale (4). In this subjective scale, presence, intensity and duration of tinnitus, as well as the changes in the quality of life and drug intake to relieve tinnitus were each rated from 0 (none/low) to 3 (always/severe). The control group did not show a significant change in the personal tinnitus rating with only 16 per cent reduction, whereas 100 mg Pycnogenol® per day improved the tinnitus rating by 41 per cent and 150mg Pycnogenol® per day even led to a reduction of 63 per cent on the tinnitus scale.

The study further investigated the effects of Pycnogenol® supplementation on microcirculation in the inner ear. For that, the blood flow velocity in the cochlea was measured using ultra-sonography. Only one ear of the patients was affected by tinnitus, the "tinnitus ear," while the other ear was referenced as the "healthy ear." The effect of a four-week supplementation of Pycnogenol® on the microcirculation in the healthy ear was neglectable, whereas the very low cochlear blood flow velocity in the tinnitus ear could be normalised with four weeks of Pycnogenol® supplementation. Systolic as well as diastolic blood flow velocity was increased to almost normal values by 48 per cent and 95 per cent, respectively. There was, however, no observable change of the microcirculation in the control group.



Another study found beneficial effects of Pycnogenol® supplementation on tinnitus in patients, suffering from Ménière's disease (5). This condition is a disorder of the inner ear, presenting with symptoms such as vertigo, hearing loss and tinnitus. 107 patients took part in the six-month study. The tinnitus scale of the patients taking Pycnogenol® was significantly reduced by 53 per cent, compared to the control group with a reduction of only 28 per cent. Interestingly, 87 per cent of the patients, supplemented with Pycnogenol® stated to be asymptomatic after six months, and only 35 per cent of the patients in the control group were symptomless. Furthermore, Pycnogenol® supplementation could significantly improve the working and social life by 72 per cent and 81 per cent, respectively, compared to 50 per cent and nine per cent in the control group. As in the first study, blood flow velocity in the inner ear was drastically improved after Pycnogenol® supplementation, which helps explain the beneficial effects of Pycnogenol® on tinnitus symptoms.

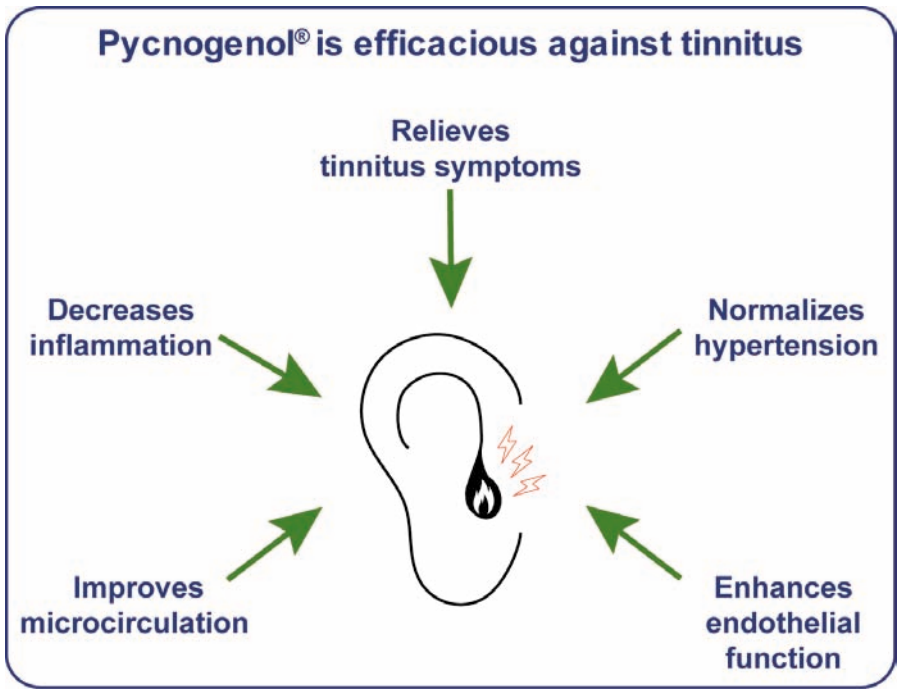
Pycnogenol® improves microcirculation, normalises hypertension and ameliorates endothelial health.

The development of tinnitus has been associated with cochlear microcirculatory dysfunction (21). As described in the previously mentioned studies, Pycnogenol® positively affects microcirculation in the inner ear (4, 5). This beneficial effect was not only observed in the ear, but could be confirmed in other small blood vessels in the body, like the retinal capillaries in the eye or the very fine micro vessels in the fingertip (6-8). In a three-month study on diabetic retinopathy, Pycnogenol® supplementation improved the retinal blood flow by around 30 per cent compared

to no change in the control patients (6). In another study with patients suffering from coronary heart disease, microcirculation on the fingertip improved significantly in 54 per cent of the patients, taking Pycnogenol® and in 33 per cent of the placebo patients after four weeks (7). A third study showed improved microcirculation in the legs by 34 per cent after Pycnogenol® intake, in patients with diabetic microangiopathy (8).

Elevated blood pressure (hypertension) can also be a causal or at least an adjuvant factor for tinnitus (21). The normalising effect of Pycnogenol® supplementation on hypertension was investigated in several studies (9-12). A double-blind, placebo-controlled, crossover study with borderline hypertension patients showed that Pycnogenol® supplementation for eight weeks significantly lowered elevated systolic blood pressure by five per cent compared to placebo (10). Diastolic pressure was found to be lowered by two per cent. Another study with hypertensive patients, treated with calcium channel blockers found that after three months, 57 per cent of the patients supplemented with Pycnogenol® were able to cut their individual hypertension medication dosage to a quarter of the previous dose to keep their blood pressure in a healthy range (11). Only 13 per cent of the placebo patients were able to do so.

Microcirculatory problems and hypertension can both be explained by endothelial dysfunction, an impairment of the inner lining of blood vessels. Consistently, endothelial dysfunction has been described in patients with tinnitus (22). There is strong evidence that Pycnogenol® improves endothelial health (11-17). One study, among others, showed that in patients with coronary artery disease, Pycnogenol® supplementation had a beneficial effect on endothelial function (13). Endothelial function was assessed by flow-mediated dilatation of the brachial artery (the widening of the artery in response to elevations in blood flow-associated shear stress). This eight-week randomised, double-blind, placebo-controlled cross-over study showed that flow-mediated dilation was improved by 32 per cent in the Pycnogenol® group, whereas it slightly decreased in the placebo group.



Pycnogenol® reduces inflammatory processes

Recent research has shown that inflammation, specifically, neuroinflammation, is involved in the development of several hearing disorders, including tinnitus (23).

In several studies, Pycnogenol® exhibited potent anti-inflammatory activities (18-20). Already after five days of daily intake, a study reported that Pycnogenol® significantly prevented the up-regulation of the pro-inflammatory enzymes 5-LOX and COX-2 (18). In another study, plasma samples of volunteers after intake of Pycnogenol® showed to significantly inhibit NF-κB activation by 15.5 per cent and matrix metalloproteinase 9 (MMP-9) release by 25 per cent, two important regulators in the inflammation process (19). In a similar study, significant inhibition of inflammatory molecules COX-1 and COX- 2 was observed after intake of 300 mg Pycnogenol® (20).

Pycnogenol® French maritime pine bark extract is an effective, safe and evidence-based natural solution to manage tinnitus by improving microcirculation, normalising hypertension, enhancing endothelial health and reducing inflammation. For more information on Pycnogenol®, please visit www.pycnogenol.com.

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Reversed-Phase HPFC to overcome major purification challenges in peptide therapeutic development

The High Performance Flash Column Chromatography (HPFC) from Biotage with the Biotage® Sfär Bio C18/C4 columns can prove to be very effective for reversed phase purification of peptides

Preparative Reversed phase HPLC is the traditional, established and most sought-after technique for routine purification of crude synthetic peptides. However, chemists can encounter major purification challenges with this technique, such as low loading amounts, long purification time, high solvent usage, and low recovery amounts with the requirement of multiple injections to enhance recovery. In addition, crude peptide may contain impurities with similar retention time as that of the parent peptide making it even more challenging to purify. Clearly, peptide purification remains the major bottleneck in the peptide synthesis workflow; can we not then search for a solution - an alternative purification platform to overcome this bottleneck. The High Performance Flash Column Chromatography (HPFC) from Biotage with the Biotage® Sfär Bio C18/C4 columns can prove to be very effective for reversed phase purification of peptides. Depending on the peptide sequence and characteristics, it can be used either as the standalone purification system (sole purification method) or as a pre-purification clean-up tool enriching the purity of the crude peptide prior to the final HPLC purification.

Biotage column features small spherical particles of size of 20 micron and a large pore size of 300 Å for increased resolution and efficient separation of crude peptide impurities. It allows higher loading in a single batch with shorter purification times using less amounts of solvent and significant recovery. Moreover, one can load sample even when it is not fully soluble in mobile phase buffer or peptides solubilise in high boiling solvents such as DMSO/DMF.

Collaborating with Jensen Lab at the University of Copenhagen, Biotage demonstrated the credibility of its Flash systems on an anti-parallel coiled coil peptide containing 44 amino acids. The peptide sequence is shown below:

H-KRKKQKRKRKRAKQL RKRLQALEWQLAQIRKELQ AAEKEEAQIE-CONH2

The crude peptide purity was 35 per cent. The crude peptide was divided into two fractions of 150 mg each, for purification; each fraction was dissolved in 2 mL of 50 per cent aqueous acetonitrile. One 150 mg fraction was purified by RP HPLC and the other by RP HPFC. The chromatographic method adopted in the HPFC is as follows:

- ◆ Cartridge: Biotage® SNAP Bio C18 or Biotage® Sfär Bio C18, 25 g
- ◆ Flow rate: 45 mL/min
- ◆ Solvent A: H2O (0.1 % Formic Acid)
- ◆ Solvent B: CH3CN (0.1 % Formic Acid)
- ◆ Equilibrium: 10 % B, 3 CV (CV means column volume)
- ◆ Gradient: 10 % B, 3 CV; 10-50% B, 10 CV; 50-100 % B, 1CV; 100 % B, 4CV; 100-10 % B, 1CV, 10 % B, 3CV.

The HPFC fractions containing the peptide were collected, combined and freeze dried. The purity the freeze-dried peptide was slightly greater than 97 per cent.

Now, the important question is how does it compare with traditional and the most established HPLC purification? Both techniques purified the peptide by greater than 95 per cent, but the HPFC purification is faster, consumes less solvent and purification of bulk amount can be completed in one single injection compared to repeated injection by HPLC. Moreover, in this scenario, the HPFC can be used as the sole method for purification of this 44-mer coiled coil peptide. The table below presents the comparison of peptide purification between HPLC and HPFC.

In another example, a

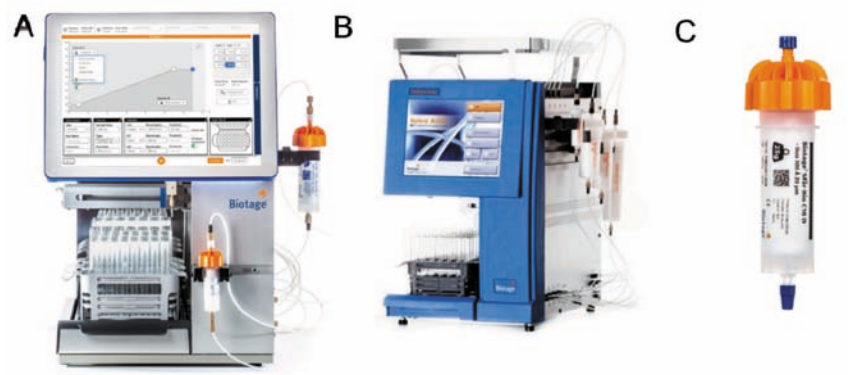

Fig 1. Range of systems and columns offered by Biotage for reversed phase HPFC. A: Biotage® Selekt Flash System B: Isolera One Flash System C: Biotage® Sfär Bio C18 Columns compatible with Selekt and Isolera Systems

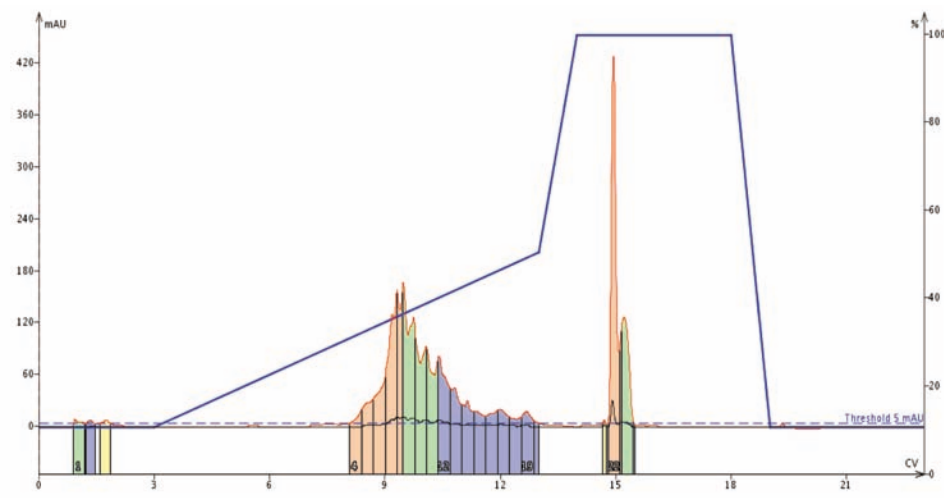

Fig. 2 HPFC performed using Biotage® C18 300 Å 25g cartridge on Isolera Flash System. The green bar indicates the collected fractions

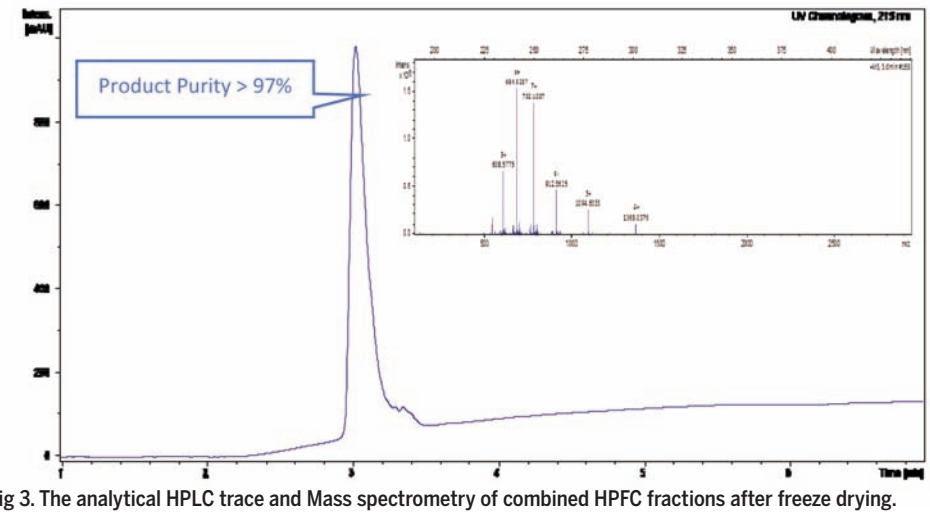

Fig 3. The analytical HPLC trace and Mass spectrometry of combined HPFC fractions after freeze drying. Purity obtained was more than 97 per cent.

54-amino acid peptide, with the given sequence H-ETYVTY-TAQSPNLLSLTNISDIFDIS PLSIARASNIDAGKDKLVPG QVLLVPVT-NH2 (Lys M1), [derived from Lys M1 subdomain of Lotus Japanicus from the nod-factor receptor 5 (Nfr 5)], was synthesised with a crude purity of 20 per cent as determined by LCMS (Fig. 4)

The Lys M1 peptide contains more than 50 amino acid in length, and, therefore, we can consider it as a mini-protein, which is particularly challenging to purify due to its low inherent solubility and very low crude purity. Hence, multiple consecutive runs in small amount are required when purified by preparative RP-HPLC; 5 mg of crude peptide could be injected per batch for RP HPLC. However, using Biotage® HPFC system, the company purified 50 mg of this crude peptide dissolved in H2O-CH3CN (2:3). The fraction size collected was at 2 mL intervals across the peak to obtain fractions of higher purity of the required peptide. Following partial purification by flash chromatography, the purity was increased to 66 per cent (13 mg).

Although HPFC did not fully purify the Lys M1 peptide, it provided fast separation of many of the impurities to make the subsequent HPLC purification easier. Moreover, the solubility of the enriched crude peptide was significantly improved, which is crucial for higher loading in the prep-HPLC. Importantly, several purification steps were avoided, which would normally be required when this peptide was purified by RP-HPLC alone.

In short, the company has demonstrated that reversed-phase High Performance Flash Chromatography (HPFC) is an efficient alternative strategy for rapid purification of large laboratory-scale quantities of crude synthetic peptides with significant recovery and purity. HPFC can be used either as the sole method of peptide purification or as part of a multi-step process to initially remove most of the undesired impurities by HPFC prior to a final purification step by RP-HPLC, especially in case of challenging peptide sequences with poor solubility. The High Performance Flash Chromatography allows more peptide to be processed in a single injection and significant amounts of impurities can be removed that would otherwise require more time and effort to purify by RP-HPLC alone, thereby increasing the speed and throughput of peptide purification, while reducing the cost.

> HPFC can be used either as the sole method of peptide purification or as part of a multi-step process to initially remove most of the undesired impurities by HPFC prior to a final purification step by RP-HPLC, especially in case of challenging peptide sequences with poor solubility

Purification Technique	HPLC	HPFC
Column/Cartridge	Phenomenex Gemini® 5 µm NXC18 110 Å, 100 x 21.2 mm	Biotage® Sfär Bio C18 (previously Biotage® SNAP Bio C18), 25 g
Amount of crude peptide purified	150 mg	150 mg
Number of Injections	4	1
Total amount of peptide recovered	33 mg	30 mg
Total solvent A (H2O)	1777 mL	1041 mL
Total solvent B (CH3CN)	1514 mL	477 mL
Total Time for purification	160 mins (40 mins per run)	27 mins

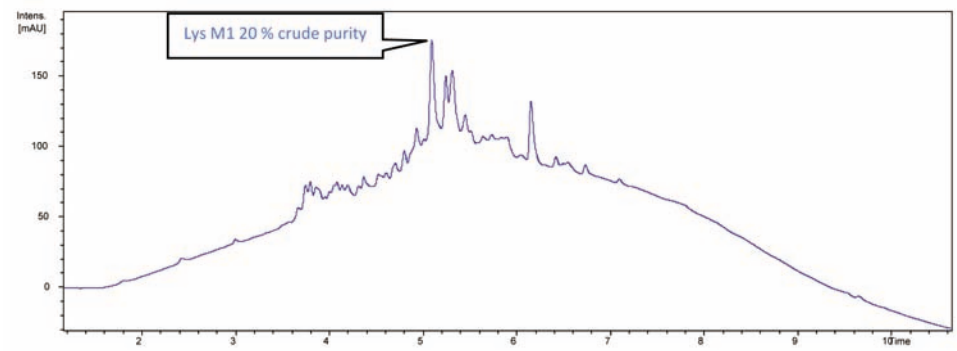

Fig.4 Analysis of crude Lys M1 peptide

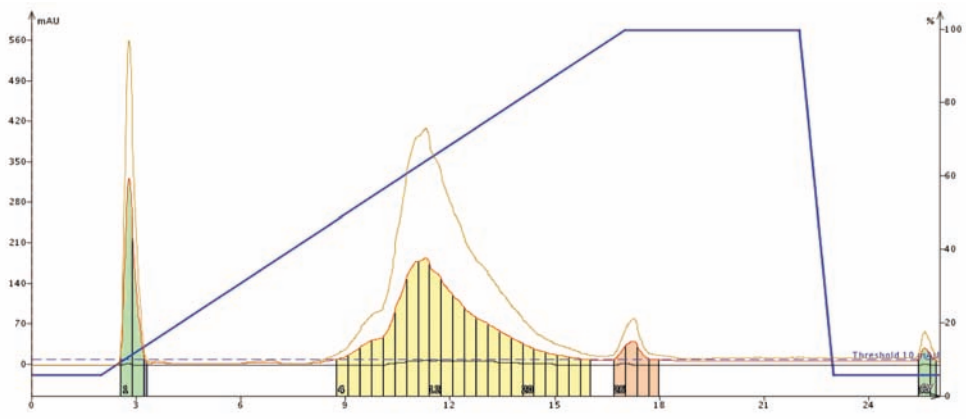

Fig 5. Flash purification chromatogram of Lys M1 peptide purified on Biotage® C18 300 Å flash cartridge.

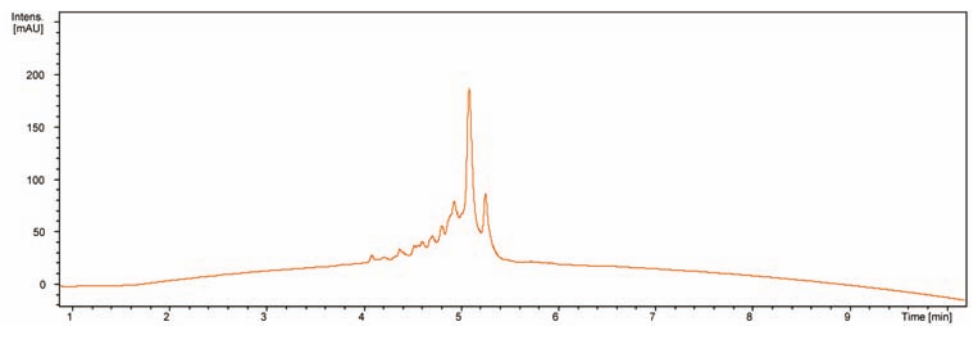

Fig 6. Analytical HPLC profile of collected fraction of Lys M1 peptide after Flash Purification. The crude peptide purity was enriched from 20 per cent to 66 per cent. The objective here was not to isolate pure peptide fractions, but to quickly remove many of the impurities to make the subsequent HPLC purification easier by reducing the quantity to be purified.

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SCADA for pharma

To meet the demands of the pharmaceutical 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

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.

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 integrated PharmaEdge solution helps users optimise the performance of their automation systems while improving cost and energy efficiency

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 pharmaceutical 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.

DuPont™ Liveo™ Pharma TPE Tubing for biopharma processing

DuPont is accelerating its investments for the future of the biopharma processing industry by expanding its supply capacity of silicone elastomers and tubing and by enlarging its single-use pharma product lines with new thermoplastic elastomer (TPE) tubing

For several years, the development of new therapeutic agents beyond traditional small molecules has profitably supported the biopharma industry, which has experienced steady and rapid growth. Cell and gene therapies, cancer treatments, the continuing trend of increasing life expectancy, and the unexpected and unprecedented demand for vaccines to control the COVID-19 pandemic blew up the most optimistic forecasts. This unpredictable growth in demand has put notable challenges on the upstream supply chain - especially the single-use-system supply.

While the bioprocessing supply sector works hard to adapt to this expansion, DuPont is accelerating its investments for the future of the biopharma processing industry by expanding its supply capacity of silicone elastomers and tubing and by enlarging its single-use pharma product lines with new thermoplastic elastomer (TPE) tubing.

DuPont successfully launched its new DuPont™ Liveo™ Pharma TPE Tubing product line in Q4 2021. This thermoweldable tubing effectively complements the Liveo™ Pharma Tubing and Overmolded Assemblies (OMA) line, the well-established DuPont product offering for bioprocessing.

This product launch marks a historic milestone for Liveo™, as it adds a range of extruded pharma tubing based on TPE technology - dedicated to fluid transport and single-use bioprocessing applications - produced under similar high-quality and high-performance principles as the recognised Liveo™ Silicone Pharma Tubing product lines.

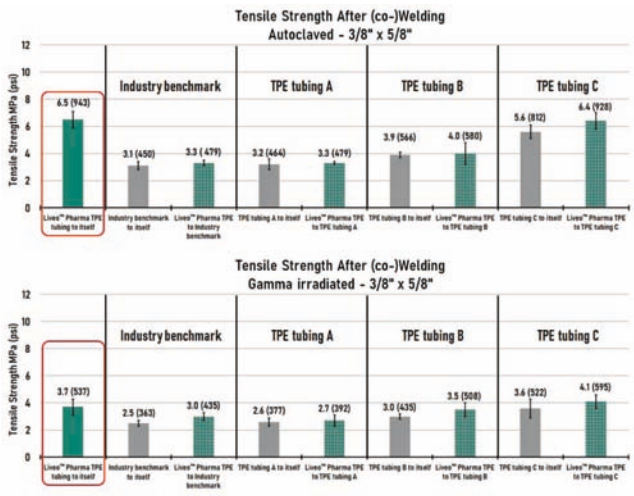

Fig. 1 - Improved tensile strength of Liveo™ Pharma TPE Tubing after heat welding to itself and compatibility with other kinds of TPE tubing

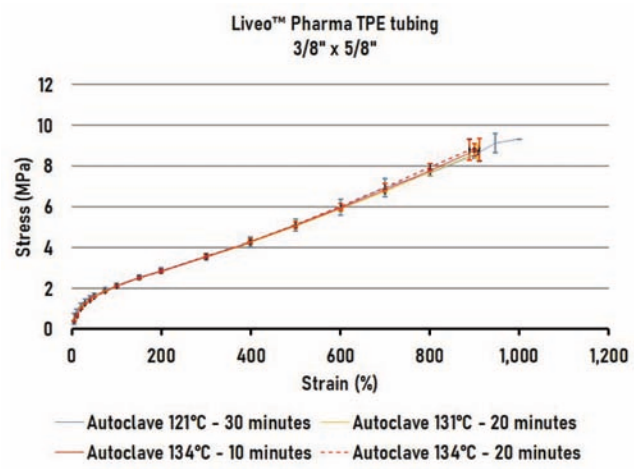

Fig. 2 - Stability of Liveo™ Pharma TPE Tubing under different autoclave sterilisation conditions

Liveo™ Pharma TPE Tubing is targetted for use in biopharma processes to enable aseptic connection and disconnection of tubing without connectors (e.g., sampling) and can be used in peristaltic pump applications. Strong from its heritage built on purity, quality and performance, the new ISO Class 7 manufactured TPE tubing offers an outstanding purity profile and low extractables. This new generation of high-purity tubing meets the most stringent requirements by enabling improved heat-welding to itself and unquestionable compatibility with any kind of TPE tubing. Not only is Liveo™ Pharma TPE Tubing weldable and compatible with other brands of TPE tubing, but it also improves the weld strength (Fig. 1).

Liveo™ Pharma TPE Tubing also demonstrates high tensile strength, burst resistance before and after welding, excellent resistance to chemicals, minimal spallation after 24 hours of pumping, and suitable stability under different sterilisation routes (Fig. 2).

These exceptional properties and characteristics are substantiated by a comprehensive set of data results compliant with required, demanding standards: USP <665> to assess the risk profile of the equipment part and potential impact on patient safety; USP <788> for particle counting and identification; USP <85> bacterial endotoxins test; biocompatibility testing according to USP Class VI and ISO 10993; ISO 11737-1 validation of sterilisation process; and elemental impurities testing. This data package will help accelerate the qualification process at customer manufacturing facilities. In addition, the performance of Liveo™ Pharma TPE Tubing and excellence in its category have been confirmed by a comparative benchmark study.

TPE tubing has been adopted increasingly in single-use bioprocessing applications, thanks to their thermoweldability. In the current context of accelerated demand for single-use tubing in the biopharmaceutical industry and the stress on supply chains due to the COVID-19 pandemic, Liveo™ Pharma TPE Tubing represents an additional competitive offering - one with the quality and performance that DuPont Healthcare customers are accustomed to receiving.

"By adding a complementary pharma TPE tubing range to our Liveo™ Silicone Pharma Tubing and OMA lines, DuPont is committed to meeting customers' requirements in terms of supply flexibility and a broader portfolio of solutions while maintaining our long-standing promises related to product performance, quality and reliability," said DuPont Healthcare Global Marketing Manager Jennifer Gemo. "We are pleased to add this new line of TPE tubing under the DuPont™ Liveo™ name for our biopharma processing customers."

Key benefits	Liveo™ qualification health data
• Liveo™ purity — Manufactured in ISO Class 7 cleanroom? — Low extractables • Improved performance — Welding and welding compatibility with other TPE tubing — Burst resistance before and after welding — Low level of spallation after 24 hours of pumping • Good chemical resistance • Good and stable clarity after sterilisation • Comprehensive data package to accelerate qualification and validation	• USP <665>: Extractables and leachables with autoclave and gamma sterilisation methods • USP Class VI — Intracutaneous Toxicity — Systemic Toxicity — Muscle Implantation • USP <85>: Endotoxins • USP <151>: Pyrogenicity • USP <232>: Elemental Impurities • USP <788>: Particulates • ISO 11737-1: Bioburdens • ISO 10993: Biocompatibility — Part 5: Cytotoxicity — Part 6: Muscle Implantation — Part 10: Irritation and Skin Sensitisation — Part 11: Acute Systemic Toxicity

Waters introduces Xevo TQ Absolute

It's the most sensitive and compact benchtop tandem quadrupole mass spectrometer

Waters Corporation recently introduced the new Xevo™ TQ Absolute system, the most sensitive and compact benchtop tandem mass spec in its class. (i)

The exceptionally sensitive Waters Xevo TQ Absolute tandem quadrupole mass spectrometer is up to 45 per cent smaller, uses up to 50 per cent less power and nitrogen, and generates up to 50 per cent less heat than competing tandem quadrupole mass spectrometers.

Waters' newest high-performance mass spectrometer is up to 15x more sensitive for quantifying negatively-ionising compounds than its predecessor (ii) and is 45 per cent smaller, and uses up to 50 per cent less electricity and gas supply than other high-performance tandem quadrupole mass spectrometers available in the market (iii). The Xevo TQ Absolute is designed to help pharma, food and beverage, and environmental analytical laboratories meet regulations requiring trace-level quantitative mass spectrometry analyses for a broad set of applications.

"The Xevo TQ Absolute is for laboratories looking for industry-leading quantitative sensitivity, accuracy, reproducibility, efficiency and sustainability," said Jon Pratt, Waters Division Senior Vice President, Waters Corporation. He further said, "It offers more analytical firepower in a much smaller footprint than any other mass spec in its class, reaches exceptionally low limits of quantitation, and aids laboratory managers to best optimise their equipment utilisation and analytical output."

For optimal performance, Waters pairs the Xevo TQ Absolute mass spectrometer with Waters' ACQUITY™ Premier UPLC System with MaxPeak™ HPS technology which eliminates non-specific adsorption of compounds containing phosphate and/or carboxylate groups and improves their recovery. Together, this integrated LC-MS/MS system is designed to drive the limits of quantitation to exceptionally low levels for many applications, including:

- quantifying regulated impurities in drug products
- performing oligonucleotide bioanalytical assays
- measuring concentrations of endogenous metabolites in large cohort clinical studies
- quantifying residues and contaminants in food and environmental samples
- measuring low-level drugs and toxicants in physiological matrices
- detecting trace-level leachables from food packaging

The Xevo TQ Absolute incorporates thoughtful design features that enable consistent and reproducible analyses, allowing labs to maintain performance and uptime for longer periods in between routine cleaning and service intervals. This is achieved with new guidance on optimal probe positioning for both sensitivity and robustness and a source shield that helps minimise source contamination by the sample matrix or mobile phase salts.

The Xevo TQ Absolute is optimised for use with the waters_connect™ software platform, and is also compatible with Waters MassLynx™ mass spectrometry software. For laboratories painstakingly reviewing the results from large numbers of samples, or those quantifying hundreds of small molecule components and contaminants in a single run, the MS Quan app on waters_connect and its unique Exception Focused Review (XFR) functionality, lets scientists review data in up to half the time it used to take them (iv).

Worldwide customer shipments of the Xevo TQ Absolute are expected to commence in May.

Additional Resources

Learn more about the Xevo TQ Absolute features and benefits
Read the blog post Can Ever-Increasing Analytical Sensitivity and Sustainability Go Hand-in-Hand?
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, Xevo, ACQUITY, MaxPeak, MassLynx and waters_connect are trademarks of Waters Corporation.

References:
i Based on a comparison of the sensitivity and product specifications of currently available instruments on the market

ii Waters Xevo TQ- XS

iii Based on a comparison of product specifications for the Sciex 7500, Sciex 6500, Agilent 6495C and Thermo TSQ Altis

iv Estimate based on time on task comparison of a batch of pesticides in a food safety analysis

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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 as the testo Saveris Pharma

A sector like pharma, which is governed by strict norms and regulations, must operate with the 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 as the testo Saveris Pharma. It is an automated system that is integrated in the facility, and constitutes of 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

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.

Application areas

◆ Manufacturing
◆ Production area
◆ Research and QC labs
◆ Cleanrooms and data centers
◆ 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

The company's specially-trained service team supports its customers 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 our website www.testo.com or write back to us on info@testo.in

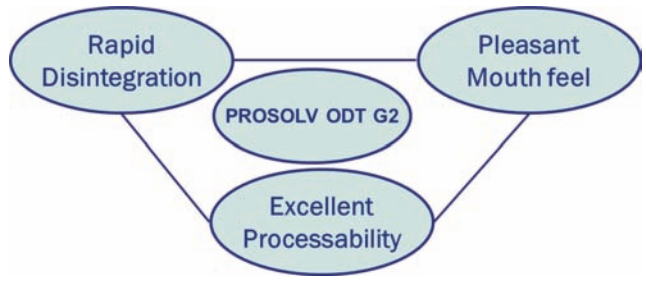
PROSOLV® ODT G2: Directly compressible composite built on proven co-processing technology

Compared to conventional tablets, ODTs have the advantages of improving the patient's compliance because they can be easily swallowed without drinking or chewing, thereby minimising swallowing problems or fear of choking

Orodispersible tablets (ODTs), also referred to as orally disintegrating or fast-disintegrating tablets, are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed. Compared to conventional tablets, ODTs have the advantages of improving the patient's compliance because they can be easily swallowed without drinking or chewing, thereby minimising swallowing problems or fear of choking. In this way, ODTs can be used in paediatric, geriatric, dysphagic, bed-ridden, psychiatric, or neurologic patients. Moreover, ODTs may enhance the bioavailability of some APIs as well as provide a faster onset of action favoured by pre-gastric absorption. Compared to oral liquid dosage forms, ODTs assure dose accuracy and are more stable. [1]

High demands are placed on ODTs, especially in terms of their disintegration time. According to the European Pharmacopoeia (Council of Europe, 2020), it is important that the disintegration time of ODTs does not exceed three minutes. However, the requirements of the USP (USP, 2015) and the FDA are stricter, demanding a disintegration time of up to 30 seconds. Therefore, the tablets must have sufficient porosity or contain a highly efficient superdisintegrant. [2]

ODTs can be manufactured by wet or dry granulation, lyophilisation (freeze-drying), spray-drying, or molding; nevertheless, the simplest and most cost-effective method is direct compression. Direct compression can be used for thermolabile and moisture-sensitive APIs, but the flow and compaction properties of the formula's constituents are crucial for the quality of the tablets.[2]



PHYSICAL PROPERTIES OF PROSOLV® ODT G2: [5]

Bulk density	0.45-0.65 g/ml
Average particle size	40-80 µm
Compactability	Highly compactible having excellent flowability as well
Mouth feel	Good mouth feel
Disintegration	Rapidly hydrating allowing faster disintegration

Need of co-processed excipients for ODT manufacturing

The development of ODTs by direct compression for poorly soluble and poorly flowable APIs, with fast disintegration and suitable hardness, is still a formulation challenge. [1]

Several studies have been performed to compare critical parameters of co-processed dry binders to the parameters of their physical mixtures. It has been shown that co-processed dry binders manifest improved dilution potential, flowability, compressibility, decreased lubricant sensitivity and higher tensile strength of compacts. The incorporation of a number of excipients into the monoparticle structure also eliminates problems caused by physical mixtures such as segregation, inhomogeneity of the mixture and tablet weight variability. Furthermore, fewer production steps are required to prepare the directly compressed mixtures resulting in a faster and more cost-effective procedure.[2]

ODTs, compared to conventional tablets, are more prone to breaking during packaging and/or transportation due to their brittle structure. It has been proved that co-processed dry binders exhibit higher energy of plastic deformation with higher tablet tensile strength and lower friability.[2]

Excipients for ODTs have to be selected based on material characteristics (plastic, elastic or brittle material) and desired functionalities like defined particle size distribution, good flowability, enhanced compactability or fast disintegration. Mannitol represents an often used excipient for fast-dissolving drug formulations. However, when used as untreated powder, the poor flowability, insufficient binding properties and compactability are limiting factors. Hence, co-processed excipients with mannitol is a good option which is possible with PROSOLV® ODT G2.[3]

PROSOLV® ODT G2

It is a high-functionality excipient for orally disintegrating tablet formulation, development and manufacture. It provides a creamy, smoothy and cool mouth feel. This innovative Orally Disintegrating Tablet (ODT) matrix is a unique combination of soluble and insoluble ingredients manufactured using JRS Pharma's co-processing technology.

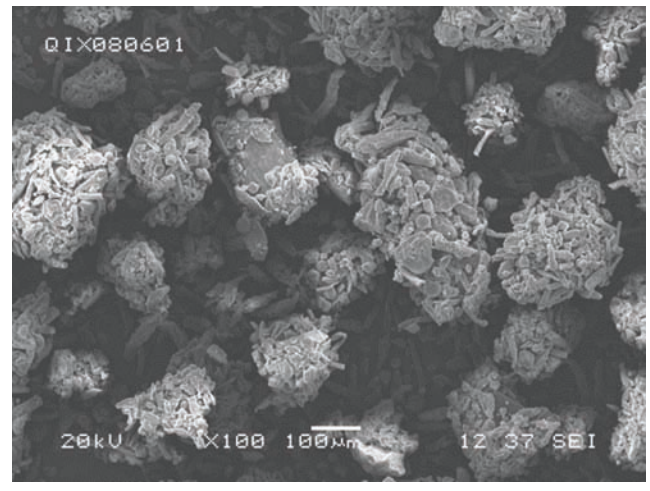


Fig.1 SEM picture of the individual ingredients of PROSOLV® ODT G2 after conventional granulation

It provides a pleasing, convenient and discreet form of administration for active pharmaceutical and nutritional ingredients without the need for water. PROSOLV® ODT G2 offers the functional performance needed for today's Orally Disintegrating Tablet formulation challenges and complies with globally accepted and monographed raw materials.

PROSOLV® ODT G2 addresses formulation and manufacturing challenges with a robust functional performance that high-speed tablet manufacturing requires. Patients experience tablets with pleasing mouth-feel and fast disintegration in the oral cavity, with no need for water. [4]

Composition [5]:

1) Microcrystalline cellulose and colloidal silicon dioxide: The combination of microcrystalline cellulose and colloidal silicon dioxide (PROSOLV®) has established superior functional performance providing improved compaction to agglomerated particles and having excellent flow and blending properties

2) Mannitol : Has proven effect in ODT matrices and formulations possessing negative heat of solution and element of creaminess

3) Crospovidone: Superdisintegrant, non-gelling even at higher concentrations

4) Fructose: For enhanced performance, taste and mouth feel

Co-processing leads to a uniform, homogeneous composite with synergistic effects compared to the physical blend.

Benefits of using PROSOLV® ODT G2 [5]

1) Directly compressible, simple to use leading to greater productivity

2) Free flowing powder having superior compaction profile as compared to other matrices

3) Excellent blending characteristics for improved content uniformity

4) Requires no additional binders or disintegrants

The use of PROSOLV® ODT G2 enables fast disintegration and can be used via direct compression process making the end formulation convenient and patient compliant.

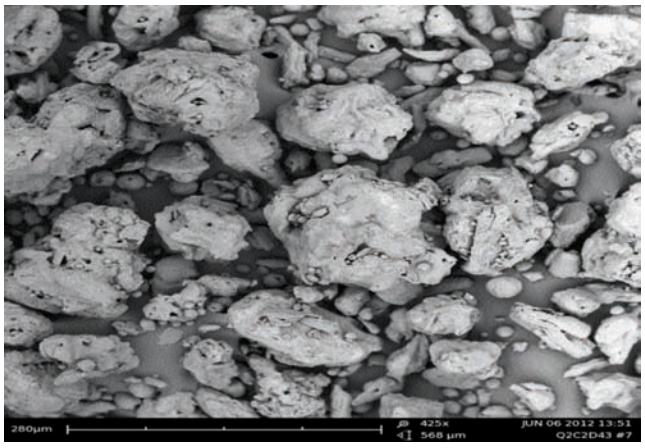


Fig.2 SEM image of PROSOLV® ODT G2 produced by co-processed technique

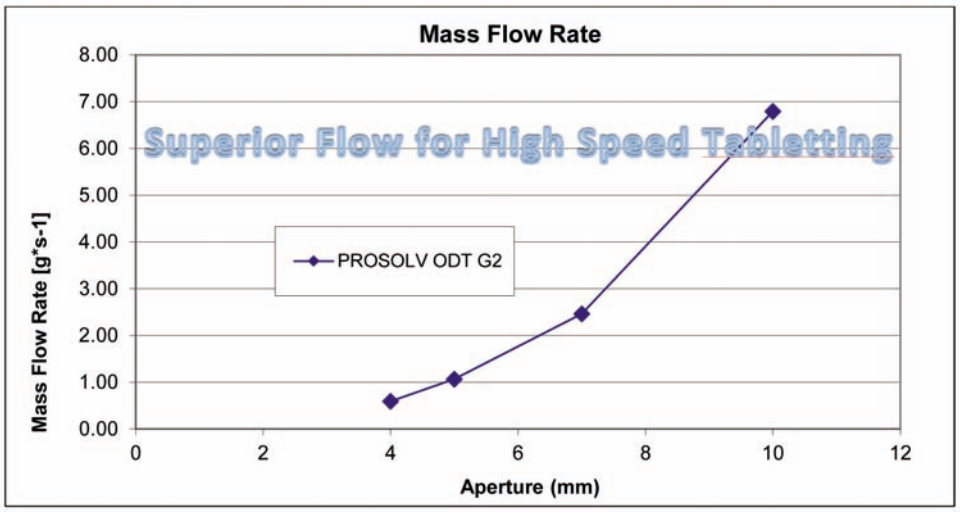


Fig.3 Flow rate of PROSOLV® ODT G2

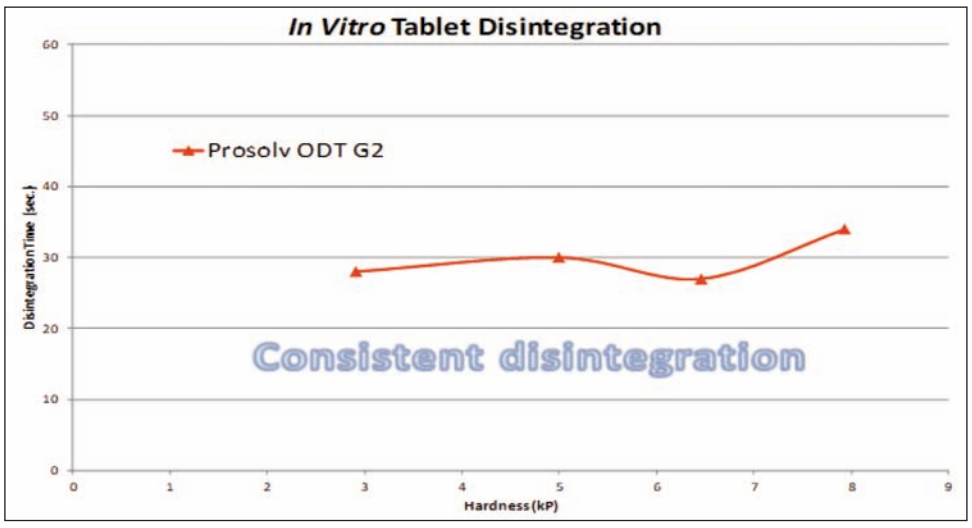


Fig. 4 Placebo with 99.5 % PROSOLV® ODT G2 showing consistent disintegration

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CASE STUDY OF PIROXICAM WITH PROSOLV® ODT G2[5]

Tablet components	Amount per tablet (%)
Piroxicam	10
PROSOLV ODT	89
Flavor (Cream & Vanilla)	0.5
PRUV	0.5

Procedure: API and ODT matrix are blended for five minutes. Flavours and lubricant are added and blended for five minutes. Tablets are compacted at 50 rpm to ~3kP crushing strength

Properties	Piroxicam tablet 10 mg
Weight	99.9 mg
Form	0.25" sc round
Hardness	3.5kP
Friability	0.0%
Disintegration time (USP)	27 sec
Dissolution	Pass USP-NLT 75% in 45 min. (92% in 10 min.)
Weight variation (% RSD)	0.8
Content Uniformity (%RSD)	0.87

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A critical review on Remdesivir and other anti-COVID-19 drugs

Dr Naseem Khan, Head India-Drug Delivery and Excipients, Sredstva Regionale Chemie; **Dr Rajiv Kumar**, Managing Director, Raptech Labs; and **Zoltán Kovács**, Senior Business Development Specialist, CYCLOLAB, Budapest, trace down the various factors associated with different drugs that help in treating COVID-19

Clinical-trial data showed that Molnupiravir, developed by pharma firm Merck, based in Kenilworth, New Jersey, and the biotechnology company Ridgeback Biotherapeutics in Miami, Florida, cut hospitalisations and deaths by 30 per cent, compared with people who took placebos. Meanwhile, Paxlovid (Nirmatrelvir and Ritonavir), made by Pfizer, based in New York City, cut hospitalisations and deaths by 89 per cent. The UK regulators approved Molnupiravir in November and Paxlovid in December, and the US regulators granted emergency authorisations for both the drugs in December.

Paxlovid inhibits SARS-CoV-2's main protease, whereas Molnupiravir tricks its RNA polymerase into incorporating part of the drug into the virus's RNA, creating so many errors that it cannot survive. A third drug - Remdesivir, developed by Gilead, based in Foster City, California - inhibits RNA polymerase, but the treatment is expensive, and currently requires intravenous infusions over three consecutive days, making it inaccessible to many people.

If the treatment does not completely wipe out the virus in a patient, some of the RNA errors it creates might inadvertently give the virus resistance against the other drug in the combination. That's why it's a key priority for researchers to find an accessible drug that effectively blocks the virus's RNA polymerase, which could be used in partnership with a protease inhibitor such as Paxlovid. One option may be an oral version of Remdesivir, which Gilead is currently testing.

Dr Naseem Khan

Dr Rajiv Kumar

Zoltán Kovács

> Remdesivir acts by inhibiting the activity of RNA polymerase, a protein that is more conserved in different SARS-Cov-2 variants than the spike protein, the target of vaccines, and Remdesivir has also shown inhibitory activity against variants

A critical review on Remdesivir

The aim of this report is to review the literature and shed light on the uncertainties surrounding the use of anti-viral agents, in general, and Remdesivir in COVID-19 patients. This review evaluated a battery of anti-viral compounds and their effectiveness in the treatment of COVID-19 since the beginning of the pandemic. Remdesivir is the only antiviral approved by the EMA and FDA for the treatment of SARS-CoV-2 infection. This work extensively reviews Remdesivir data generated from clinical trials and observational studies, paying attention to the most recent data, and focussing on outcomes to give readers a more comprehensive understanding of the results. This review also discusses the recommendations issued by official bodies during the pandemic in the light of the current knowledge. The use of Remdesivir in the treatment of SARS-CoV-2 infection is justified because a virus is the causative agent that triggers the inflammatory responses and its consequences. More trials are needed to improve the management of this disease.

It was concluded that the use of Remdesivir, when indicated, would shorten hospital stays and reduce the risk of progression to the Intensive Care Unit (ICU), and, therefore, represents a saving in staff hours and other resources. Remdesivir acts by inhibiting the activity of RNA polymerase, a protein that is more conserved in different SARS-Cov-2 variants than the spike protein, the target of vaccines, and Remdesivir has also shown inhibitory activity against variants.

Remdesivir is marketed as intravenous agent formulated by sulfobutyl beta.cyclodextrin (SBECD, Captisol, Dexolve) under the trade name Veklury (Gilead Sciences).

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Gandhi Automations's dock levelers

Electro-hydraulic dock levelers offered by Gandhi Automations are not only "a bridge for connecting a vehicle," but these also facilitate fast, smooth and safe transition by compensating the difference in heights between the loading bay and the vehicle

Gandhi Automations's widely recognised position has been achieved over years of hard work, innovation, commitment to quality and reliable customer service. The company is also proud to be certified to ISO 9001 : 2015, ISO 14001 : 2015 & ISO 45001 : 2018. Since its inception in 1996, the company has been manufacturing, importing, distributing and installing products that are problem-free and easy to operate.

The company offers complete logistics solutions by providing dock levelers, dock shelters, sectional overhead doors and dock houses.

Electro-hydraulic dock levelers offered by Gandhi Automations are not only "a bridge for connecting a vehicle," but these also facilitate fast, smooth and safe transition by compensating the difference in heights between the loading bay and the vehicle. This contributes to minimising the energy used and savings on heating and chilling costs resulting in maintaining the quality of the transported goods. Dock levelers offered by Gandhi Automations are designed as per EN 1398 standard for the most demanding loading and unloading operations.

Efficient loading and unloading of the goods

The importance of efficient loading of the goods has always been evident, and it has increased over the years, essentially for two reasons: the lesser availability and the higher cost of manpower. Consequently, lesser qualified manpower is being utilised which leads to damage to the goods.

The cost of loading and unloading the goods can be calculated precisely and is exactly definable, which allows for a scientific approach to find out the investment that goes into the process. Gandhi Automations has always designed solutions based on such scientific approach and feedback from clients. The dock levelers offered by the company ensure loading and unloading with lesser effort and minimal cost.

It is possible to load and unload products in a safe way, and, in the process, obtain remarkable energy savings. The dock leveler remains with the loading bay in rest position and the sectional overhead door closed, until the vehicle is positioned. The driver drives back centring to the dock shelter and stops the vehicle the moment it gets in contact with the bumpers.

The sectional overhead Ddoor is then opened only when the vehicle is positioned, brakes are applied and engine is shut off. This eliminates the exit of hot air, intake of cold air (or the opposite in hot area and inside conditioned places) and intake of exhausting gases in the warehouse. After the sectional overhead door opens, the lip of the dock leveler connects to the truck bed for loading/unloading to take place.

At the end of the loading/unloading, the dock leveler is put in rest position and the sectional overhead door is closed, without moving the vehicle. The vehicle then departs at the end of the process. Following are the types of dock levelers

a) Radius Lip dock levelers: These are available in multiple size and capacities. It allows the dock to connect with the truck bed, thus making it convenient to drive directly on and off with forklift trucks etc. Moreover, the Self-Cleaning Lip - Hinge System does not retain dust and dirt, which allows a smooth operation.

b) Telescopic Lip dock levelers: These are ideal for connecting vehicles unable to drive near dock i.e. sea containers, side loading railway wagons, etc. These dock levelers can be supplied with a lip extending up to 1 m.

c) Edge-of-dock levelers: It is developed in compliance with the latest European safety standard, EN 1398. It has a capacity of 6,000 kgs and is suitable for use with all types of material-handling equipment.

d) Forklift Roll-Off Barrier Lip dock levelers: The newly introduced product adds a run-off protection, which prevents accidental forklift roll-off when the overhead door is open and no trailer is stationed at the dock. These dock levelers are designed and built to provide all the benefits of the hydraulic dock leveler along with the additional benefit of providing a formidable barrier.

Gandhi Automation's dock levelers are equipped with the most secure safety devices and accessories.

For further details, contact:
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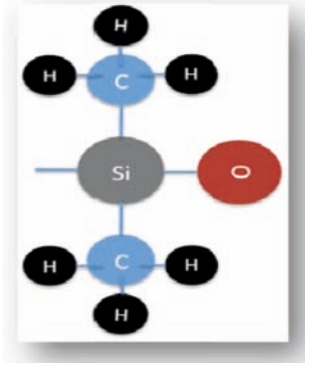
Email: sales@geapl.co.in
Website: www.geapl.co.in

Demand of Silicone hose in pharma industry

Silicone hoses are the tubes that are extruded into tubulous shapes at high temperature and cross—linking and solidity, which have a certain softness and tensile strength

In the modern market of elastomers, consumers have a huge choice of hoses options. However, the numerical number can often cause confusion as to which type of rubber, silicone or polymer is the best suited for a particular application.

Silicone is a polymer that mainly consists of silicon. The starting material from which silicones are made is silica, common in sandstone, beach sand and quartz. Silica is also widely used in glass production. Silicone can thus have different physical forms, such as oils, gels and solids, and is, therefore, a versatile type of rubber that can be used in many applications where large working temperature ranges, stability, resistance, etc. are required. VMQ (High Consistency Silicones) is used for food and drug use and medical applications.



Silicone hoses are the tubes that are extruded into tubulous shapes at high temperature and cross—linking and solidity, which have a certain softness and tensile strength. Thus, they are widely used in many industries. Silicone hoses are an excellent choice for transporting liquids in medicine, pharmaceuticals, biotechnology, machine-building, construction, power industry and food industry. Silicone is one of the most flexible elastomers, thanks to its wide operating temperature range, biocompatibility, high dielectric strength and the ability to be pigmented to almost any colour. For these reasons and more, the use of silicone hoses continues to expand in spheres that traditionally use materials such as PVC, polyurethanes and natural rubber, which required curing. Silicone hoses are made of silicone which has been widely applied in a variety of fitness equipment that takes advantages of their excellent elasticity to replace commonly used metal spring, their merits including portability, beauty, practicality and low risk, etc... Generally, they can be stretched more than six times and they are also hard to be broken. Even though there is a breach, they will not be broken immediately, which minimises the harm to human body.

Features

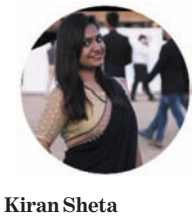
Silicone hose has many features. Let us know some of them.

- Low temperature flexibility
- Shape option
- High temperature resistance
- Water resistance
- Weather resistance
- Tasteless and odourless
- Chemical resistance
- Colourful

Why choose AMI Polymer hoses?

Ami polymer silicone hoses is registered as Imafit®, Imavac®, Imavacfit®, Imawrap® and Imaflexxie®. All Hoses are manufactured by advance grade of silicone rubber which conforms to FDA 21 CFR 177.2600 food grade standard.

- High-quality designed silicone hoses
- Fulfill all regulatory and compliance requirement
- Customisation available
- Fast delivery
- Competitive prices



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Hose Production – Sr Executive
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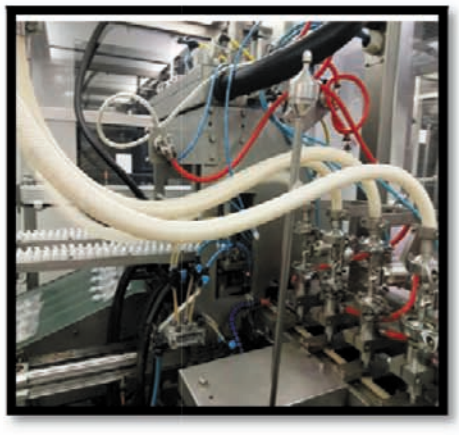
APPLICATIONS

FOOD INDUSTRIES

MEDICINE MANUFACTURING INDUSTRIES

PHARMACEUTICAL INDUSTRIES



CRITICAL LIQUID TRANSFER

LOAD CELL APPLICATION

CIP, WFI TRANSFER

FormWeigh.Net®: Powerful solution for dispensing application in pharma industry

FormWeigh.NET® offers full formulation control with visual displays that guide operators easily through the recipe-weighing process

Challenges associated with weighing in dispensing area

Inaccurate measurements, addition of wrong materials, false labelling or lost documentation are some of the reasons for inefficiencies. Experience has shown that manual inputs are more error-prone than automatic methods.

Solution

FormWeigh.NET® offers full formulation control with visual displays that guide operators easily through the recipe-weighing process. It captures weight values automatically, storing them in a central database. Qualification manuals and checklists complete the package and speed up validation process.

FormWeigh.Net® encompasses a full set of possibilities needed for successful formulation of pharma production without quality problems, and in compliance with regulations.

Automatic quantity adjustment of active ingredients makes it at the same time to a powerful tool to increase production yield and realise considerable savings in time and money.

Implement FDA 21 CFR Part 11 compliance

The US FDA has implemented 21 CFR Part 11 on request of the pharma industry with the target to simplify drug approval, specifically to move away from the huge amount of paper-based documents toward electronic documentation. With 21 CFR Part 11, the electronic documents become the originals, while printouts on paper are non-binding copies. Companies wishing to comply with 21 CFR Part 11 will have to implement systems supporting it. One of those is FormWeigh.Net®. With the 21 CFR Part 11 module, a major step towards compliance is achieved.

Automatically adjust the potency of APIs in the recipe

The optional Active Substances Module helps in making full use of API stock, even if its potency varies from batch to batch. This intelligent FormWeigh.Net® option automatically calculates the required amount of material in order to achieve the required potency in the end product. FormWeigh.Net® calculates the new target weight as well as the new quantity of compensation material. The result is a stable product quality even if important parameters differ from one raw material batch to the other.

Designed for compliance from beginning

Thanks to full batch control in the dispensing and formulation process, one gains important benefits within the process:

- Full knowledge about the batch status in every production step
- Traceability over the material flow in the production process
- Assignment of end product batches to used raw materials

About Mettler Toledo

Mettler Toledo is a leading global supplier of precision instruments and services. The company is the world's largest manufacturer and marketer of weighing instruments for use in laboratory, industrial and food retailing applications. Mettler Toledo also holds top-three market positions in several related analytical instruments, and is a leading provider of automated chemistry systems used in drug and chemical compound discovery and development. In addition, the company is the world's largest manufacturer and marketer of metal detection and other end-of-line inspection systems used in production and packaging, and holds a leading position in certain process analytics applications. Additional information about Mettler Toledo can be found at www.mt.com

For more information, visit:
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Analytical Intelligence - Analytical workflow automation

Analytical Intelligence is a new concept for analytical instruments offered by Shimadzu for supporting automation of analytical operations and ensuring acquisition of highly reliable data

Automation in analytical operations have led to a remarkable improvement in productivity, prevention of human errors, implementation of more efficient and flexible work styles. Nevertheless, differences in the functionality, performance, operability of instruments and software can affect the reliability of results and the condition of instruments. Overall operating efficiency also depends on the knowledge and expertise of users. Experienced and inexperienced analysts approach the same problem in different manners affecting reliability of data. Furthermore, improving the knowledge and skill level of users requires a time-consuming process of training personnel. This trend is a major issue currently being faced by the analysis and testing industries. It can only be truly solved if highly reliable results can be acquired at any time by any users, regardless of their knowledge or skill.

Analytical Intelligence is a new concept for analytical instruments offered by Shimadzu for supporting automation of analytical operations and ensuring acquisition of highly reliable data. Analytical Intelligence consists of systems and software that simulate expert operators automatically determining whether or not conditions and results are good or bad, providing feedback to users, and solving common problems. It increases data reliability by compensating for any differences between users in their instrument knowledge or experience. This article describes the new Analytical Intelligence functionality included in the latest Shimadzu HPLC and UHPLC systems.

Liquid chromatography workflow involves several risks that could interrupt continuous analysis or compromise data reliability. Analytical Intelligence helps minimise each of the risks when using Nexera series and new Ai-Series systems.

Flow pilot enabling fully automated workflow for analysis

When starting up the system and equilibrating the column, expert analysts will gradually increase the flowrate as the column temperature is controlled to prevent exposing the column to any excessive pressure loads. When the auto-start-up function starts up the system at the specified date and time, the flow pilot function starts equilibrating the column by gradually increasing the mobile phase flowrate as the column temperature increases replacing manual operations. Scheduled shutdown automatically turns off the system and switches it to power-saving mode when all analytical operations are complete. The combination of these functions allows the user to fully automate an entire analytical cycle: Shutdown → Start-up → SST→ Analysis → Results report → Shutdown.

Mobile phase monitor prevents mobile phase depletion

Using the mobile phase monitor prevents depletion of mobile phase and eliminates the need to visually check the level. It also eliminates the need to perform bothersome consumption rate calculations. The MPM-40 unit, which comprises a weight sensor and controller with dedicated MPM Checker notifies the user for decreasing mobile phase levels. It also stops the LC system if specified criteria are satisfied. The function also reduces the risk of bubbles getting inside the column and prevents loss of scarce samples caused by injecting samples when the mobile phase supply is depleted.

Automatic detection and resolution of solvent delivery problems during analysis by auto-diagnostics and auto-recovery functions

Air bubbles within HPLC/UHPLC flow channels can cause solvent delivery problems if they enter the solvent delivery pump significantly reducing the reliability of quantitative results. The auto-diagnostics and auto-recovery functions included in Nexera series solvent delivery pumps detect abnormal pressure fluctuations (pulsation) caused by bubbles in flow channels and automatically purge the pump to restore the system to normal. Consequently, instead of the user, the instrument monitors and manages the relationship between easily overlooked chromatogram abnormalities and flowrate changes that can cause pulsation, thereby preventing analysis failures.

Peak intelligence™ for peak processing

Until now, peak-finding algorithms have required the user to fiddle with multiple parameter settings before they can start data processing. Additionally, when the algorithm can't deal with a chromatogram, an experienced user has to select the peak by hand. This all adds up to extra time and hassle. Peak intelligence is a world-first algorithm incorporating AI assistance to search for chromatography peaks and process data with the same skill level as experienced users. The algorithm can be implemented immediately without adjusting any parameters and reduce wrong detection by 1/3 compared conventional algorithm with default setting.

Separating unseparated peaks using a PDA detector detecting overlapping peaks with i-PDeA II

Coelution of target peaks affects quantitative accuracy and may require checking for such peaks with a mass spectrometer or any other instrument with high selectivity is used for detection. Further, if unseparated peaks are discovered, it usually requires reassessing peak separation in the column. The i-PDeA II (Intelligent Peak Deconvolution Analysis II) uses a PDA detector to identify overlapping peaks that were not adequately separated by the column and either separates those peaks in the chromatogram or determines the UV spectrum of each peak. Consequently, it can be used to check for impurity peaks hidden by key component peaks, extract chromatograms for individual components.

LabSolutions MD-solution for method development and Analytical Quality by Design

LabSolutions MD software uses an "Analytical Quality by Design" (AQbD) approach for achieving efficient method development by designing analysis methods based on science and risk. All workflow steps, including analysing samples with the experimental design, building a design space by using the analytical results, and evaluating robustness after deciding the optimal analytical conditions can be completed using LabSolutions MD software. The software outputs a report that summarises the experimental design, design space, chromatograms and other relevant information. It also manages the information in a database to ensure data integrity.

To summarise, Shimadzu LC systems, owing to its highly proven and prominent performance, added the Analytical Intelligence (AI), supports the data acquisition regardless of the user's experience. Analytical Intelligence consists of various supporting functionalities that were developed for the purpose of promoting higher efficiency through workflow improvements. Automatic operation of the system, which simulates operation by an expert analyst, reduces the risk of system problems. The Analytical Intelligence establishes a new style of workflow which ensures for more reliable data, more efficiency and less burden, enhancing automation in analytical testing and operations.

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