VOL. 17 NO. 3 PAGES 72 www.expresspharma.in

EXPRESS PHARMA

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

MARKET

Virtual Clinical Trials: A renaissance in the making?

avantor™

Chromatography Solutions

Avantor® Hichrom® GC capillary columns for gas chromatography applications

Offering more than 50 different phases in GC capillary columns to provide an access to the widest range of chemistries for your GC application requirements.

RANGE OF DIMENSIONS AVAILABLE:

- Length: 1 to 150 m
- Internal Diameter: 0.05 to 0.53 mm
- Film Thickness: 0.05 to 7.00 µm
- Temperature max. limits: 150 to 400 °C (depend on phase & film thickness)

RANGE OF FORMATS AVAILABLE:

e.g. Hichrom® HI-5 GC column (5% phenyl 95% methylpolysiloxane) is avalable in following formats.

HI-5	Standard
HI-5 HT	High Temperature
HI-5 MS	Low bleed for MS
HI-5 MS XIL	Ultra-low bleed for sensetive MS

Find out more on GC applications:

For enquiries:
chromatography.India@avantorsciences.com

01/2022-EL-KS
ZPROVWRI36877-IN

VOL. 17 NO. 3 PAGES 72
www.expresspharma.in

EXPRESS PHARMA

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

+

Market

The slowing trend of ANDA approvals in 2021: Pandemic effect or selective filings?

Strategy

Analysing decriminalisation of biodiversity provisions under 'The Biological Diversity (Amendment) Bill, 2021

VIRTUAL CONFERENCE

IDEAL CURES

PRESENTS

FDD CONCLAVE 2021

FORMULATION DEVELOPMENT & DRUG DELIVERY CONCLAVE

IN PURSUIT OF EXCELLENCE

The fourth edition of FDD Conclave witnessed FR&D leaders and experts congregate to confer and converse on the new global realities and share learnings to leverage different dosage forms and drug delivery systems

WHIRL-PAK®

a Nasco SAMPLING brand

OVER 60 YEARS

TRUSTED, PUNCTURE-PROOF CLOSURE TABS

- worry-free, no-leak closure for sample integrity

+1 POST-MANUFACTURING STERILIZATION

- increased sample integrity
- perforated closure to maintain sterility

OPAQUE POLYETHYLENE FILM

- maximum protection for samples that are sensitive to light
- FDA approved for food contact
- ideal for pharmaceuticals, supplements, and many other liquid and solid samples·

"the black bags provide maximum protection for photosensitive samples"

THE COST EFFECTIVE, PREMIUM QUALITY SAMPLING MUST-HAVE YOU CAN TRUST, WHIRL-PAK.

Whirl-Pak® sterilized sampling bags are R-Nase, D-Nase, Pyrogen and BPH free and comply with regulatory and industrial requirements: FDA

LEARN MORE

whirl-pak.com

+91 75060 42889

abisen@whirl-pak.com

CELEBRATING 25th ANNIVERSARY

GANDHI Automations Pvt Ltd

India's No.1 Entrance Automation & Loading Bay Equipment Company

Stainless Steel Rolling Shutters

- Stainless Steel Rolling Shutters are made of SS304 or SS316 interlocked profiles and are high grade high performance.
- They are capable of withstanding adverse weather conditions, thus providing 100% safety and security.
- They are easy to clean, have longevity and are low maintenance.
- These shutters are easy to operate, install and have a very good corrosion resistance while providing an appealing finish.
- The shutter slats are also available in larger sizes and can be customized to clients requirements.
- Operational safety is ensured through power limit.

Dock Levelers | Dock Shelters | Fire Rated Shutters / Doors | High Speed Doors | Sectional Overhead Doors

STAR EXPORT HOUSE (Government of India Recognised)

World's Safest Rolling Shutter

CE

INDIAN GREEN BUILDING COUNCIL IGBC MEMBER

TUV NORD ISO 9001 / ISO 14001 / ISO 45001

ISO 9001 : 2015, ISO 14001 : 2015
ISO 45001 : 2018

24X7 TOLL FREE 1800 209 0200
From Anywhere in India

Corporate Office : Chawda Commercial Centre, Link Road, Malad (W), Mumbai - 400064, India
Tel : +91 22 6672 0200 / 0300 (200 Lines) | Fax : +91 22 6672 0201 | Email : sales@geapl.co.in | Website : www.geapl.co.in

PROSOLV® SMCC

Silicified Microcrystalline Cellulose

- Excellent compactibility
- Better content uniformity
- Cushioning effect owing to silicification
- Better synergy with compression sensitive API
- Improves DT
- Extra-ordinary compressibility
- Ideal for Wet granulation, Multi-particulate system and Direct compression
- Pharmacopoeia status - USP/NF, JPE
- Multi-functionality co-processed concept

JRS PHARMA FAMILY
A Member of the JRS Group

• Excipients • Coatings
• Biopharma Services • Technical Services

RETTENMAIER INDIA PVT. LTD.
B/816, Lodha Supremus II,
Road No. 22, Wagale Estate,
Thane (W) Maharashtra - 400604.
Tel: 022 4024 3817-21
Email: info-india@jrs.de

www.jrspharma.com

EXPRESS PHARMA

Chairman of the Board
Viveck Goenka

Sr. Vice President-BPD
Neil Viegas

Asst. Vice President-BPD
Harit Mohanty

Editor
Viveka Roychowdhury*

BUREAUS
Mumbai
Lakshmipriya Nair, Kalyani Sharma

Delhi
Akanki Sharma

DESIGN
Asst. Art Director
Pravin Temble

Senior Designer
Rekha Bisht

Senior Artist
Rakesh Sharma

Digital Team
Viraj Mehta (Head of Internet)

Marketing Team
Rajesh Bhatkal
Ambuj Kumar
Ashish Rampure
Debnarayan Dutta

PRODUCTION
General Manager
BR Tipnis

Production Co-ordinator
Dhananjay Nidre

Scheduling & Coordination
Arvind Mane

CIRCULATION
Circulation Team
Mohan Varadkar

CONTENTS

MARKET

12 | **VIRTUAL CLINICAL TRIALS: A RENAISSANCE IN THE MAKING**


Sowmya Kaur


Jinu Jose


Henry McNamara

18 | **SLOWING TREND OF ANDA APPROVALS IN 2021: PANDEMIC EFFECT OR SELECTIVE FILINGS?**


Meenu Grover Sharma


Dr Professor Harvinder Popli

STRATEGY

36 | **ANALYSING DECRIMINALISATION OF BIODIVERSITY PROVISIONS UNDER 'THE BIOLOGICAL DIVERSITY (AMENDMENT) BILL, 2021**


Aditya Bhattacharya


Kunal Kapoor

Express Pharma®

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

Editor: Viveka Roychowdhury.* (Editorial & Administrative Offices: Mafatlal Centre, 7th floor, Ramnath Goenka Marg, Nariman Point, Mumbai 400021)

Filling the gaps in India's pharma manufacturing supply chain

This Republic Day, the nation honoured the vaccine makers – Serum Institute of India's Dr Cyrus Poonawalla, and Bharat Biotech's Dr Krishna Ella and Suchitra Ella – with Padma Bhushans, the third highest civilian award. As we start the third year under the shadow of the COVID-19 pandemic, there is no greater acknowledgement of the importance of the sector, vital to India's future health, both at the citizen and corporate level. Will this sentiment also be reflected in Budget 2022 allocations? Will the Finance Minister have the fiscal space to do so? We will know this by 1st February, but as I write this on 27th January, it is anyone's guess.

However, even if Budget 2022 falls short of support, PE and VC players are stepping up to support key parts of the sector, most notably the much neglected API segment.

Most recently, on 24th January, Advent International acquired a controlling stake in Hyderabad-based Avra Labs, a contract manufacturing and research services (CRAMs) and speciality Active Pharmaceutical Ingredients (APIs) manufacturer. The PE player has reportedly invested in over 20 businesses in pharma R&D, production and distribution with the goal of "creating a top five merchant API Platform in India" – a goal, which presumably predates the pandemic by at least three decades. Since 1990, Advent has invested $10.5 billion in 52 companies in the sector worldwide. In addition to Avra Laboratories, recent pharma and healthcare investments by Advent include GS Capsule, BioDuro-Sundia, RxBenefits, RA Chem Pharma, ZCL Chemicals, Bharat Serums and Vaccines, Industria Chimica Emiliana, Vitaldent, Definitive Healthcare, Zentiva, AccentCare and Iodine Software.

Carlyle is another global PE player investing to create a global generics player based out of India. The group made significant investments last June and November in Viyash Life Sciences, which is already a leading manufacturer of APIs and intermediates. Viyash was set up by ex-Mylan veteran Dr Hari Babu in partnership with Dr Srihari Raju Kalidindi, with a strategy to 'consolidate other pharma intermediates, API and formulation assets to create an integrated offering for large generics customers', as per a release. With the acquisitions so far, Viyash already has ten manufacturing facilities in India with a combined capacity of ~2000 KL as well as one formulation facility in the US, and CEO Dr Hari Babu has indicated that the next phase will be about integration across these businesses.

The lessons of the past – of spiralling API costs, over-dependence on a shrinking list of API makers – have been well learnt

In November 2020, Asia-focussed PE firm PAG, with consortium partners CX Partners and Samara Capital, acquired a controlling stake in Chennai-based API manufacturer Anjan Drugs. Again, this was of the consortium's strategy to 'create a best-in-class platform for the development and production of bulk drug ingredients.'

Clearly, the lessons of the past – of spiralling API costs, over-dependence on a shrinking list of API makers – have been well learnt. As larger pharma companies look to de-risk their supply chain, API and ingredient makers have seen PEs and VCs lining up to invest in their scale up.

Many pharma companies are implementing various strategies, like the Government of India's PLI scheme, to de-risk from dependency on China for key raw materials and fill the gaps in India's pharma manufacturing supply chain. In fact, the pharma segment, and APIs, in particular, could see much more investment as new sectors emerge as contenders for PE/VC investments in the years ahead.

The Drugs Controller General of India's (DCGI) nod for regular market sales of Covishield and Covaxin for adults, albeit under certain conditions, is another affirmation of the importance of the biopharma sector. Even though the vaccines will still not be available for sale at chemists, hospitals and clinics can now purchase the vaccines. Hospitals and clinics will have to submit vaccination data to DCGI every six months and related data will be updated on CoWIN app, as per news agency reports. As these are still relatively newer vaccines, the government has indicated that adverse events following immunisation will continue to be monitored.

All in all, as we enter the third year of the COVID-19 pandemic, the country seems better placed to ride out the Omicron-driven third wave. Let this year's Padma Bhushans be a reminder that hard work pays off but let us not wait for a pandemic to invest in pharma and healthcare infrastructure.

VIVEKA ROYCHOWDHURY, *Editor*
viveka.r@expressindia.com
viveka.roy3@gmail.com

CRAFTSMANSHIP

BEYOND COMPARE. IT'S WHAT WE ARE KNOWN FOR.

Dear Partner,

Providing our customers with the highest quality products means having a great design understanding, for a variety of applications. Thankfully, we do, with the backing of partners like Hanns G Werner GmbH+ Co. KG.

As the leading manufacturers of exceptionally high-quality neutral sugar pellets used as drug-free cores for sustained release formulations, Hanns G Werner GmbH+ Co. KG is well-regarded for their stringent quality control, cutting-edge technology, ever-evolving research and innovation.

Signet-ure craftsmanship

pharm-a-spheres™

Particle Size Range (Mesh ASTM)	Diameter (in microns)
170-100	150-90
80-100	180-150
70-80	212-180
60-70	250-212
50-60	300-250
40-60	425-250
40-50	425-300
40-45	425-355
35-40	500-425
30-35	600-500
25-30	710-600
20-25	850-710
18-20	1000-850
16-20	1180-850
16-18	1180-1000
14-16	1400-1180
12-14	1700-1400
10-12	2000-1700

Signet

The Complete Excipients Company

SIGACHI®

HiCel™ SMCC

Overspeed on your Tablet Press

HiCel™ Silicified Microcrystalline Cellulose, a high functionality excipient for Direct Compressible tablets, is a combination of binder, filler Microcrystalline Cellulose and glidant Silicon dioxide. **HiCel™ SMCC** delivers benefits such as,

- Excellent Flowability
- Less Disintegration Time
- Superior Physio-mechanical Properties
- Improved blending properties and tablet hardness
- Increased Production Capacity,
- Minimal Dust Formation during Blending.

Different grades of HiCel™ SMCC manufactured by Sigachi®

Sr No.	Grades	Average particle size (µm)	Bulk density (g/ml)	Application
1.	HiCel™ SMCC 90M	125	0.25-0.37	Formulas in which a balance of flow andcompaction are required.
2.	HiCel™ SMCC 50M	65	0.25-0.37	Formulas in which optimal compaction and decent flow are required.
3.	HiCel™ SMCC LM90	125	0.27-0.39	It is low moisture content (3.0%) grade and recommended for extremely moisture sensitive active ingredients.
4.	HiCel™ SMCC HD90	125	0.38-0.50	This is higher density grade of SMCC, it has excellent flowability and facilitates thinner tablets. This grade gives the best disintegration time.
5.	HiCel™ SMCC SCG 90	165	0.27-0.30	This grade has been specially developed for high density with fine particles API's, it improves compressibility and flowability of the poor flowable API's.

SIGACHI® has been synonymous with highest excipient and service quality. Since the last 30 years, Products manufactured and supplied by Sigachi has been gaining traction in the Regulated markets all across the world. The Government of India approved R&D Lab and Excipient Application lab has been providing relentless support to customers, across more than 36 countries.

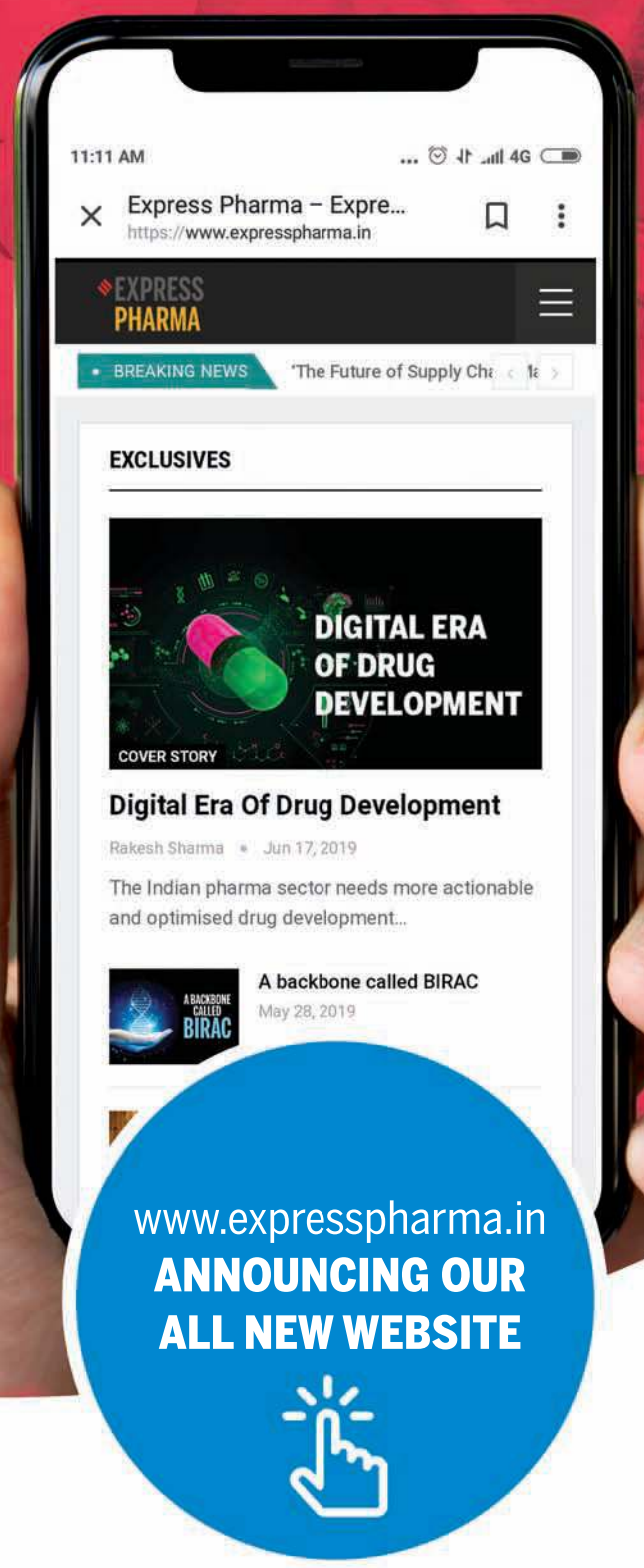
Corp Office: 4th Floor, Kalyan's Tulsiram Chamber's, Madinaguda, Hyderabad - 500 049, T.S. India.

www.sigachi.com

Tel: +91 - 40-40114874 / 75 76
E-mail: mktg.bd@sigachi.com, mktg@sigachi.com

THE INDUSTRY IN YOUR POCKET

And it is just the way you want it!



NOW, FIND ALL YOU WANT. INDEPTH.

- DRUG APPROVALS
- DEALS
- REGULATIONS/POLICIES
- TECHNOLOGY
- THOUGHT LEADERSHIP
- BUSINESS STRATEGIES
- RESEARCH
- LOGISTICS
- INFRASTRUCTURE
- MARKETING
- HUMAN RESOURCES
- AYUSH
- BIOTECH
- NUTRACEUTICALS

www.expresspharma.in

ANNOUNCING OUR ALL NEW WEBSITE

RE-IMAGINED AND REDESIGNED FOR YOUR READING PLEASURE.

- NEWS AND ANALYSIS
- EDITORIAL FEATURES
- GUEST BLOGS FROM INDUSTRY LEADERS
- EBOOKS AND DOWNLOADABLE CONTENT
- BUSINESS VIDEOS AND INTERVIEWS
- WEBINARS AND EVENTS

VISIT US ON YOUR MOBILE, TABLET OR PC TO EXPERIENCE THE DIFFERENCE TODAY.

Facebook
Join us on Facebook

Linkedin
Follow us

Twitter
Join us on Twitter

RSS
Subscribe our RSS

Virtual Clinical Trials
A Renaissance in the Making

The shift towards virtual clinical trials, spurred by the pandemic, is ushering newer research models that are more convenient, transparent and patient-centric. India needs to invest in the right technologies, policies and people to be a leader in this space and leverage its huge potential

By **Lakshmipriya Nair**

Since the onset of the COVID-19 pandemic, we have seen Austrian economist *Joseph Schumpeter's* concept of creative destruction come into play often. As the wily virus caused chaos and mayhem to social and economic activity globally and challenged existing models and current systems, it left no one with any option but to adapt and innovate. As a result, we have witnessed businesses and systems replace their long-standing and sometime obsolete practices, products and services with more effective and innovative approaches and offerings to survive and thrive during the pandemic. Decentralisation of clinical trials is a case in point.

Trials and tribulations

An article published online in *The Lancet* in December 2021 informs that the COVID-19 pandemic affected scientific research worldwide and over 2000 trials registered on *ClinicalTrials.gov* were stopped. Delays in regulatory approvals, hassles with site set-ups and delegation of responsibilities, limited scope for site visits, lack of participation by health units and clinicians, enrollment of patients for the study, etc were some of the challenges of doing clinical research during the pandemic.

KEY STEPS IN A VIRTUAL CLINICAL TRIAL (VCT)

Patient recruitment: In VCTs a combination of traditional patient recruitment and digital recruitment is used. When happening digitally, patients are targeted directly via web-based platforms. This allows faster recruitments without geographical limitations. Patients don't have to travel to sites to sign up for the study; instead, they could send in e-consent forms. Technology reaches patients who would be most suitable for the study, ensuring that they participated with minimal travel to the site, significantly increasing patient participation and retention during clinical research studies.

Phone-based visits: While some in-person office visits will always be required (e.g. to perform certain testing, and conduct physical examinations), the hybrid approach with replacing few in person visits with phone based visits can lead to increase patient retention as well as cost optimisation.

Remote electronic monitoring: As both the complexity of clinical trials and demand for remote site connectivity is increasing, research organisations are looking for solutions to lower cost and remove inefficient workflows. COVID-19 has further emphasised the need for remote clinical trial monitoring solutions.

Patient retention: VCTs are patient centered, meaning that they are based from the patient's home and connect with the patient's own smart phone. This increases the convenience for patients, especially for elderly and disabled.

Digital health data collection: After patients are recruited for a study, it is important to collect data during the clinical research study process. There are multiple ways to collect this data using digital tools. Demographic and medical health data, patient activity, and physiological parameters, patient-reported outcomes, along with images, can now be collected using electronic medical records, smartphones, or tablets.

Safety monitoring in virtual trials: The fast pace of digital technology movement into routine processes in a clinical trial has helped in significantly improving efficiency, reducing time and cost for sponsors. New tools are now being paired with traditional biomarker assessments to enhance safety and validation.

Data Security: To develop intelligent clinical trials that do not require constant human monitoring but are dependent on advancements in technology, certain challenges need to be addressed. There is an increased need to tighten data security during collection, transmission, and analysis. To overcome this, the FDA has put forward specific guidelines, like conveying information collected by the digital tools to all stakeholders. Medical device certification has been developed as a measure to control data breach.

Data analytics: Flexible, extensible, and scalable clinical trials can be carried out only with the support of effective data analysis. For example, an AI and ML powered platform enables study investigators to connect remotely and access data from clinical trials in near real-time. Such emerging technology helps automate processes and mapping data, with advanced analytic methods applied to manage multiple facets of clinical trials.

Optimising trial methods: There are multiple ways in which virtual resources support clinical trials optimisation. A method of intervention optimisation, called micro-randomised trials, involves identifying factors like dose and timing that can be managed better using reminders. Such engagement strategies are best suited for patient recruitment, enrolling and retention. The personalisation of the clinical trial process helps in enhanced patient participation in clinical trials.

Limited number of sites in VCTs: Number of sites in VCTs are limited. For the same principal investigator, a team of multiple sub investigators can ensure health and safety of participants via remote visits where patients contribute with data virtually via their smart phones.

- ***Sowmya Kaur***, *EVP – Navitas Clinical Research and BU Head Clinical APAC*

Henry McNamara, Sr VP and GM, Oracle Health Sciences shares his views on this situation and explains, "The COVID-19 pandemic radically changed clinical operations forcing the clinical research community to re-evaluate how to manage clinical trials. In a flash, physical access to patients across the globe became infeasible, causing a significant impact on clinical data collection and patient monitoring."

"The biggest factor delaying clinical trials today – exacerbated by COVID-19 – is enrolment. It's difficult to find enough patients to participate in trials. The study found that more than half (51 per cent) of respondents identified longer enrolment timelines as one of the key ramifications of the pandemic. This is partly due to the inconvenience of trial participation for the patient. For instance, some patients may be living away from the site, so in-person visits can be a large inconvenience," he adds.

These circumstances have paved the way for accelerated adoption of virtual clinical trials (VCTs) worldwide, altering the traditional approaches to clinical trials, probably for ever.

The age of VCTs

A GlobalData report titled *'Virtual Clinical Trials – Thematic Research'*, states, "COVID-19 lockdowns and social distancing measures caused significant disruption to clinical trials and accelerated the use of virtual trials. Companies that had not considered this model before had no option but to rapidly implement new technologies and procedures to maintain business continuity, and many companies will continue to use virtual trials post-pandemic. 67 per cent of the participants cited COVID-19 as the reason they plan to use decentralised clinical trials in the future."

McNamara shares data from an Oracle-commissioned study by Informa Pharma Intelligence that reveals "76 per cent of respondents accelerated their adoption of decentralised clinical trial methods during the COVID-19 pandemic."

Why? Well, as Sowmya Kaur EVP – Navitas Clinical Research and BU Head Clinical APAC explains, "A virtual clinical trial harnesses the power of technology to improve patient recruitment, retention,

> The market outlook for virtual clinical trials is very bright. The global virtual clinical trials market is expected to grow from $ 2,092.67 million in 2020 to $5,521.67 million by the end of 2025

collection of data, and analysis. They support efficient trials as they tap into digital technologies, like apps, monitoring devices, and online social engagement platforms to conduct each stage of the clinical trial. This includes enhanced support for recruitment, informed consent, patient counseling, measuring clinical endpoints, and in determining adverse reactions."

"The advent of digital solutions in clinical trial management and conduct has improved transparency, with an onus on delivering better healthcare. Consumers or patients have access to a wide range of information, and, with this dissemination of information, there is increased expectancy. This has initiated a need for rethinking clinical trials to maximise benefits. There has been a significant shift towards embracing the incredible advantages of data analytics, along with digital models of engagement, to forge clinical trials that cater to the current demands," opines Kaur. *(Check Box: Key steps in a virtual clinical trial)*

"Virtual trials ease the patient burden of traveling to sites for multiple visits and tests, remove geographic and logistical constraints to participation, and leverage technology for real-time information access and communication between sites and patients. Investments in technology and remote trials were underway before COVID-19 due to cost and efficiency considerations and the pandemic will only catalyse these developments", points out Jinu Jose, VP, Head – Sales and Clinical Operations, R&D Solutions, IQVIA India.

Thus, the market outlook for virtual clinical trials is very bright. The global virtual clinical trials market is expected to grow from $ 2,092.67 million in 2020 to $5,521.67 million by the end of 2025, as per a report by *ResearchandMarkets.com*. Another recent report by *ResearchandMarkets.com* states that the global eClinical solutions market is expected to grow from $6,784.59 million in 2021 to $14,897.53 million by 2027at a CAGR of 14 per cent.

KEY AREAS FROM AN ETHICAL PERSPECTIVE AS VIRTUAL TRIAL ECOSYSTEM IN INDIA EVOLVES

Informed consent: Linguistic differences, literacy levels, therapeutic misconceptions, socio-cultural aspects, and perceptions about the medical system make informed consent an important focus area. The compliance issue of participants with digital tools needs to be considered throughout the ongoing trial, especially for trials involving certain vulnerable populations for whom the use of technology is an arduous task for them.
Vulnerable populations: Working with these populations requires careful consideration
Investigational Medicinal Product (IMP) management: Shipping, administering, and tracking the IMP poses certain challenges in terms of storage at the patient's residence, logistics and adherence.

*- **Jinu Jose,** VP, Head – Sales and Clinical Operations, R&D Solutions, IQVIA India*

MANAGING THE DELUGE OF DATA

The amount of data is far more information than humans can process or manage and outsourcing or throwing more people at the problem is no longer sustainable or effective. Not only is there more data, but it is also much more complex.
AI and ML are currently being incorporated into advanced, cloud-based life sciences technology platforms to support trial design, data monitoring, and safety case management. But this is only the beginning. Five years from now, a patient's clinical trial experience could be very different. Wearables combined with cloud technologies will enable continuous and instantaneous data collection and advanced analytics that is fed back to the study teams developing new treatments. Each enrolled patient could be creating millions of data points a week—or even per day. That could mean more accurate assessments as the data will reflect the patient's everyday experiences.
To support the move to decentralised clinical trials and the variety and volume of patient data that is going to come with it, organisations need a single platform where the data can be collected, harmonised, and analysed quickly and efficiently. In the past, sponsors and CROs may have used point solutions designed to improve specific processes in clinical trials, such as electronic data capture (EDC), and drug randomisation and supplies management (RTSM). But as these systems weren't built to work together, it causes process redundancy and data quality issues. The data streaming in from remote devices and patient apps further add to the complexity.

*- **Henry McNamara,** Sr VP and GM, Oracle Health Sciences*

Advantage India

Clearly, virtual clinical trials are set to increase, but what does this mean for India? Well, industry stakeholders seem to share a positive outlook about India's potential for growth in this sphere.

Jose informs, "The investments we have seen in building the decentralised trial infrastructure have been unprecedented. These developments, coupled with the introduction of the *New Drugs and Clinical Trials Rules, 2019,* which was a significant milestone, will encourage more global clinical studies to be conducted in India, thus improving access to treatment for patients."

He shares, "Given its large population and growing disease burden, unmet medical needs, highly trained, English-speaking healthcare professionals, clinical research professionals, leadership in information technology, advancements in mobile and internet accessibility and burgeoning patient population, India possesses immense potential for conducting global decentralised clinical trials."

"The growing number of pharma companies in developing Asian countries such as China, India, Taiwan, and Korea has also opened up growth opportunities for the eClinical solutions market in this region," states Kaur.

Preparing for progress

However, to leverage the advantage and optimise the growth potential, there is a need to put certain measures into place. So, what do the industry experts recommend?

◆ **Invest in the right technologies:** GlobalData's report titled 'Virtual Clinical Trials – Thematic Research' highlights a considerable increase in deal-making activity in the virtual trials space over the past 18 months. Nine M&As linked to virtual trials were witnessed in 2020, instead of one in 2018 and two in 2019, as per the report. In 2021, this segment has seen some major M&As including Thermo Fisher's acquisition of PPD for $17.4 billion in April 2021 and ICON's acquisition of PRA Health Sciences for $12 billion in February 2021.

India needs to learn from the global playbook and invest in existing and emerging technologies to build and fortify its position in the virtual clinical trials space.

Industry experts also underscore this fact and elaborate on the importance of emerging technology in this space. McNamara points out, "The ability to do home health, virtual visits, and telemedicine are key to making trials easier for patients, which lessens the enrolment barrier. Whilst the technology has existed, two key barriers have precluded its adoption: state/regulatory support and end-user (physician) acceptance. COVID-19 has broken down these barriers almost overnight, triggering mass relaxation of regulatory hurdles, and likewise immediate realisation by the medical community that video can work, and in many cases, is better than face-to-face interactions."

Jose adds, "Great advances have been made in AI and machine learning (ML), which can be applied to automate many data-heavy processes to lessen

the pressure. AI and ML not only process data faster than humans, but they can also point to patterns and trends that humans can't see. This ideally leads to a more accurate and detailed view of how patients are responding in trials, which can lead to better patient experience, better therapies, and treatments in the long run."

Kaur weighs in, "The need to invest in digital tools like Artificial intelligence (AI) and Machine Learning (ML) tools is crucial. These tools help ensure clinical trial continuity during and post the pandemic era. Significant strides in incorporating digital health solutions began a few years ago, more as experimental solutions or as support for certain sections of clinical trials. Such investments have paved the way for hybrid clinical trials that are guiding forces for successful and efficiently run clinical trials."

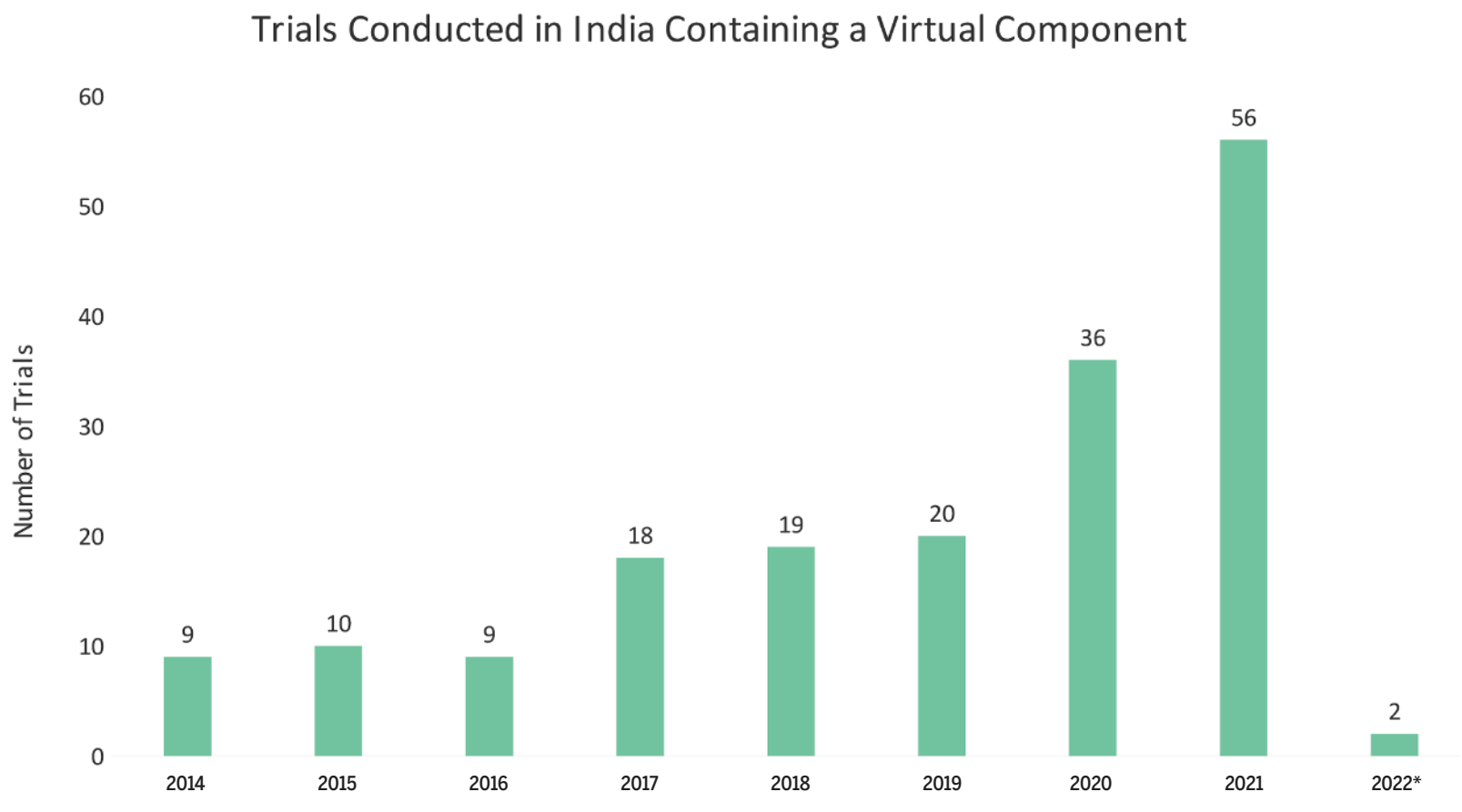
◆ **Adequate regulatory support:** Regulatory support and flexibility to accommodate novel approaches and interventions for disease management is crucial. Indian regulators should promote and encourage initiation and conduct of virtual clinical trials in an ethical manner with appropriate processes and policies. Fortunately, industry stakeholders inform that regulatory pathways in India for clinical trials are evolving to keep pace with changing demands.

Jose updates, "Indian clinical trials regulations have evolved over the last few years and introduction of the *New Drugs and Clinical Trials Rules, 2019* has been a significant milestone infusing significant interest and confidence in the clinical trials industry. During the pandemic, the clinical trial industry worked very closely with regulators on innovative trial designs, improvised pathways for approvals, and use of digital health platforms in various aspects of the clinical trial continuum. We hope that these will continue beyond the pandemic to sustain the momentum and fast track the clinical trial application review process."

He further opines, "While these were short term measures, we are confident that this opens many possibilities to further improve the overall clinical trials process and leverage technology and automation to bring drugs to markets faster while reducing the overall cost of development. Some of the specific areas in virtual trials that require focus from a regulatory perspective include – IMP management, patient consent, use of digital platforms, documentation, and access to data. We also believe that there are significant opportunities for the industry to proactively partner with regulators to drive continued innovations and faster adoption of newer ways of working."

"In the context of the pandemic, the regulators have been willing and flexible to adopt new technologies and provide quicker approvals. As the pandemic situation spiraled, regulators moved with speed to issue guidance enabling sponsors to introduce new approaches and protocols for clinical trials,' states Kaur.

◆ **Build better security management systems:** Jose explains, "Cyber security, privacy and data protection are



Source: Priya Nair, Clinical Trials Analyst, GlobalData

key tenets of managing a clinical trial. Any service delivery model that has a backbone of data and technology is prone to cyber-attacks and data thefts. The conventional clinical trial processes are largely automated (electronic data capture, trial management, document exchange, IMP management etc.) and while virtual trials introduce a layer of technology, the risk does not significantly rise."

"While continuing to invest in world class technology, cyber security and digital capability can help mitigate the risks to a larger extent. We believe that investments in training, education, and increasing awareness of employees and the larger clinical research ecosystem we operate can significantly help better manage these risks," he adds.

Kaur enlightens, "As clinical trials take a digital approach the complexity grows along with the risk to data integrity. The challenge is the difficulty in securing a clinical trial eco system that may involve hundreds of data input points, trial sites, networks and applications, including patient's own devices like wearables, smart phone apps being on the constant rise."

She adds, "It is critical when designing a clinical study, to map the data flow, from where the data is generated, how it is stored and how many software systems it flows through. Clear controls need to be in place at the sponsor's site, at the sponsor's trial partners to scan for malware and incorporate patch applications as soon as patches become available, and train/inform personnel on how to protect data."

However, Kaur also informs that increased use of technology is being accompanied by development of better security management systems. She says, "Industry as well as regulators understand the utmost importance of data protection. The importance of data protection increases as the amount of data created and stored continues to grow at unprecedented rates. There is also little tolerance for downtime that can make it impossible to access important information. There are many storage and management options that can help to restrict access, monitor activity, and respond to threats (e.g.,Data loss prevention, Storage with built-in data protection, Firewalls, Encryption, Endpoint protection etc.,)"

◆ **Create a tech-savvy, digitally-skilled workforce:** A barrier to progress in virtual trial field is skill-shortage. GlobalData's State of the Biopharmaceutical Industry 2021 report cites lack of specific skills and talents as the key hurdle barrier to digital transformation initiatives. It is an imperative to recruit and train digital talent on priority to enable utilisation of remote technologies in clinical trials. The industry needs a workforce that is skilled in digital, advanced data analytics and AI/ML to leverage these tech solutions to generate and analyse datasets.

As Jose highlights, "The future of work in our industry will be at the intersection of strong clinical/medical expertise, use of data/analytics and digital platforms to achieve better outcomes for our patients. The foundation skill is and will continue to remain the ability to apply clinical and medical expertise in different contexts in a clinical trial. Data and analytics will be pervasive in our decision making and the use of new technology platforms will drive the future of our work. Therefore, we need to continue to invest in building skills in emerging areas including data, analytics and digital platforms.

He adds, "Remote working lends itself well to the decentralised trial model. Virtual trials will open new opportunities for professionals in the areas of information technology, logistics, patient care (home health nursing/phlebotomy support) and training."

Kaur emphasises, "Virtual trials mandate the need for a digital-savvy workforce which is required to satisfy patient health and well-being demands, which will be frequently delivered through innovative technology-based applications. The focus for professionals in the industry should be on developing skills in technology like AI, ML etc., data analytics, governance of data and more."

On an optimistic note, Kaur shares, "About 50 per cent of workers find themselves as digital natives, with the figure set to rise to 75 per cent by 2025. Within the next few decades, the entire workforce will have grown up under the ubiquitous influence of the Internet and other technologies. Digital natives are already shaping the future of working life: as a new generation enters the workforce, business processes will continue to modernise in view of evolving skill sets."

VCTs are here to stay

Jose says, "The process, technology and infrastructure supporting virtual trials is evolving. Like with most emerging industry solutions, we do expect that over a period there will be consolidation, standardisation, and greater maturity of the

ecosystem supporting virtual trials. In the future, we believe that this will pave the way for not only for reduced R&D costs but also better data quality, access to patients, better diversity, improved protocol adherence, reduce study drop-out, faster patient recruitment and reduced cycle times for clinical trials."

McNamara opines, "Today's environment has helped push the industry from looking at decentralised trials as a series of pilots to accelerating adoption because they are simply a better way to operate. Organisations have adapted to decentralised trials quickly in the face of the global pandemic, but the industry needs to embrace this change not as situational, but as a permanent evolution. With the right processes and technologies in place, the shift can be advantageous to patients, sites, and sponsors moving forward. Ultimately, decentralised trials will change clinical research forever, driving patient centricity, richer real-world data, and faster development of life-enhancing therapies and treatments.

"Virtual clinical trials enable improving patient-centric experience, offers a cost-effective, and easy to manage solution. All these indicators provide a compelling insight for virtual trials to become the default in the post COVID era," asserts Kaur.

Thus, the outlook for VCTs is very positive given the myriad advantages they offer over traditional, site-based clinical trials. Therefore, as Kitty Whitney, Director of Thematic Analysis at GlobalData highlights, "While COVID-19 shone a spotlight on virtual trials, data show that the shift towards virtual trials was underway before the pandemic. Companies who are not already integrating virtual components into trials need to adapt their research models to become more patient-centric in order to recruit and retain more participants and improve trial efficiencies overall."

laxmipriyanair@gmail.com
lakshmipriyanair@expressindia.com

A barrier to progress in the virtual trial field is skill-shortage. GlobalData's State of the Biopharmaceutical Industry 2021 report cites lack of specific skills and talents as the key hurdle barrier to digital transformation initiatives

INSIGHT

Slowing trend of ANDA approvals in 2021: Pandemic effect or selective filings?

Meenu Grover Sharma, Principal Consultant, BusinessAssociar Consultants, New Delhi and **Dr Professor Harvinder Popli**, Director, School of Pharmaceutical Sciences, Delhi Pharmaceutical Sciences & Research University, New Delhi, analyse the changing market landscape and increasing costs of filing and maintaining ANDAs

Meenu Grover Sharma

Dr Professor Harvinder Popli

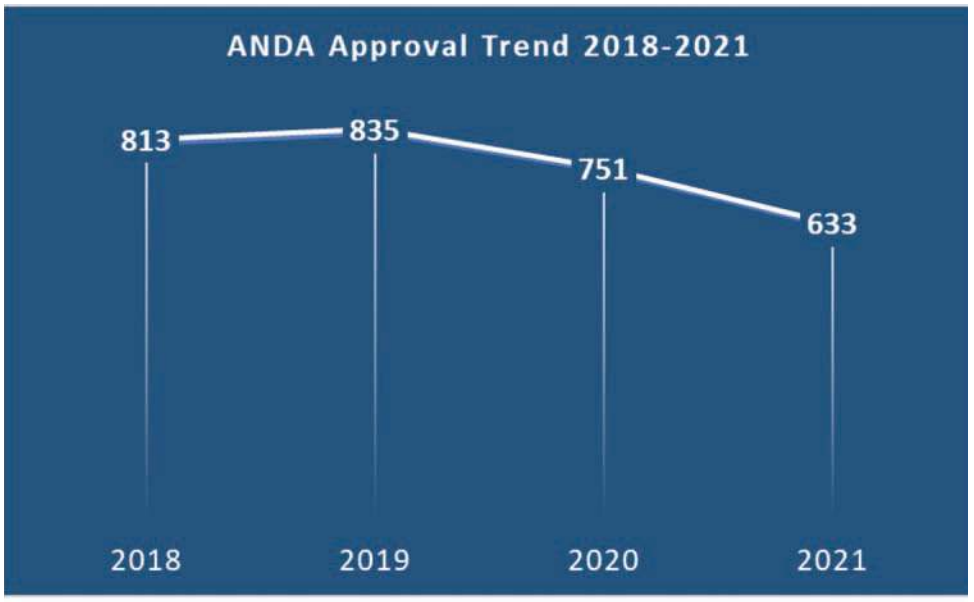
The dip in ANDA approvals that we witnessed in 2020 continued further in 2021 with a total of 631 final ANDA approvals granted during the calendar year, declining by further 16 per cent from the previous year. Additionally, 117 tentative approvals were also granted during the calendar year 2021, in the same range as tentative approvals during 2020 (123).

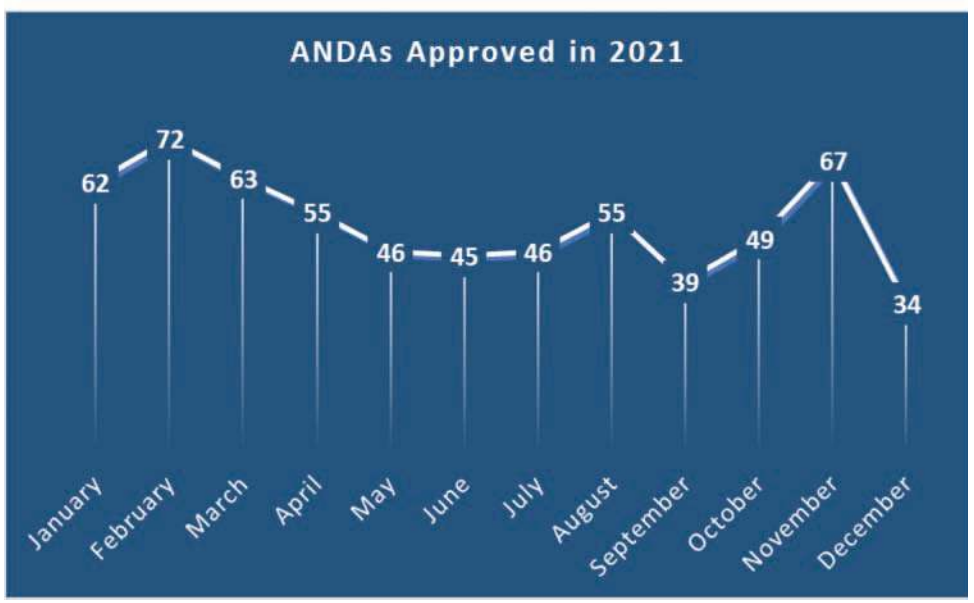
ANDA applicants were mapped to the parent company as recorded in the FDA database and the location/headquarter of the parent company was used for analysing the regional trends. As always, Indian companies dominated the ANDA approvals, with 267 or 42 per cent of total ANDA approvals. This was followed by the US, China, Europe and Israel in that order. Chinese companies (without Taiwan and Hong Kong) garnered 66 approvals during the year, maintaining their strong interest in playing in the forward-integrated space of formulations as well. There was one approval also for Bangladesh-based Beximco Pharmaceuticals. With at least a couple more companies from Bangladesh targetting the US market, we can see a small stream of ANDAs continuing from this country in the future. Taiwan is another geography with eight ANDA approvals for products filed by five different companies.

> As generic players become more selective, preferring the more complex and low-competition products, over higher number of filings, a slowing trend in ANDA approval is becoming evident

Oral dosage forms get the highest share of approvals as always, followed by injectables and topicals

With 394 approvals, oral dosage forms held about 62 per cent of ANDA approvals granted in 2021, followed by injectables with 146 and topicals with 44 approvals. Within the oral dosage forms, 79 are extended release/delayed release formulations and 55 approvals are for liquid formulations. Separately, one buccal film (Buprenorphine)





Regional trend: Indian companies continue to dominate, China maintaining presence

and three sub-lingual formulations also got approval. In injectables, Paliperidone Palmitate approval to Teva, Ferumoxytol approval to Sandoz, Calcitonin (Salmon) approval to Custopharm and Liposomal Amphotericin B to Sun Pharma are some of the notable ones. Within inhalations, most approvals were for inhalation solution vials except Budesonide suspension vials to Sun Pharma and Advair diskus generic to Teva. Ophthalmic category saw some of the more complex product approvals, including Loteprednol gel for Akorn, Brinzolamide suspension for Bausch Health, Difluprednate emulsion for Amneal and Cipla, and Tobradex suspension to Amneal. Another complex dosage form, vaginal ring, saw two approvals for Teva and DRL, both for Nuvaring generic taking the total of generics to this complex product to three.

ANDA approvals in 2021, dosage forms

First-time generics and CGT approvals: Indian companies again hold a significant share

There were 88 first-time-generics approved in 2021 and 52 approvals through the Competitive Generic Therapy (CGT) route. For the first-time generics approvals, 12 approvals were only for Droxidopa and five for Pregabalin extended-release tablets; 32 of the 88 first-time Gx approvals were garnered by the Indian companies, mostly for oral solid dosage forms (24). Teva, with nine approvals, is the leading company targetting the first-time-generics products, followed by Fresenius with seven approvals. Zydus and Sun Pharma with six approvals each are the top Indian companies with maximum first-time-generics approvals in 2021.

The US-based companies led the table for CGT approvals, getting 22 of the 52 approvals followed closely by the Indian companies with 20 approvals. Novitium Pharma, with its liquids capability, is the leading player for five CGT approvals in 2021, followed by Glenmark and Amneal with four each.

Several ANDAs continue to be discontinued in the approval year itself, increasing significantly by the following year

About nine per cent (55 of 633) ANDAs are already listed as discontinued in the approval year itself, in line with the trends seen in the previous years. Indian companies discontinued relatively fewer proportion of ANDAs. While in overall approvals, Indian companies hold 42 per cent share, for discontinued ANDAs, the share is about 31 per cent (17). Interestingly, 13 first-time-generics approvals are already showing as status "discontinued" within the approval year. One product approved through CGT route is also showing up as discontinued already.

Checking for ANDAs approved in 2020, about 21 per cent are already discontinued by now (154 of 751). The same number for 2019-approved ANDA is showing status as discontinued (152). So, about 10 per cent of ANDAs get discontinued in the same year and about 20 per cent by the next two years.

Seven of the top 15 parent companies are from India

Hetero, with 28 approvals (including its affiliates Annora

Pharma and Ascent Pharmaceuticals Inc), topped the overall list of companies getting final ANDA approvals in 2021 followed by Aurobindo (Including Eugia Pharma) with 24 and Teva (including Watson, Actavis and Arrow International) with 23 approvals. Fosun (Gland Pharma) was the leading Chinese parent company with 14 approvals which are expectedly mostly injectables.

Among the top 15, Teva had the highest number of first-time generic approvals (nine) followed by Sun Pharma and Zydus with six each.

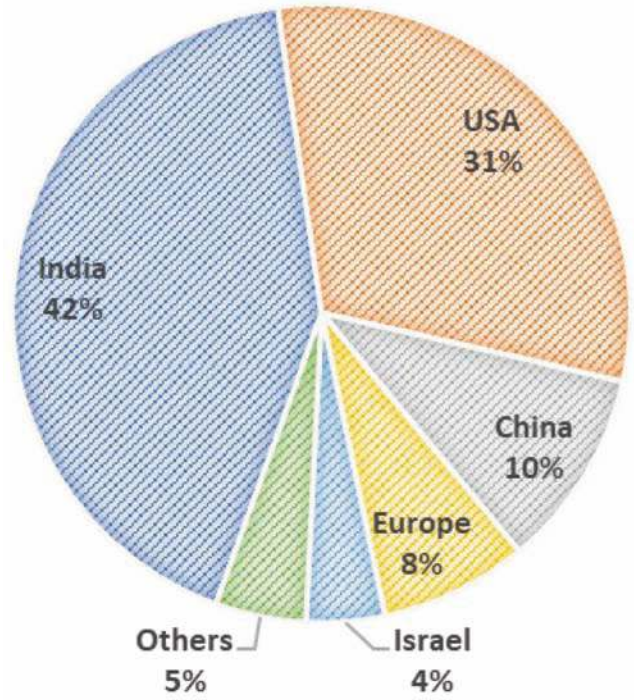
Key Highlights

- 633 Final ANDA Approvals granted in 2021, down from 751 in 2020
- Additionally, 117 Tentative Approvals
- Indian Companies account for 42% of total approvals, followed by US (31%) and China (10%)
- 62% ANDA approvals were for Oral dosage forms, proportion higher for Indian Companies (71%)
- 88 First-time-Generics approved in 2021 and 52 approvals through the Competitive Generic Therapy (CGT) route
- Zydus and Sun Pharma with 6 approvals each are the top Indian companies with the highest first-time-generics approvals in 2021
- Hetero with 28 Approvals topped the list of companies getting final ANDA approvals in 2021 followed by Aurobindo with 24 and Teva with 23 approvals
- 7 of the top 15 companies with the highest ANDA approvals are from India

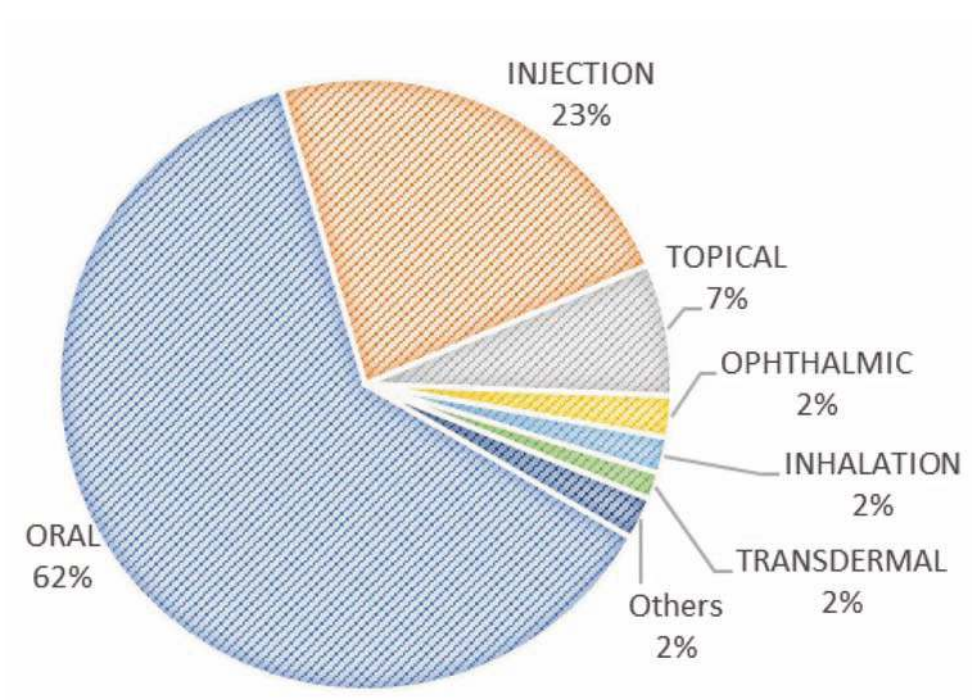
more complex and low-competition products, over higher number of filings, a slowing trend in ANDA approval is becoming evident, as we predicted in our analysis of 2019 approvals.

The changing market landscape and increasing costs of filing and maintaining ANDAs appears to be the more important driver of this change than the ongoing pandemic. We anticipate this trend to continue in the near future as well as companies continue to choose their investments carefully.

REGIONAL BREAKDOWN OF ANDA APPROVALS IN 2021



ANDA APPROVALS IN 2021, DOSAGE FORMS



(Location based on HQ of the parent company of the ANDA applicant)

All the approvals for Hetero were for oral dosage forms, including some for oral liquids. On the other hand, the other Indian companies in the top 15 had a much-varied presence across dosage forms, including complex dosage forms as well.

Harman Finochem (one ANDA - Metformin tablets), AET Pharma (two ANDAs- Posaconazole DR Tablets, Leflunomide tablets) and Enaltec Labs (two ANDAs- Chlorpromazine tablets, Fluphenazine tablets) are the Indian companies that got first-time ANDA approvals in 2021.

As generic players become more selective, preferring the

LEADING COMPANIES BY NUMBER OF ANDA APPROVALS IN 2021

	Parent Company	ORAL	INJECTION	TOPICAL	OPHTHA	INHAL.	TRANSDER.	VAGINAL	Total	1st Gx
1	HETERO LABS LIMITED	28							28	2
2	AUROBINDO PHARMA LIMITED	12	10	1	1				24	1
3	TEVA PHARMACEUTICALS USA	17	1			3	1	1	23	9
4	ALKEM LABORATORIES LIMITED	21*				1			22	2
5	SUN PHARMACEUTICAL INDUSTRIES IN	8	3	5	1	1			18	6
6	ZYDUS PHARMACEUTICALS USA INC	14	4						18	6
7	AMNEAL PHARMACEUTICALS LLC	11	2	1	2		1		17	2
8	NOVITIUM PHARMA LLC	15							15	4
9	ALEMBIC PHARMACEUTICALS LTD	7	1	3	1	1	2		15	-
10	DR REDDYS LABORATORIES LTD	13		1				1	15	2
11	MYLAN INC.	13	1				1		15	2
12	SHANGHAI FOSUN PHARMACEUTICAL		13		1				14	1
13	APOTEX INC.	7	2		1		1		11	4
14	NANJING KING-FRIEND BIOCHEMICAL		10						10	-
15	HIKMA PHARMACEUTICALS	3	7						10	1

Yellow-shaded companies are from India-parent company considered for all ANDAs

THE PURSUIT OF
EXCELLENCE

EXPRESS PHARMA

IDEAL CURES

PRESENTS

FDD
CONCLAVE 2021

FORMULATION DEVELOPMENT
& DRUG DELIVERY CONCLAVE

VIRTUAL CONFERENCE

16-17
DECEMBER, 2021

THANK YOU

WE THANK OUR PARTNERS, SPEAKERS AND PARTICIPANTS FOR EXTENDING THEIR SUPPORT IN MAKING THE CONFERENCE A GRAND SUCCESS

PARTNERS

IDEAL CURES
PRESENTING PARTNER

West
By your side
for a healthier world™
GOLD PARTNER

BECKMAN COULTER
Life Sciences
GOLD PARTNER

#FDDConclave

https://fdd.expresspharmaonline.com/


VIRTUAL CONFERENCE
IDEAL CURES
PRESENTS
FDD
CONCLAVE 2021
FORMULATION DEVELOPMENT
& DRUG DELIVERY CONCLAVE
IN PURSUIT OF
EXCELLENCE

Welcome Address

Viveka Roychowdhury, Editor, Express Pharma & Express Healthcare

Express Pharma recently hosted the fourth edition and the first-ever digital edition of the Formulation Development and Drug Delivery (FDD) Conclave.

FDD Conclave 2021 witnessed formulation scientists and R&D leaders came together to confer and converse on the current and future trends in the industry, their growth drivers and challenges under the theme "in Pursuit of Excellence".

It commenced with a Welcome Address by Viveka Roychowdhury, Editor, *Express Pharma & Express Healthcare*.

Welcoming the august audience, she said, "When we launched the FDD Conclave in 2017, it was with the sole aim of recognising the tireless efforts of the unseen champions in pharma formulation R&D. Of creating a networking space for FR&D scientists to discuss and debate the latest technologies and share best practices on topics ranging from the opportunities across dosage forms from OSDs to injectables.

Speaking on this year's edition, she added, "We take the next step on this journey today 'In pursuit of excellence', our theme for this year's edition. Over these two days, we plan to celebrate how these unseen champions have not just repurposed medicines for a coronavirus but also give new purpose to the sector as a truly frontline lifesaving sector for the millions across the globe who are COVID recovered."

In pursuit of excellence

Ravi Udaya Bhaskar, Director-General, Pharmexcil

The conclave also witnessed a special address by Ravi Udaya Bhaskar, Director-General, Pharmexcil. Beginning his address, he informed the audience that India exported $24.4 billion worth of drugs to different countries with 18 per cent growth rate in FY2021. In addition, the scientists of India have played a crucial role, particularly in the development of indigenous vaccines during the COVID-19 pandemic. Mentioning about the efforts made during the development of a formulation, he said that people are coming up with different kinds of formulations. For instance, Zydus is coming up with a needleless vaccine, as well as there have been development from sustained release to transdermal patches, nasal vaccines, etc.

He highlighted that the world is moving in a different direction and it is also thinking about developing the complex generics as well as the biosimilars. Bisosimilars is the area where scientists are seriously working. Thus, the future of the pharmaceutical industry depends upon the Novel Drug Delivery System (NDDS). The role of the scientists who are working in the industry is much valued, he emphasised.

He also said that India is known for producing quality generic medicines at an affordable price. However, the country needs to shift its focus to develop new formulations and new drug delivery systems and complex generics and innovation and research, particularly the role of the scientists who are working in the formulation development and drug delivery. He further stated that the Indian pharma industry and its scientists have surprised the world by developing two indegeneous vaccines on their own. This shows that India is not only capable of producing generics, but is also capable of manufacturing vaccines and providing new drug delivery systems to the world.

Documented Solutions - How customers benefit from Ideal Cures

Suresh Pareek, MD, Ideal Cures

Suresh Pareek, MD, Ideal Cures spoke on Documented Solutions - How customers benefit from Ideal Cures at FDD Concave 2021. His presentation was very informative as it drew from his vast experience spanning over 40 years experience in coating technology.

He began his session by alluding to Ideal Cures' long association with *Express Pharma* and said that it has been partnering with the leading pharma magazine for the FDD Conclave since its inception in 2017.

He went on to explain how coating needs of the pharma industry have changed and evolved over time, with scientific advancements in the drug development process.

He shared details about Ideal Cures' Instacoat solutions, their key features and how they can be used can be used for a wide range of nutra and pharma products. Pareek also explained how the company's Instacoat 4G solution can ensure significant advantages in terms of time and cost savings, thereby making it a preferred choice for the pharma sector. He said that Instacoat 4G ensures 80 per cent reduction in carbon emissions and energy consumption, thereby making it a more eco-friendly choice as well.

He assured the industry Ideal Cures has been keeping pace with the advancements in the industry and is fully geared to be the ideal partner for all its coating requirements.

Application of Quality by Design in development of NovaPure closures

Sharing his views with the audience, Prabhaharan Sankaran, Technical Account Specialist, West Pharmaceutical Services, India, talked about the evolving product and patient needs that drive industry trend. He notified that year on year, the number of biologics and cell gene therapy are increasing around the globe. He also mentioned that by 2025, about 55 per cent of the top 100 molecules around the globe will be based on biologics.

According to him, the things required for the growth of the market are patient safety and compliance, increase in home care and self administration, increasingly stringent regulations and quality standards. Whereas, the challenges are drug-closure compatibility, drive to quality, design excellence, risk mitigation, ease of use, product lifecycle management, particulate control and yield maximisation. He further told that FDA encourages risk-based approaches and adoption of QbD principle during the drug development and manufacturing. He also made comparisons between the traditional (conventional) and QbD (ideal) processes of product development. Besides, he talked about the various applications of QbD in product development that include mitigating risk, optimised functional profile, high visual quality and low product-to-product variation, among others.

He concluded that QbD principle has been adopted to develop NovaPure closures which focusses on understanding changing regulatory requirements, customer needs and relevant guidances and principles in development.

Panel Discussion: The pandemic effect on FDD

The first panel discussion at FDD Conclave 2021 witnessed FR&D leaders and experts reflect and discuss on the experiences and learnings for pharma scientists since the outbreak of the COVID-19 pandemic.

The eminent panenlists for this session were Dr Alagumurugan Alagarswamy, VP & Head - R&D, Maiva Pharma (Moderator); Dr Rakesh Kumar Bhasin, VP and Head R&D (Formulations), Biocon Pharma; Dr Sumedha Nadkar, Site Head and Sr Director, Perrigo Labs and Dr Pirthi Pal Singh, VP, Tirupati Group.

The panelists discussed how the pandemic, one of the biggest health crises of this century, has also been instrumental in furthering progress in formulation development and drug delivery.

They looked at various aspects like the challenges faced by the R&D community due to the pandemic such as working in very restricted conditions, supply chain disruptions, the urgency to find drugs and vaccines to battle the pandemic while ensuring that the focus on the coronavirus did not affect the search for medicines to deal with other ailments. The panelists also discussed how clinical trials were adversely affected by the pandemic as they had to deal with escalating costs, challenges in recruitment of participants, etc.

For instance, experts informed that the majority of R&D leaders have been spending an average of 40 to 50 per cent of their time in crisis management.

But at the same time, it was a period of great learning as well since the sector learnt

newer methods to deal with challenges and devised newer approaches to make their processes and operations more efficient.

It also allowed the industry's professionals to expand their knowledge base and optimise R&D outcomes. For instance, as scientists and researchers were exploring different drugs for efficacy against COVID-19, it was found that drug formulation and delivery strategies like controlled release and targeted delivery could expand the use of such repurposed drugs and mitigate their side effects.

The discussion was very wide ranging and the experts addressed several vital topics such as recent scientific advancements spurred by the pandemic, the growing use of technology and digitalisation to enhance efficiency and efficacy of pharma operations, especially in pharma R&D, the growth potential for India Pharma Inc, the impact, growth potential and challenges in herbal formulations and nutraceuticals, etc.

Thus the session was very insightful and had several takeways which will be pivotal for the sector's growth trajectory in future.

KEY HIGHLIGHTS

- COVID-19 has affected each one of us and even in these unprecedented times, we have been at the forefront responding to the challenges and bringing new therapies to continue to thrive in the changing business scenario:
  Dr Alagumurugan Alagarswamy, VP & Head - R&D, Maiva Pharma
- The rapid development of novel vaccines for COVID-19 demonstrates that a new type of streamlining and efficiency is indeed possible:
  Dr Rakesh Kumar Bhasin, VP and Head R&D (Formulations), Biocon Pharma
- The demand for cough and cold medicines actually went down during the pandemic, while the drugs for pain, inflammation and dehydration saw a surge in sales:
  Dr Sumedha Nadkar, Site head and Sr Director, Perrigo Labs
- 3D printing has a lot of potential for drug delivery:
  Dr Pirthi Pal Singh, VP, Tirupati Group

> It was a period of learning since the sector learnt newer methods to deal with challenges and devised newer approaches to make their processes and operations more efficient

Two high-resolution measuring systems for Research and Development and Quality Control

Uwe Killeman, Field Marketing Manager - Particle Counting and Characterisation - Europe, Beckman Coulter Life Sciences

In his presentation, Uwe Killeman talked about the two high-resolution measuring systems for Research and Development (R&D) and Quality Control (QC) that are being provided by Beckman Coulter to the industry, namely Multisizer 4e and LS 13 320XR. He referred to the several qualities of Multisizer 4e which include its measuring range, and that it has got direct computer control. DPP pulse evaluation, measurement of concentrations, measured number distributions and electrical sensing zone are the other qualities of Multisizer 4e that Killeman mentioned in his address to the audience. He also talked about its functioning and notified that when a cell passes through the measuring port, there is a change in resistance in the solution due to the cell volume. He further said that the change in resistance when the particles pass through the measuring zone is proportional to the particle volume.

He also said that for different applications, the company uses different kinds of beakers ranging from 100 ml to 400 ml, accuvette ranging from 10-20 ml and small volume cups of 3 ml. He mentioned about high-resolution digital pulse analysis and informed that the Digital Pulse Processing (DPP) analysis enables the acquisition, storage and display of each individual pulse, which means that individual areas of the pulse spectrum can be evaluated separately at a later date. DPP allows raw data re-analysis of single sample components, he further informed.

He then talked about injectable fat emulsions, while also giving some examples like nutritional fat emulsions, vitamin E emulsion and purified soyabean oil/olive oil emulsions. Its general use includes as that of a carrier for better and controlled release. These are used as carriers in clinical trials for neuroleptic drugs, dexamethasone, propofol, diazepam, fat dissolvable vitamins, etc. He also said that more drugs are being researched as candidates to be carried by fat emulsion.

Automation and AI for Formulations Development

Dr Ranjit Barshikar, CEO-QbD International; United Nations Adviser - Geneva, gave an insightful presentation about the role of automation and AI for formulations development at the FDD Conclave 2021 organised by *Express Pharma*. The sessions focused on how traditional approaches to drug formulation development are giving ways to newer approaches as a result of groundbreaking advances in technology. The session also looked at how artificial intelligence (AI) and automation technologies have been gaining momentum in pharma processes with their potential to eliminate errors, optimise resources and reduce time in experiments.

Dr Barshikar gave an overview on the three distinct types of AI that are being widely used, i.e. human-created algorithms, machine learning and deep learning. He also explained how and why digitalisation and automation are finding increasing application across sectors, including the life sciences industry with their potential to lower costs, improve revenues, speed-up launches and reduce product recalls. He also explained AI's role in transforming quality control work in labs and on shop floors by introducing new ways of working with more efficient and automated processes, data-driven decisions and better predictive analytics tools. He asserted that this is crucial to increase R&D success, develop new drugs and fasten speed to market.

Thus, Dr Barshikar's session had some good takeaways on how AI can be used in formulation development and drug delivery, for clinical trial design and monitoring, QA and QC, pharma manufacturing, pharma product management, drug discovery and pharma product development.

Panel Discussion : Optimising FR&D to expedite regulatory compliance

The moderator of this panel discussion Dr Vinod Arora, Principal Advisor, Institute of Good Manufacturing Practices India (IGMPI), began the session by saying that FR&D activity can be divided into three parts – prototype development, analytical evaluations and exhibit batches and regulatory filings, etc. On the development part, together, there are almost 3,000 companies in India and about 10,500 manufacturing facilities – API companies or API plus dosage form companies or only dosage form companies. He pointed out that businesses request products for multiple markets, but there are various challenges when it comes to developing formulations for multiple markets because different markets have different Reference Listed Drugs (RLDs) and then there are API sources, DMF sources, non-DMF sources, etc and FR&D resources are limited. The panellists talked about these challenges and the solutions required for such global development programmes.

The panellists also shared their views with the audience on overcoming the challenges with respect to PCS Class-II and Class-IV drugs, and Class-III drugs where the inter-subject variability is high. They threw light on the kind of evaluation that is done to minimise or avoid the failures before initiating the pilot studies in such cases

The panellists also shared their views with the audience on overcoming the challenges with respect to PCS Class-II and Class-IV drugs, and Class-III drugs where the inter-subject variability is high. They threw light on the kind of evaluation that is done to minimise or avoid the failures before initiating the pilot studies in such cases.

Apart from it, the panellists also pondered upon the clinical development programmes, which are time-consuming,

challenging as well as expensive. They talked about the challenges faced while planning biostudies since the RLD and regulatory requirements are different in different countries. They focussed on the strategies that are worked out during such scenarios. Further, talking about the differentiated products, where unmet needs are there, the panellists also deliberated upon the approaches needed for successful formulation development of generics.

Mentioning about the molecule-based multiple geographies' simultaneous development, one panellist said that a critical aspect in this regard is IP alignment. In the initial phase itself, the scope of the project needs to be properly defined for all the geographies put together, whatever is of interest. He further said that these days, IP extensions that come in different geographies, while the filing date might be same for the same pattern, but then the pattern extension paradigm that sets in different geographies, actually shift the launch dates, in some cases, by several years. From that perspective, the scope of the project has to be defined keeping in mind IP scenario, packaging requirement and zonal stability requirement. For the formulator, there are challenges of reference products performance being different and all other things. That is something which has to be experimented and taken care of, but then definition scope is crucial for such type of development.

KEY HIGHLIGHTS

- To enter new markets/countries, for e.g. China, ensure that all ingredients and excipients used for formulations are compliant with the pharmacopoeias of these countries:
  Ravikumar N, Senior VP, MSN Laboratories
- An integrated and effective reverse engineering approach is key for successful formulation development of generics and to ensure their compliance with global regulations:
  Dr C Muthulingam, VP-Formulations, Mankind Pharma
- Formulation development should not be done in silos. FR&D scientists should get involved with different processes like dissolution to improve the efficiency of their formulations:
  Dr Sukhjeet Singh, Chief Scientific Officer, Sentiss Pharma
- Today, FR&D is being done through integrated and evidence-based strategies with cross-functional inputs to improve outcomes, but certain blind spots need to be eliminated:
  Dr Sajeev Chandran, Director, Adv Drug Delivery Research & IVIVC/ Biopharmaceutics, Pharma R&D, Lupin
- Molecule-based R&D approach in formulation development might offer greater advantages vis-à-vis market-based R&D approach, in enabling regulatory compliance across global markets:
  Vinod Arora, Principal Advisor, Institute of Good Manufacturing Practices India (IGMPI)

Special Address: S.M.A.R.T Pharmaceuticals

Dr Ajaz Hussain, Independent Advisor - Life Sciences

Dr Ajaz Hussain gave a very interesting presentation as part of his Special Address at FDD Conclave 2021 on how and why S.M.A.R.T Pharmaceuticals, as a category, is poised to dominate the market in this decade. He said that they should not be confused with 'smart pharmaceuticals' such as digital therapeutics and pills with embedded sensors that digitally track behaviours and described S.M.A.R.T as an acronym for Specific Self, Measurable Monitoring, Achievable Analysis, Relevant Reporting and Timely Technology.

Dr Hussain also advised the life sciences industry to hone their adaptive learning skills to remain relevant in the coming times and gave some points for consideration while investing in S.M.A.R.T objectives and tools. He said that it is time for the life sciences sector to get ready for an era of rapid change and this necessitates the adoption of a smart 'development stance' to prepare for 2022 and beyond. His advice was that a mix of the right education, training and experience is vital for this.

Moving on, he said that as the pharma industry embarks on a journey of transformation driven by technology it has to ensure data integrity. He asserted that it is vital to build a culture of GMP and opined that empowered workers are the key to data integrity. He ended the session with the take away that the need of the hour for the industry is to be self-transforming and the step to get there is self-authorship.

Clean label coatings

Sanjay Negi, GM, Ideal Cures

Speaking about the clean label coatings, Sanjay Negi, GM, Ideal Cures, said that the company offers clean label products to various pharmaceutical as well as nutraceutical companies. He informed that clean label refers to food products that have fewer ingredients and simpler ingredients at that. It alludes to more than just being honest about what's in one's product; it means moving away from highly processed ingredients and toward ingredients from natural sources. Some of the benefits of the clean label products are that these contain natural, familiar, safe and simple ingredients, and the ingredients are easy to recognise, understand and pronounce. Further, there are no synthetic chemicals and these have a good acceptability, he mentioned.

While sharing his presentation with the audience, Negi also spoke about the two products offered by Ideal Cures – INSTANUTE MB-II and INSTACOAT T2F. Regarding the application of INSTANUTE MB-II in a project, he highlighted that it was free from titanium dioxide, talc, iron oxide and carmine, contained no synthetic/artificial colours, and had global acceptability, among other benefits. He also informed that INSTANUTE MB-II is an innovative, ready-to-use product with high solids moisture barrier film coating system, and is available with and without titanium dioxide. It is talc- and preservative-free dry blend of polymer, plasticiser and synthetic or natural colours.

Speaking of INSTACOAT T2F, he said that it is a novel, ready-to-use titanium dioxide- and talc-free coating system and is a dry blend of polymers, plasticisers, opacifiers and other excipients. He also shed light on its features and benefits. For instance, it can be formulated with aluminium lakes, iron oxides and natural pigments and can also include flavours and cooling booster. Further, it is easy to scale up and transfer to different equipment types or manufacturing sites. He also said that INSTACOAT T2F coating formulations provide a good alternative to typical coatings containing titanium di oxide for pharmaceuticals/nutraceuticals exhibiting good hiding and colouring properties. Ideal Cures is further evaluating few more potential ingredients (polymers and opacifiers) to offer more choices to the customers, he concluded.

Green formulation development: Strategies and challenges

Arjun Singh Dasoondi, AVP, Innovation & Science, Amway

There is a growing need for sustainable drug discovery and development methods across the global pharma industry and experts feel that a myriad of opportunities exist for the generic pharma industries to reduce the E-factor and develop cost effective and green synthetic routes of medicines. Arjun Dasoondi, AVP Amway I&S addressed this issue and spoke on 'Green formulation development: Strategies and challenges' at FDD Conclave 2021.

He spoke on the global growth potential in this segment and informed that in all life stages, it is about $10 billion in market size with a three-year projected CAGR of 11 percent. He also informed that the consumer penetration opportunity for green formulations is 50 per cent. He pointed out that green formulations are becoming increasingly popular on the back of growing consumer awareness. Clean labels, no artificial colours, no preservatives etc are some of the buzzwords today which are driving the growth of green formulations in pharma and nutrition.

However, challenges such as availability of raw materials, logistics, high cost of ingredients etc, complex regulations, use of contemporary and advanced formulation technologies like sustained release, delayed release nano technologies etc in natural or green formulation development are challenges that hinder progress in this field, globally. Explaining the Indian context, he said that green formulations segment is still at a nascent stage and face major market challenges such as low category penetration, low average product consumption and low compliance. These issues need to be dealt with effectively to accelerate development.

Emphasising how green formulation development is a way of life for Amway, he also assured that they focus on human health, ecosystem health and environment system health in equal measures, while developing a product.

Panel Discussion: Oral solid dosage forms: Trends and opportunities

On the second day too, the panel discussion on the trends and opportunities regarding the oral solid dosage forms saw Dr Vinod Arora, Principal Advisor, Institute of Good Manufacturing Practices India (IGMPI) as the moderator of the session. The other panellists included Dr Kavita Inamdar, CTO, Indoco Remedies; Dr Krishnakanth Gandhi, MD, Solinova Life Sciences and Ravi Kochhar, Head-R&D, Beximco Pharmaceuticals, Bangladesh. The panellists began the discussion by deliberating on various dosage forms like mini tabs, micro tabs, etc. One of the panellists, Kochar, said that such tablets are the way forward. Further, moving along patient-centric dosage forms and ease of dosing, this trend will go on and one has to build upon it, he

stressed.

Going forward, the panellists discussed about the fixed-dose combinations and their clinical as well as business advantages, along with the role of continuous manufacturing in the Indian pharma industry. Dr Gandhi highlighted that continuous manufacturing is not new in the industry. Before the pharmaceuticals, oil refineries, chemicals, synthetic fibres, fertilisers, power generation, natural gas and waste water management are the various areas where continuous manufacturing concept is being used, he informed. He also said that there are three major factors driving continuous manufacturing – initial investment set up, regulation and technology. Thus, it is the right time to focus on it.

KEY HIGHLIGHTS

- Biologics is growing at a CAGR of 35 per cent plus, and, by 2028, it will be a $119 billion market: **Vinod Arora,** Principal Advisor, Institute of Good Manufacturing Practices India (IGMPI)
- Fixed-dose combinations have clinical advantage like better safety profile and business advantage like better pricing: **Dr Kavita Inamdar,** CTO, Indoco Remedies
- Continuous manufacturing offers flexibility, robustness and reduction in manpower and energy, but there are also challenges associated with mindset, regulation and technology balance: **Dr Krishnakanth Gandhi,** MD, Solinova Life Sciences
- Dosage forms like mini tabs and micro tabs are the way forward. As we move along patient-centric dosage forms and ease of dosing, this trend will go on and we have to build upon it: **Ravi Kochhar,** Head-R&D, Beximco Pharmaceuticals, Bangladesh

In addition to it, the panellists also shared their views on digital medicine. Dr Inamdar, in this regard, informed that Abilify – a drug approved for schizophrenia that has an ingestible sensor embedded in the pill that records that the medication was taken – is the only US FDA-approved product at present. According to Dr Gandhi, digital medicine is still an emerging technology, and will take a lot of time to come up in a market. Kochar said that this technology is being used more in inhalers incorporated with a chip. Nowadays, there are inhalers that measure the force at which inhaler was taken, whether the dosages were taken in time or not – all that information is recorded and gets conveyed to the physician, he mentioned.

The panellists later discussed upon the oral biologics, and, during the discussion, Dr Gandhi notified that all big generic companies are currently focussing on injectables and a lot of small startups in the Europe and the US are working in the area of biologics, in terms of giving it by the oral route. He also said that currently, the biologics are taking a pace because of the capabilities in the metabolic disorder, ageing-related factors, inflammatory diseases and other chronic conditions.

Panel Discussion - Biologics and Biosimilars: Challenges and opportunities in FDD

The last panel discussion of FDD Conclave 2021 was on 'Biologics and Biosimilars: Challenges and opportunities in FDD'. In this discussion, our eminent panelists sought to understand and address the formulation challenges in biologics and vaccines, understand the potential of less traditional delivery routes, regulatory and quality issues, emerging therapies etc.

Dr Shrikant Mishra, Professor & Head, Technology & Translation Laboratory, School of Biotechnology, KIIT University, Bhubaneshwar (Moderator); Dr Jaby Jacob, Sr President – R&D, Bharat Serums & Vaccines; Dr Dinesh Kundu, Co-founder & CEO, QbD Biosciences; Jayant Gangakhedkar, Asst Drugs Controller (I), Biologicals Div, CDSCO; and Dr Ramakrishna Bangaru, Sr VP, Clinical Pharmacology Research, Viatris were the participants in this discussion.

The panelists discussed the progress in this field and the

emerging opportunities, in India and globally, in this arena. One of them informed that though only 10-20 biologics have been approved in the last 15-20 years, over 470+ trials have been reviewed in the past 18 months, thus signifying how the COVID-19 pandemic has accelerated growth. At the same time, they also discussed the myriad challenges that exist and are emerging in this segment and deliberated on the various approaches to tackle them.

Dr Mishra, an industry veteran and an academician, as the moderator for this session, steered the discussion to address several pertinent aspects

in biologicals and biosimilars such as evolving regulations and ways to comply with them, quality and non-compliance issues, FDA rejects and recalls of these products, measures to leverage opportunities and minimise restraints, importance of training the human resources to optimise growth potential and more, during the course of this discussion.

Dr Jacob elaborated on formulation challenges in biologics and biosimilars such as stability issues, storage requirements, viscosity, complexities in formulation, and how they have been overcome. He spoke on quality issues and non-compliance in marketed drugs of rDNA origin. He also gave details on the opportunities and growth potential in this field. Dr Kundu shared information on regulatory issues in MSC therapy, Plasma therapy, and COVID-19 specific MAbs. He informed that more than 670 development programmes have been initiated for COVID related treatments and vaccines in two years across the globe.

Gangakhedkar from the CDSCO, on the other hand, gave the regulator's perspective and detailed on the various pathways and measures taken by the regulatory authority to ensure quality, safety and efficacy of biological drugs. He assured that there are multiple stringent checks done at multiple levels, before regulatory approvals are given to biological and biosimilars in India.

Dr Bangaru shared information on the regulatory approval process for biologicals and biosimilars and gave insights on the different kinds of recalls, their causes and impact. He cautioned that these recalls actually hurt both the industry and the patients. The pharma companies have to deal with loss of time, money and reputation while the patients have to face issues with drugs that are not top quality. Hence, it is essential to prevent or minimise them by ensuring top most quality and regulatory compliance. Thus, the discussion had a lot of learnings and takeaways for the audience of the session.

KEY HIGHLIGHTS

- There has been a lot of progress in the field of biological and biosimilars in terms of drug delivery, for instance, micro needles, to improve patient-compliance:
  Dr Jaby Jacob, Sr President – R&D, Bharat Serums and Vaccines
- Indigenous manufacturers of biologics and biosimilars must generate data of minimum consecutive batches of their product to ensure quality, safety and efficacy:
  Jayant Gangakhedkar, Asst Drugs Controller Biologicals Division, CDSCO
- Be it cell and gene therapies or biologics approval, the pathways have been clear with elaborate checks in place. So, we are seeing double digit and triple digit numbers getting approved in US and Europe:
  Dr Dinesh Kundu, Co-founder & CEO, QbD Biosciences
- Education, training and safety awareness are key to reduce recalls of biological and biosimilar drugs:
  Dr Shrikant Mishra, Professor and Head, Technology, and Translation Laboratory, School of Biotechnology, KIIT University
- Patients and pharma companies, both, end up paying the cost of errors and drug recalls. We need to improve input quality and ensure stringent checks across the development lifecycle:
  Dr Ramakrishna Bangaru, Sr VP, Clinical Pharmacology Research, Viatris

SUBSCRIBE NOW

Note:

Payment should be made in the name of
'' The Indian Express (P) Ltd.''

DDs should be payable at Mumbai.

Please mail to:
Subscription Cell,
Express Pharma,
Business Publications Division,
The Indian Express (P) Ltd.,
Mafatlal Centre, 7th floor, Ramnath Goenka Marg,
Nariman Point, Mumbai - 400021
Mob.: 9867145028 / 8879199787
Tel: 67440002, 67440451,
E-mail: bpd.subscription@expressindia.com

Kindly allow 4-5 weeks for delivery of first issue.
Please add ₹ 20/- for cheques from outside Mumbai.

Subscribe Online
www.expresspharmaonline.in

Yes! I Want to ☐ Subscribe ☐ Renew

Tick Terms	Subsription
☐ 1 Year (12 issues)	₹ 450/-
☐ 2 Year (24 issues)	₹ 900/-

International Subscription rate for 1 year US $ 100

Mailing Address: _____

Name: _____ Subscription No: _____

Company Name: _____ Designation: _____

Address: _____

_____

City: _____ State: _____ Pin: _____

Phone: _____ Fax: _____ Mobile No: _____ E-mail: _____

Payment enclosed Cheque/Demand Draft No.: _____ Dated: _____

For ₹.: _____ Drawn on: _____

For Office Use: _____

Bp No.: _____ Order No.: _____ Docket No.: _____ Period.: _____

INSIGHT

Analysing decriminalisation of biodiversity provisions under 'The Biological Diversity (Amendment) Bill, 2021

Aditya Bhattacharya, Partner and **Kunal Kapoor**, Principal Associate, **Lakshmikumaran** and **Sridharan Attorneys**, examine the various factors associated with the act

The Biological Diversity (Amendment) Bill, 2021 introduced in the Lok Sabha seeks to bring some fundamental changes in the way the Indian legislature regulates the Biological Diversity Act, 2002 (Act). The present Act, which was a product of India's commitment to Nagoya Protocol, was enacted with a fundamental ideology, to ensure equitable benefit sharing arising from the use of biological resources. The Nagoya protocol, which came into force in 2014, was enacted with the endeavour to create global ethos of equitable sharing of biological resources and genetic material. The protocol's agenda was to ensure that all stakeholders who come into the picture during the sharing of a biological resource must share the benefits of the genetic resource in a fair and equitable manner. The 2002 Act enacted by the Indian legislature created authorities such as the National Biodiversity Authority (NBA) and the State Biodiversity Authorities (BDA) and entrusted them with the task of ensuring equitable sharing of biological resources. These authorities, amongst other things, were also entrusted with powers to file FIR and initiate magisterial enquiry in a situation an entity violated specific provisions of the Act.

Aditya Bhattacharya

Kunal Kapoor

The 2021 bill aims to streamline the legislation by bringing changes both in the realm of substantive law as well as procedures. One issue, within the bill, which requires a special mention is the proposed amendment to decriminalise violation of the substantive provisions of the legislation. The bill aims to establish a regime where violation of the substantive provisions will not make an entity criminally liable. The power to file FIR given to the National Biodiversity Authority against the defaulting entity has been withdrawn under the bill. The proposed bill has created an inquiry officer (of the rank of Joint Secretary) who will now conduct enquiry in the matters of violation and accordingly impose penalty that can go upto Rs 1 crore in cases of continuous violations. If enacted, the provision will bring closure to the much-debated issue and apprehension of criminal liability that could be fastened upon entities for violation. The proposed measure may be interpreted as a step by the Indian legislature to give assurance to the commercial stakeholders that the legislation is not an arm-twisting device, but rather a regulator to ensure compliance by the entities. In a way, it also gives assurance to the Global Inc that the Indian BD Act is not an anti-business legislation. The proposed change in the legislation is unique as many other biodiverse countries following the Nagoya protocol continue to criminalise the non-adherence to the respective legislations, prominent examples can be the National Environmental Management Biodiversity Act, 2004 (South Africa) and the Canadian Environmental Protection Act, 1999 that continue to criminalise non-compliance.

> The present Act, which was a product of India's commitment to Nagoya Protocol, was enacted with a fundamental ideology, to ensure equitable benefit sharing arising from the use of biological resources

However, amendments in the legislations also bring with it various issues which can only be understood in its true scale once the provisions are implemented. It is pertinent to mention here that, the proposed bill, if implemented, will create two separate authorities, the Biodiversity Authorities at the Central and state level to determine equitable sharing of resources and a separate adjudicatory body or officer to impose penalties for violation of substantive provisions. If a comparison is made in this regard with other similarly-placed legislations, then legislature could have drawn analogy and entrusted all powers upon the authorities and manned it with both judicial and technical members. Another way could have been to make an investigative body like under DG (enquiry) office which could investigate on allegations of non-compliance and place its report before the authorities for adjudication. Such practices have been crystalised in other laws such as the 'Competition Act and allied regulations' as well as the 'erstwhile and present 'Indirect Tax-Goods and Service Tax regime.' However, all these issues can only be left to the wisdom of the legislature.

The proposal to decriminalise provisions under the new bill and its consequence will be closely watched world over. The amendments, if implemented, will have its own share of issues (both good and bad) which will only be known in the time to come. It is hoped that the proposed changes succeed in taking Indian BD regime to a higher level where the interests of all stakeholders are balanced and secured.

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

Our Esteemed Clients

Head Office:
Kilitch Healthcare LLP,
902/B Godrej Colesium, Behind Everad Nagar,
Near Priyadarshani Cirlce, Sion (East),
Mumbai – 400022.
Tel. : 022 6137 2222
Mr. Divya Mehta : +91 9819724957

Factory:
Kilitch Healthcare India Ltd.
R-905/904, T.T.C. Indl. Area,
M.I.D.C, Rabale, Navi Mumbai - 400 701.
Tel. : 022 2769 9174, 6516 2146

www.kilitchhealthcare.com | info@kilitchhealthcare.com

Replace "Fumed Silica + Talc" with Sylysia 350/770 FCP

Dr S K Chauhan, Center for Food Technology, University of Allahabad, India; **Dr Umakant Mishra**, Head – Production, Associated Biotech, Baddi, India and **Dr Naseem Khan**, Head India-Drug Delivery and Excipients, Sredstva Regionale Chemie, Mumbai, India explain the several benefits of Sylysia 350/770 FCP over (Fumed Silica+Talc)

Impurities in pharmaceuticals are unwanted chemicals that remain with Active Pharmaceutical Ingredients (APIs) or develop during formulation or upon aging of both API and formulation. The presence of these unwanted chemicals even in trace amounts may influence the efficacy and safety of pharmaceutical product. The control of impurities is currently a critical issue for the pharmaceutical industry. International Conference on Harmonisation (ICH) formulates guidelines regarding the control of impurities.

Dr S K Chauhan

Dr Umakant Mishra

Dr Naseem Khan

There are many APIs, plant extracts and oil-based tablets that tend to be hygroscopic in nature. They can absorb moisture from the environment, cake together or adhere to equipment depending on RH. Sylysia is a highly porous, micronised silica powder. When added to a formulation, the high porosity of Sylysia 350/770 is capable of adsorbing a considerable amount of moisture and oil, keeping the active ingredient dry and improving stability.

It can be replaced with Sylysia 350/770 for (Fumed Silica+Talc), As to highlight talc, it has many impurities and nitrosamine profile enough to destablise the product. So, Sylysia can be used instead of (Fumed Silica+Talc) in any formulation for many benefits:

SYLYSIA 350/770*FCP shows better tensile strength and disintegration time than Aerosil 200.

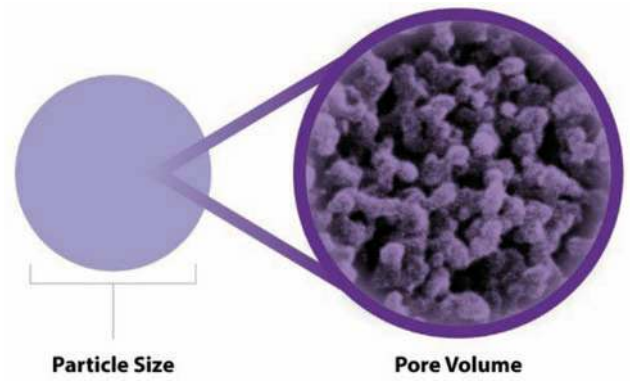
As a result of ICP analysis, both grades are high SiO2 purity, more than 99.7 per cent talc has lower density and poor performance than Sylysia. Talc density is normally 0.2 gm/cc and Sylysia 350 FCP is 0.06. In Japan, talc is not majorly used for Pharma excipients and lubricants due to impurities, magnesium and a crystal component. If there is too much magnesium, the taste of the tablets will be bitter.

Many more benefits:

◆ Less dust, reduces the potential for cross contamination
◆ Improves flavour retention and oxidative stability
◆ Less bulky, easier to handle and store
◆ Reduces downtime from static build-up
◆ Eliminates or reduces need for sieving before
◆ Work as glidant and improve homogeneity
◆ Increases tablet hardness at a lower compression force
◆ Decreases friability, capping and lamination
◆ Improves flow for standard and challenging formulations
◆ Acts as an anti-static agent and reduces API loss
◆ Facilitates wetting to aid in disintegration and dispersion
◆ Improves dissolution
◆ Improves mouthfeel of medicated chewing gums

(Mg3Si4O10(OH)2, Talc), generates many impurities as it contains Mg, Si. Due to porous structure of silicon dioxide, the formulation and a fine glidant, many impurities can be avoided and the formulation can be more thermostat and better stability.

It is possible to remove impurities with options to replace them with Sylysia 350/770. Similarly, many formulations can be discussed to derive solutions.



< Tableting Condition >	
Tableting machine	Tab A II (OKADA SEIKO CO. LTD.)
Compression Pressure	100 MPa
Compression Speed	10 RPM
Beetle	Flat beetle (Diameter 8mm)
Tablet Weight	180 mg
< Tableting Formulation >	
Composition	**Formula (%)**
Ginkgo biloba extract (Nippon F. Yakuhin C.L.)	27
Fast Flo 316 (Foremost Farms)	65
Croscarmellose Sodium (JRS PHARMA)	3
Carboxymethyl Starch Sodium (JRS PHARMA)	3
Silica (SYLYSIA 350 / 770 FCP, Aerosil 200)	1
Magnesium Stearate (Mallinckrodt)	1
Total	100

< Tableting Test Results >			
	Hardness (N)	**Tensile Strength (Mpa)**	**Disintegration Time (S)**
SYLYSIA 350 FCP	36.2 ± 2.94	0.99 ± 0.05	293.0 ± 9.5
SYLYSIA 770 FCP	30.9 ± 0.57	0.84 ± 0.02	292.2 ± 7.0
Aerosil 200	34.1 ± 2.73	0.92 ± 0.07	318.8 ± 12.5

Bibliography:

1. U.S. Food and Drug Administration. Guidance for Industry, Q3A Impurities in New Drug Substances. February 2003.
2. U.S. Food and Drug Administration. Guidance for Industry, Q3B Impurities in New Drug Products. July 2006.
3. Renbourn ET. The history of sweat and prickly heat, 19th-20th century. J Invest Dermatol. 1958;30(5):249-259. doi:10.1038/jid.1958.50
4. Shelar J. Report on 'toxic' talc worries India. The Hindu. https://www.thehindu.com/news/national/ canada-report-on-toxic-talc-worries-india/article25699760.ece. Published December 8, 2018. Accessed December 4, 2020.
5. Rohl AN, Langer AM. Identification and quantitation of asbestos in talc. Environ Health Perspect. 1974; 9:95-109. doi:10.1289/ehp.74995

Connectivity gives product data its true digital meaning

Data that stays on the machine that is collected is not good to anyone – it must be shared and utilised elsewhere to fulfil its purpose. Software connectivity is a critical part of making that happen. **Jürgen Kress**, General Manager, Checkweighing and Vision Inspection, Mettler-Toledo Product Inspection, explains how liquid pharma manufacturers should approach this issue

In the previous two columns of this series, the articles looked at ways in which product inspection equipment such as checkweighers and vision inspection systems can help liquid pharmaceutical manufacturers to manage the quality of their products.

This third and final article talks about the importance of software connectivity to bring this all together. It is a technical challenge to integrate software, but one, where pharma manufacturers and their technology suppliers must not cut corners, because the benefits of getting this right can reach into every aspect of a manufacturer's operation.

Connectivity

Equipping product inspection systems with the right software connectivity gives manufacturers a chance to gain a real-time picture of production, processing and packaging lines, allowing them to spot potential problems in advance. It might help them to avoid issues arising in the first place, but at the very least, they will be able to mitigate the damage and costs that they might incur. Being able to quickly pinpoint where something went wrong, and then quickly taking the action required to put it right, will also be appreciated by supply chain partners.

If we consider the word "connectivity" itself, we can gain a greater appreciation of why software connectivity is so important. We exist in a marketplace that is increasingly inter-connected; where the supply chain is transforming towards a fully digital utility that every partner both feeds into and taps into. To achieve true transparency, such a supply chain requires data to be automatically gathered and shared by each partner and passed on via an efficient digital handshake from machine to machine, partner to partner.

Neither the handshake, nor the exchange of data can happen efficiently without software connectivity. In the areas of serialisation and aggregation, in particular, it is crucial. The point of these activities, after all, is to enable easy tracking of products, whether individually or as batches, through the supply chain. The data and the codes are pointless if they go nowhere. Building and sharing an audit trail of actions linked to serial codes serves multiple purposes.

Importance of data

Firstly, it is a record of actions taken during manufacturing and onward processing of a product – information that might need to be referred back to in the event of a problem with the product and as reference against attempts by counterfeit operations. Secondly, the data gained is useful for proving good manufacturing practices, and are being followed and meeting the compliance requirements of different levels of regulations. Thirdly, without this access to digital data, real-time process monitoring and inventory management cannot meaningfully happen.

Role of product inspection

Pharma manufacturers will typically deploy checkweighing (as described in previous articles in this series, for fill level and completeness checks) and vision inspection, to make additional quality checks as needed. Track and trace is a requirement for serialisation and may be optional for aggregation (depending upon the region). Utilising all three of these technologies will help in supporting top-quality production methods and compliance.

Modern checkweighers and vision inspection systems should have advanced software already integrated, with robust security levels and process monitoring capabilities built in. This should be aligned to global and local regulations that follow Good Automated Manufacturing Practice (GAMP 5) guidelines. For track and trace systems, integration into MES- or ERP-systems (Level 5 software) ensures connectivity across single or multiple production sites and provides transparency into the production line data. Exchange of data should be managed through industry standard protocols and software architecture such as OPC UA, PackML and Fieldbus, which supports developments around the Internet of Things and Industry 4.0 initiatives

Compliance

For the European manufacturers, compliance with the EU Falsified Medicines Directive (FMD) requires reporting of serialisation data to the European Medicines Verification Organisation (EMVO). Solutions for tracking and tracing the data must also include connectivity to Level 5 software, which, in turn, reports the data to the EMVO. Partner organisations must be technically certified to do the reporting as they have demonstrated that they meet the technical feasibility to do so.

Additionally, the need to comply with requirements such as those set out by the US FDA CFR 21 Part 11 regulations must also be supported. This FDA clause specifically calls for machinery to create a local electronic audit trail, recording activity such as user logins and machine set-up adjustments.

Compliance, digital supply chain transparency, managing production issues and operating more efficiently, and cost effectiveness are benefits that liquid pharma manufacturers stand to gain by taking a proactive view of software connectivity.

All of these have a bearing on overall product quality – a multi-faceted aspiration for manufacturers in liquid pharma, incorporating the medication and the many processes by which that medication comes through the supply chain to market.

Conclusion

The key point to understand from this series of columns on quality assurance for liquid pharma packs is that strong product inspection capabilities are at the centre of any effective quality assurance programme. They help in making the production of liquid pharma products safe, complete, trackable and compliant with all levels of regulations. They play a critical function in creating and maintaining a transparent and connected digital supply chain.

Crucially, product inspection systems do this while supporting manufacturers in meeting productivity and profitability objectives, by keeping production lines running at the speeds required with minimal downtime. Robust and thorough product inspection solutions are a requirement for liquid pharma manufacturers, helping them to overcome some of the many challenges they face today.

For more information, visit:
www.mt.com/pi-pharma-liquid-pr

Gandhi Automations India's leading entrance automation and loading bay equipment company

This widely-recognised position has been achieved over years of hard work, innovation, commitment to quality and reliable customer service

Gandhi Automations is proud to be certified to ISO 9001 : 2015, ISO 14001 : 2015 and ISO 45001 : 2018. Since its inception in 1996 we have 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 they also facilitate fast, smooth and safe transition by compensating the difference in heights between the loading bay and the vehicle. This contributes to minimising 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 the goods

The importance of efficient loading 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 your 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 door 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 air conditioned places). 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 four types of dock levelers.

a) Radius lip dock levelers

Radius lip dock levelers are available in multiple sizes 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. Further, the self-cleaning lip - hinge system does not retain dust and dirt which allows a smooth operation.

b) Telescopic lip dock levelers

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

c) Edge-of-dock levelers

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

d) Forklift roll-off barrier lip dock levelers

The newly introduced product Forklift roll-off barrier lip dock leveler adds a run-off protection which prevents accidental forklift roll-off when the ovehead 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.

Entrance door with automations

Gandhi Automations offers Porto and Max Vista - automatic sectional overhead doors - the ideal solution for all industrial and commercial needs.

Porto: Porto sectional overhead doors are ideal for all industrial and logistics needs. The design and different solutions offered ensure the door to be aesthetically pleasing and perfectly suited to any architectural environment – from modern and traditional industrial buildings to fine commercial buildings. As these doors slide vertically, stopping in the proximity of the ceiling, they blend in with the architectural features of the building. Porto doors are built to ensure the highest ease and flexibility of use, which, in turn, ensures a quick, hassle-free and accurate replacement of old doors. Their compact size ensures more available space both inside and outside the premises. Depending on the structure of the building and the requirement, a choice can be made from a standard lift, vertical lift, horizontal lift, low headroom or inclined lift. Porto range comprises a wide series of track systems, panel options and safety features. Special glazed doors provide excellent lighting and vision into the building.

Max Vista: Max Vista sectional overhead doors are ideal for industrial and commercial buildings. The doors are made with a combination of aluminium panels and transparent acrylic, grilled or meshed windows giving it a distinctive look and enhancing the look of a building. Max Vista Doors make the environment bright and pleasant to work in as it allows natural light to pass through the large clear areas.

Gandhi Sectional Overhead Doors provide heat insulation and sound proofing thus improving the working conditions on the premises and saving energy. The products are affixed with a CE mark making them reliable and safe.

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

For further details contact:
Gandhi Automations Pvt Ltd
Chawda Commercial Centre
Link Road, Malad (W)
Mumbai – 400064, India
Off : +91 22 66720200 / 66720300
Fax: +91 22 66720201
Email: sales@geapl.co.in
Website: www.geapl.co.in

ACG introduces Smart Connected Product to enable remote machine monitoring in real-time

New solution improves machine efficiency, prevents breakdowns, lowers costs and reduces risks, all while providing anytime, anywhere remote monitoring

ACG has introduced the Smart Connected Product, a new, innovative, IIoT solution, that connects production machines at any facility and visualises relevant information on a single platform. This data can be viewed over web on any device with a secure connection and, most importantly, it is accessible only to authorised users.

The prime benefit of this technology is it enables pharmaceutical and nutraceutical companies to remotely monitor –production machine settings, performance parameters, machine downtimes and alarms, if any, over the Smart Connected dashboard – all in real-time. ACG Engineering's team of experts and data scientists can study the machine performance through remote settings and guide customers on how to better maintain and operate the machines. The Smart Connected Product, therefore, is an integrated solution that addresses the evolving needs of the healthcare industry.

As part of its mission to make manufacturing better, ACG has also launched its campaign, "Smart Connected." The campaign will raise awareness on how pharma manufacturers can collaborate with ACG to remotely monitor their ACG equipment, improve their efficiencies and reduce unplanned downtimes. The key messages will focus on how IIoT-based solutions will help pharmaceutical manufacturers use valuable data to analyse machine performance and improve the overall equipment effectiveness.

> ACG Engineering's team of experts and data scientists can study the machine performance through remote settings and guide customers on how to better maintain and operate the machines

Marcus Michel, CEO, ACG Engineering, said, "We are excited to unveil the Smart Connected Product as part of our Smart Connected campaign. This initiative demonstrates ACG's commitment to provide data-centric, end-to-end solutions under the principle of predictive maintenance. Our overall aim is to reduce costs as well as lower any safety, health, environment and quality risks – all to ensure superior manufacturing performance. Detailed insights and information from our experts will help provide guidance to our customers on how to make machines run more efficiently and prevent unplanned downtime. Amid the evolving healthcare landscape, the Smart Connected product is a step forward to ensure an undisrupted supply chain."

Yokogawa launches OpreX Managed Service – Cloud edition

Enabling cloud-based remote monitoring and maintenance of plant equipment

Yokogawa Electric Corporation has announced the release of OpreX™ Managed Service – Cloud edition, a solution that supports remote monitoring and maintenance of OT/IT field assets using a cloud platform provided by Yokogawa. By visualising information on each device's performance, reliability and security for the entire plant system, the solution will help to minimise unexpected plant shutdowns. The new service solution will be offered as part of the OpreX Sustainable Maintenance lineup.

Development background

Unexpected plant shutdowns result in unscheduled work and increased maintenance costs and lead to lost production opportunities, substantial economic losses and lowered corporate credibility. As OT/IT convergence accelerates and production facility monitoring systems are increasingly integrated with production management and information systems to improve efficiency, there is a growing need for solutions that enable appropriate maintenance activities for the entire complex system, protect the system from security threats, and optimise production efficiency in terms of both safety and efficiency.

In order to meet these needs, Yokogawa launched the OpreX Managed Service in September 2020 to digitise the monitoring and maintenance of production assets. With the development of the OpreX Managed Service – Cloud edition, it is now possible to provide a solution that more customers can deploy with minimal lead time and cost for standardised functions.

Features

◆ Shared-cloud dashboard provides real-time information on the performance, reliability and security of OT/IT devices

The shared-cloud dashboard provides real-time information on the performance, reliability and security of all registered OT/IT devices. Customers can monitor and analyse the information on OT devices such as production equipment monitoring systems and field devices, and monitor the health and security status of IT devices such as computer assets and network devices.

◆ Remote control through remote access with enhanced security

The powerful remote access function provides secure access even from outside the plant. Flexible session control with various combinations of conditions, such as limiting connections based on user role settings, site manager approval, connection time limits and standard security features like the automatic recording of access activities, provide a more secure remote access environment.

◆ Proactive 24/365 monitoring and prompt maintenance support using IT service Management (ITSM) ticketing system

Yokogawa's Network Operation Center (NOC) and Security Operation Center (SOC) monitor plant operate 24 hours a day, 365 days a year, to protect against security threats that are becoming more sophisticated every day. When an incident is detected, it is immediately registered in the ITSM ticketing system and troubleshooting is quickly initiated. This information is always shared online with the customer, who can check the status of the plant and resolve the issue as soon as possible.

◆ Provision of optional specialised remote services

The following services are available for customers who have subscribed to this service. More remote services will be developed in the future.

● Distribution of Microsoft security updates and virus definition files, and provision of security diagnosis reports

●Provision of health diagnostic reports for production equipment systems and field assets

Main target markets

Manufacturing industry in general

Applications

● Efficiency improvement and outsourcing of maintenance and preservation activities

● Remote operation monitoring infrastructure for safe access to plants

For more information, visit:
https://www.yokogawa.com/gl/solutions/products-platforms/oprex/oprex-lifecycle/oprexsustainable-maintenance/managed-service/

About OpreX

OpreX is the comprehensive brand for Yokogawa's industrial automation (IA) and control business. The OpreX name stands for excellence in the technologies and solutions that Yokogawa cultivates through the co-creation of value with its customers, and encompasses the entire range of Yokogawa's IA products, services and solutions. This brand comprises the following five categories: OpreX Transformation, OpreX Control, OpreX Measurement, OpreX Execution and OpreX Lifecycle. OpreX Managed Service is an OpreX Sustainable Maintenance family solution in the OpreX Lifecycle category. For its development of products, service, and solutions in this category, Yokogawa tapped its extensive experience in working closely with customers to optimise operations and maintenance over the entire plant lifecycle.

About Yokogawa

Yokogawa provides advanced solutions in the areas of measurement, control and information to customers across a broad range of industries, including energy, chemicals, materials, pharmaceuticals, and food. Yokogawa addresses customer issues regarding the optimizstion of production, assets, and the supply chain with the effective application of digital technologies, enabling the transition to autonomous operations. Founded in Tokyo in 1915, Yokogawa continues to work towards a sustainable society through its 17,500 employees in a global network of 119 companies spanning 61 countries.

For more information, visit www.yokogawa.com

(The names of corporations, organisations, products, services and logos herein are either registered trademarks or trademarks of Yokogawa Electric Corporation or their respective holders.)

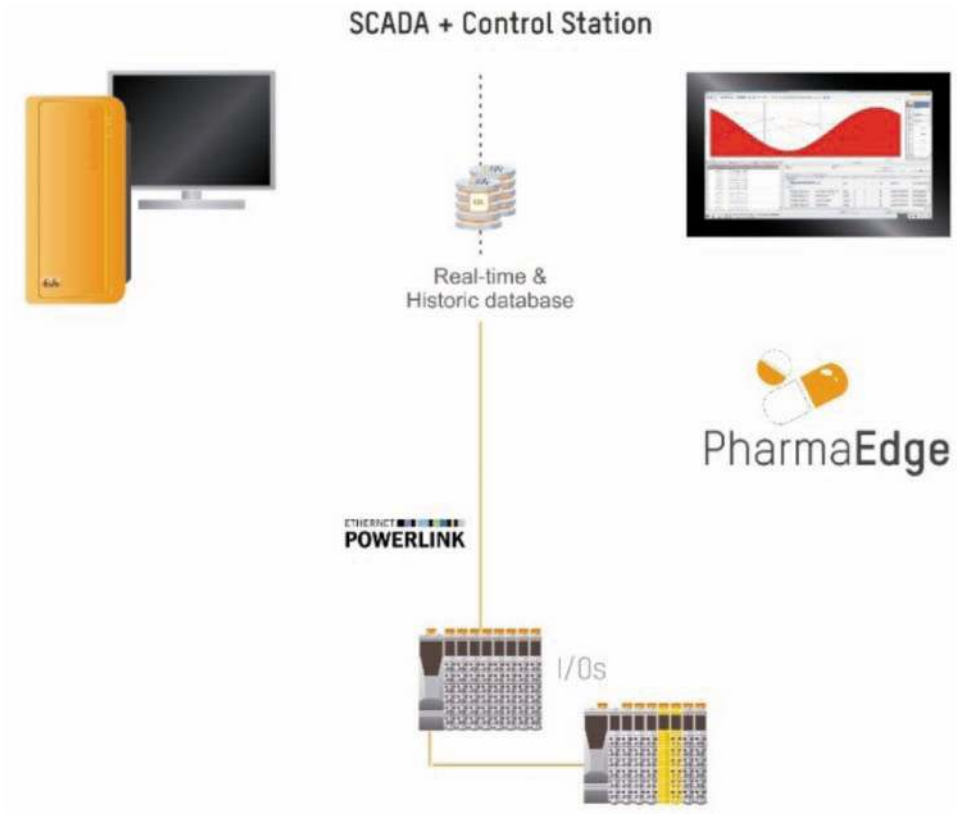
The next big digital revolution is happening in pharma industry

Digital revolution is all about creating seamless connectivity between machines, processes, and people within and beyond manufacturing facilities to increase quality, productivity and profit from the power of advanced data analytics

The Indian pharmaceutical industry offers tremendous opportunities for the automation sector. With globalisation and competitive market demands, more companies are becoming open to digitalisation as it is being used in many pharmaceutical processes, from drug discovery to manufacturing to packaging. On top of that, compliance with regulatory requirements opens new opportunities and challenges for automation suppliers.

Digital revolution is all about creating seamless connectivity between machines, processes, and people within and beyond manufacturing facilities to increase quality, productivity and profit from the power of advanced data analytics. With these next-generation automation solutions, pharma manufacturing companies can digitise their operations, increase efficiencies, enhance product quality, and fulfill regulatory compliances.

Pharma companies are usually tasked with examining data at every stage of their manufacturing process, right from the time raw materials arrive until the final product is packed and sent for distribution. In traditional pharmaceutical facilities, the references and information about drug formulation, production, equipment and data of QA-QC are manually entered in data sheets, which are prone to human errors and can even be manipulated. With such non-real-time information, it is difficult for management to take corrective actions and make timely decisions. However, with connected plant and Industrial IoT (IIoT) solutions, manufacturers can access data in real-time to monitor production, quality, OEE and equipment condition. It also enables mass customisation and batch size with cost-effective production.



PharmaEdge is an integrated solution for the pharmaceutical industry – all the benefits of SCADA and a powerful control system in one device

Demand for individualisation is creating new business opportunities. However, while executing this, a high ratio of setup costs to unit production costs acts as a bottleneck in the manufacturing process

Improved operational efficiencies

With IIoT, manufacturing facilities can monitor data from shop floors in real-time, enhancing process efficiencies. In the pharma industry, appropriate quality assurance is important. Without it, companies cannot guarantee that the product conforms to necessary quality and safety standards. Many times, product quality suffers because of machine downtime. In such cases, monitoring the conditions of assets in real-time can help in increasing equipment availability, preventing unplanned downtime.

Monitoring solutions like condition monitoring can predict device failures using real-time data helping scheduling services. Energy monitoring provides us with real-time data of the energy consumption and various other vital electrical parameters for a particular machine or process. All these data are collected from a machine or shop floor into the supervisory and control system to help us enable maximum life cycle usage of a product, maximising machine uptime resulting in improved OEE. Management can make faster and more intelligent business decisions using real-time data of operational insights. IIoT helps prioritise business decisions to reduce operating costs.

B&R's condition-monitoring modules reliably detect potential maintenance issues and are extremely easy to configure. A unique feature of these modules is that they perform vibration analysis locally. The availability of fully processed results minimises the time and cost of integration. These results also provide detailed insight into the system mechanics, allowing existing processes to be optimised with maximum efficiency.

B&R's energy-monitoring modules precisely measure all essential electrical parameters as configured. Often, it's not only the measured value that is important, but also the exact moment when a group of measured values is read out. The module is equipped with a Net-Time timestamp function which supplies a timestamp for the recorded position and trigger time with microsecond accuracy. Later, these values can be analysed as per requirements, and energy cost can be optimised, which will lead to an energy-efficient system.

Inter-connected machines or processes on the shop floor provide a massive amount of important data. B&R's PharmaEdge solution can easily collect the data. PharmaEdge is an integrated, out-of-the-box, optimised offering from B&R for the pharma industry to meet the increasing demand of

B&R's versatile industrial transport systems boosts the Overall Equipment Effectiveness (OEE), multiplies Return on Investment (ROI) and accelerates the Time To Market (TTM)

FDA compliance. It helps achieve cyber-security and advanced detailed reporting, analytics and business intelligence functionality. PharmaEdge offers all benefits of SCADA and a robust control system in one device. The possibility of adding energy monitoring, condition-based predictive maintenance, and MES/ERP connectivity enables smart and futuristic machines.

Digital remote access

Indian pharma OEMs are selling their machines, equipment and systems worldwide. Modern communication is helping to bring distant locations closer. However, for OEMs, having customers worldwide also comes with its share of new challenges. The situation becomes even complex during periods of extensive maintenance and unplanned downtimes. OEMs increasingly rely on remote maintenance to avoid incurring travel costs of service technicians and engineers worldwide. Remote maintenance makes connectivity, diagnosis and maintenance easier than ever and improves after-sales service. Service technicians can access machines from anywhere in the world. The secure remote maintenance solution utilises the latest IT and security standards and provides significant savings with low investment costs.

The new remote maintenance solution from B&R makes diagnosis and maintaining machinery and equipment easier and secure. The solution utilises the latest IT and security standards, enabling significant savings with low investment. With B&R's remote maintenance solution, a service technician can access machines from anywhere in the world to retrieve logbook entries, application data, and much more. When a customer's equipment or machine is not working, every minute counts, and there is immense pressure on maintenance and production teams to get the machine up and running. If a service technician is not available on-site, with B&R's remote maintenance solution, a technician can connect, diagnose, adjust parameters, and resolve errors – all in a matter of moments.

With B&R remote maintenance solution, a technician can connect, diagnose, adjust parameters and resolve errors – all in a matter of moments

Enabling mass customisation

Demand for individualisation is creating new business opportunities. However, while executing this, a high ratio of setup costs to unit production costs acts as a bottleneck in the manufacturing process. Next-generation innovative mechatronic systems deliver key advantages for advanced manufacturing solutions. The flexible, operator-friendly conveyors make production more efficient while improving product quality. This makes the production line more economical and effective at any volume from mass production down to batch size one.

B&R's innovative mechatronic systems ACOPOStrak, SuperTrak and ACOPOS 6D, help achieve increased demand effectively and efficiently. These systems can be fully integrated into any machine, which reduces the overall footprint of the line and improves processing precision. B&R's next-generation industrial transport systems can be implemented up to IP69K with dust and water protection and smooth surfaces easy to clean. The hygienic design certifies operation in food grade environment. The industrial-grade design ensures high availability and reliability with 24/7 operation. The mechatronic systems synchronise with robotics and CNC systems to create integrated production lines. This helps to make the production and packaging lines economical and effective at any volume from mass production down to batch size one. These systems allow products to be transported flexibly and independently and then grouped at a station to be processed as a batch. Overall, the production process can be accelerated by up to 50 per cent for a significant boost in productivity. B&R's smart-factory motion control in transport technology helps achieve key advantages: maximum availability, high-speed transport and positioning, rapid changeover, and fault-tolerant high quality.

B&R's innovative mechatronic systems boost the Overall Equipment Effectiveness (OEE), multiply the Return On Investment (ROI), and accelerate the Time To Market (TTM).

IIoT is currently in its nascent stages of adoption and started gaining interest in the Indian pharma industry, but its eventual impact across the global pharma sector is indisputable. IIoT helps in the standardisation of the manufacturing process along with data integrity. By systematically monitoring and analysing large volumes of data, manufacturers can benefit from improved production efficiency, productivity, reliability and quality. IIoT provides manufacturers with a holistic view of production, raw materials and distribution, leading to better and feasible analysis of the processes, thereby increasing operational efficiency.

Waters accelerates quantitative Mass Spectrometry with new application on waters connect informatics platform

Waters extends its waters_connect informatics platform to support tandem quad mass spectrometers with new quantitation software application

Waters Corporation recently announced that it is expanding its waters_connect™ informatics software platform to support customers analysing food and environmental samples with Waters' tandem quadrupole mass spectrometers. The new MS Quan™ application for waters_connect allows laboratories screening large numbers of samples, or those who may be quantifying hundreds of small molecule components and contaminants in a single run, a more efficient means of processing and reviewing data and identifying batch-to-batch variations.

For laboratories using Waters™ Xevo™ mass spectrometers, the MS Quan app quickly and accurately converts measurement data on compounds into meaningful results in a traceable, compliant and secure manner. Featuring a web-based user interface, the MS Quan app includes an Exception Focused Review (XFR) feature that can help cut data review time by up to 50 per cent by allowing users to focus on only those results that fall outside the user-determined ruleset.

MS Quan application reduces quantitative data review time by up to 50 per cent while allowing labs to meet compliance and data integrity requirements

"The waters_connect platform provides a backbone for the connected lab of the future where data is no longer siloed, but can be securely shared among a community of connected scientists using apps that talk to each other," said Jon Pratt, Senior Vice President, Waters Corporation.

Prat added, "MS Quan is a great example of the new applications and quality improvements we are bringing to our customers via waters_connect and its platform architecture designed for data integrity, compliance, security and accessibility."

Several scientists from Primoris (Zwijnaarde, Belgium), a global contract laboratory, participated in the beta testing of the MS Quan software application. Primoris measures pesticide residues and contaminants in food and animal feed as well as analysing food additives, supplements and essential oils.

"We've used MassLynx and TargetLynx from Waters for a very long time so we knew from the beginning the potential that this new app will offer," said Janne Dombrecht, Analysis Lead, Primoris Belgium.

Dombrecht also said, "The final product is exactly what we were looking for. Our close relationship with Waters and being able to test this product to make sure it is optimal for our methods has been a win-win situation. We're excited to roll it out across Primoris!"

The waters_connect for quantitation workflow and MS Quan app are now available worldwide as an upgrade for select Waters' tandem quadrupole mass spectrometers.

Additional resources

◆ *Learn more about the MS Quan app on waters_connect*

◆ *Read the blog: "Helping Laboratories Embrace New Era of Efficiency"*

◆ *Download the white paper: "The Benefits of waters_connect MRM Processing Application, MS Quan"*

About Waters Corporation
(www.waters.com)

Waters Corporation, 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 7,400 employees worldwide, Waters operates directly in 35 countries, including 14 manufacturing facilities, and with products available in more than 100 countries.

Waters, MS Quan, Xevo, MassLynx, TargetLynx and waters_connect are trademarks of Waters Corporation. Primoris is a trademark of Primoris Belgium.

CONTRIBUTOR'S CHECKLIST

❒ Express Pharma accepts editorial material for regular columns and from pre-approved contributors / columnists.
❒ Express Pharma has a strict non-tolerance policy of plagiarism and will blacklist all authors found to have used/refered to previously published material in any form, without giving due credit in the industry-accepted format. All authors have to declare that the article/column is an original piece of work and if not, they will bear the onus of taking permission for re-publishing in Express Pharma.
❒ Express Pharma's prime audience is senior management and pharma professionals in the industry. Editorial material addressing this audience would be given preference.
❒ The articles should cover technology and policy trends and business related discussions.
❒ Articles for columns should talk about concepts or trends without being too company or product specific.
❒ Article length for regular columns: Between 1200 - 1500 words. These should be accompanied by diagrams, illustrations, tables and photographs, wherever relevant.
❒ We welcome information on new products and services introduced by your organisation for our various sections: Pharma Ally (News, Products, Value Add), Pharma Packaging and Pharma Technology Review sections. Related photographs and brochures must accompany the information.
❒ Besides the regular columns, each issue will have a special focus on a specific topic of relevance to the Indian market.
❒ In e-mail communications, avoid large document attachments (above 1MB) as far as possible.
❒ Articles may be edited for brevity, style, and relevance.
❒ Do specify name, designation, company name, department and e-mail address for feedback, in the article.
❒ We encourage authors to send their photograph. Preferably in colour, postcard size and with a good contrast.

Email your contribution to:
The Editor,
Express Pharma,
Business Publications Division,

The Indian Express (P) Ltd,
Mafatlal Centre, 7th floor,
Ramnath Goenka Marg,
Nariman Point, Mumbai 400021
viveka.r@expressindia.com
viveka.roy3@gmail.com

Applications of Single-Use Technologies (SUTs) for upstream bioprocessing

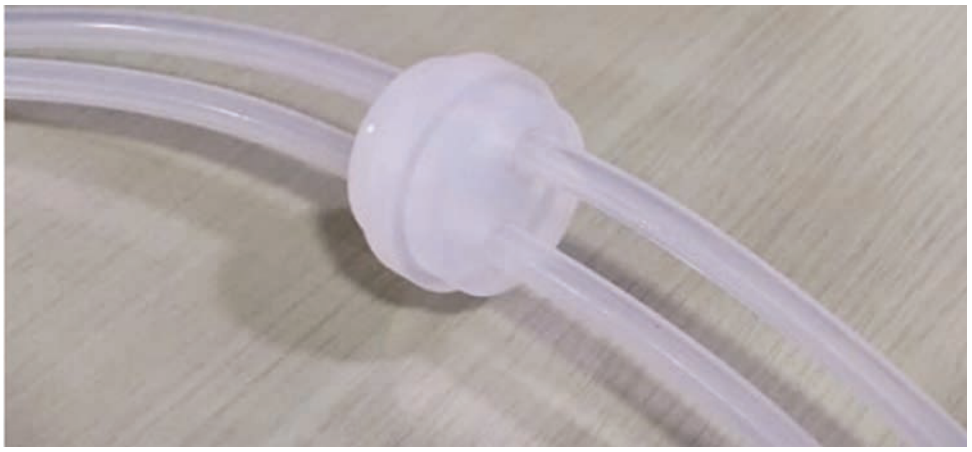
Implementation of SUTs for biopharmaceutical drug production helps to reduce the risk of contamination, reduces scheduling times, increases operational efficiencies, and reduces capital expenditures, including both fixed and consumables costs

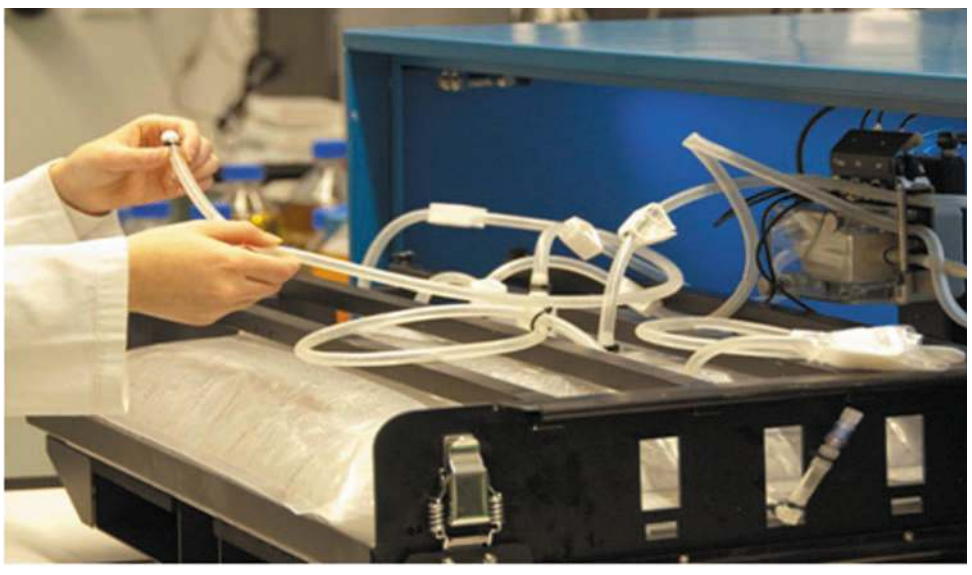
Single-Use Technologies (SUTs) have received increasing acceptance for biopharmaceutical manufacturing as companies have begun to realise their numerous benefits and equipment manufacturers have addressed key concerns, such as the potential for extractable and leachable from plastic components and interconnectivity of equipment from different suppliers.

Implementation of SUTs for biopharmaceutical drug production helps to reduce the risk of contamination, reduces scheduling times, increases operational efficiencies, and reduces capital expenditures, including both fixed and consumables costs. Single-use systems come pre-sterilised, thus eliminating the need for cleaning and sterilisation and significantly reducing setup and switch-over times. As a result, they also provide flexibility and enable manufacturers to quickly change their portfolios in response to market needs. When implementing SUTs, no clean-in place and steam-in-place (CIP/SIP) operations are required because disposable technologies generally are sterilised with gamma radiation. Thus, SUT piping and instrumentation are significantly simpler than those for traditional stainless-steel equipment.

SUTs have reduced dependency on utilities for sterilising product-contact parts of bioreactors between batches. Thus, processing times have been shortened, operational costs have been lowered and cleaning validation and training have decreased.

In particular, SUTs are ideal for scaling down biologic manufacturing processes, and are a key trend in the biopharmaceutical industry. SUTs are also well-suited for use in modular facilities, which are designed to enable high-quality production of biologic APIs and formulated products around the world, including in places where traditional facilities cannot be constructed.





Single-use systems come pre-sterilised, thus eliminating the need for cleaning and sterilisation and significantly reducing setup and switch-over times

As a result of these benefits, single-use bioreactors are widely used in upstream biopharmaceutical manufacturing processes. It is quite clear that disposable production technologies are now common place for many biopharmaceutical operations and their use can only be expected to expand further as additional innovative solutions are introduced by single-use equipment suppliers.

Ami Polymer is specialised in the production of custom assemblies for bioprocesses.

The company understands that time is important to its clients. For this reason, it fully adapts to client requirements. Plug-and-play solutions are now also available for fluid management. With its assemblies, one can easily connect multiple containers, vessels and process lines in one controllable system.

A solution towards Single-Use Assemblies

Ami Polymer offers wide range of gamma-irradiated single-use assemblies for various critical applications in biopharmaceuticals. These range from simple tubing with connector to complex manifold with several joints/connections. All the assemblies are manufactured and packed in Class 7 certified clean room. Few applications of upstream production in biopharmaceutical industry where Ami Polymer supplies assemblies are listed below:

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

Chandan Kumar Sah
Senior Manager- Quality/ Technical
Biotechnologist
Email: Chandan.s@amipolymer.com
Website:www.amipolymer.com

Ami Polymer Pvt. Ltd.
"Sealing Expert in Silicone"

testo Saveris Pharma: A complete pharma solution

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

A sector like pharmaceuticals that is governed by strict norms and regulations must operate with utmost efficiency. Testo provides the best-in-class solution for comprehensive data monitoring and management of equipment as well as environmental parameters in the pharma industry called the testo Saveris Pharma. It is an automated system that is integrated into the facility and constitutes wireless or ethernet probes installed at different locations that are connected to one base station to document and monitor all measurement data of its own. The monitoring process is uninterrupted, and the system provides a 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 includes:

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

Testo Saveris Pharma system consists of testo Saveris base V 3.0 which is the core component of the system. It manages and evaluates data from all over the facility from 3000 channels. The four testo 150 data logger modules can be flexibly combined with the three communication modules (WLAN, LAN, testo UltraRange) making it a very convenient and user-friendly system along with the web-based, intuitive cockpit to detect alarms, initiate corrective measures, and 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 you 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, log in to the company's website www.testo.com or write back to info@testo.in

PROSOLV® SMCC by JRS Pharma: Single excipient, many roles

Suyesh Kale, Technical Manager, JRS Pharma India, explains the various benefits of PROSOLV® SMCC

The development of co-processed, multi-functional excipients has enabled formulators to address multiple challenges with a single excipient, resulting in enhanced production and better finished product quality.

PROSOLV® SMCC can be used by formulators to address challenges which occur due to conventional granulation processes. It serves as a multifunctional excipient enabling fast and simpler formulation development which is hassle-free with proven benefits

Why PROSOLV® SMCC?

Attaining good hardness at low compaction forces is quite essential while considering suitability of excipient for tablet formulation. Microcrystalline cellulose is one of the widely used and accepted excipients in tablet dosage form. Compactability of microcrystalline cellulose (MCC) is of prime importance during compression.

MCC compact cohesion (which directly affects tablet strength) will be determined by the compaction pressure, all other conditions being equal. PROSOLV® SMCC is a novel high-functionality tableting excipient. The material is manufactured by co-processing MCC with colloidal silicon dioxide (CSD) and can be used to improve flow, lubricant sensitivity and tablet strength. (1) (2) (3).

The addition of CSD in MCC helps improve compactability. It has recently been reported that silicification appears to have no apparent effect on the primary chemical and polymorphic characteristics of MCC (4). This suggests that bulk modification of MCC does not occur during silicification and that the CSD, either by providing surface modification or by modifying strengthening interactions, is primarily responsible for the improvements in functionality, in particular tablet strength. This may be solely due to a morphological property or some other silicon dioxide MCC interfacial interaction.

Based on scanning electron microscopy studies together with electron microprobe analysis, it was stated that silicon dioxide is primarily located at the surface of the SMCC particles, while certain amounts of silicon dioxide were detected in the internal regions of some particles, the colloidal silicon dioxide particles present at the surfaces of the SMCC particles are shown to be uniformly distributed (5).

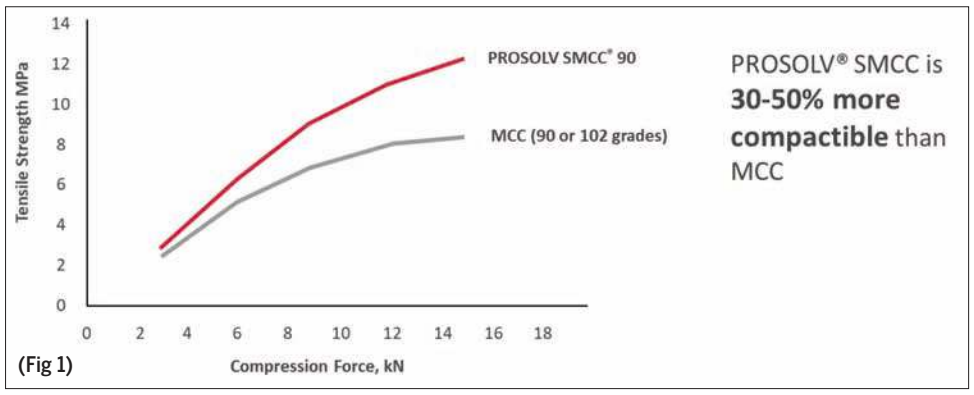
PROSOLV® SMCC for robust tablet production...

Taking the evolution of cellulose-based excipients further, JRS Pharma has improved MCC for direct compression by co-processing colloidal silicon dioxide and MCC in a spray-drying process. The result is PROSOLV® SMCC, which is almost dust-free and flows significantly better than non-direct compression grade MCC. It also offers superior compactability as compared to regular grade MCC.

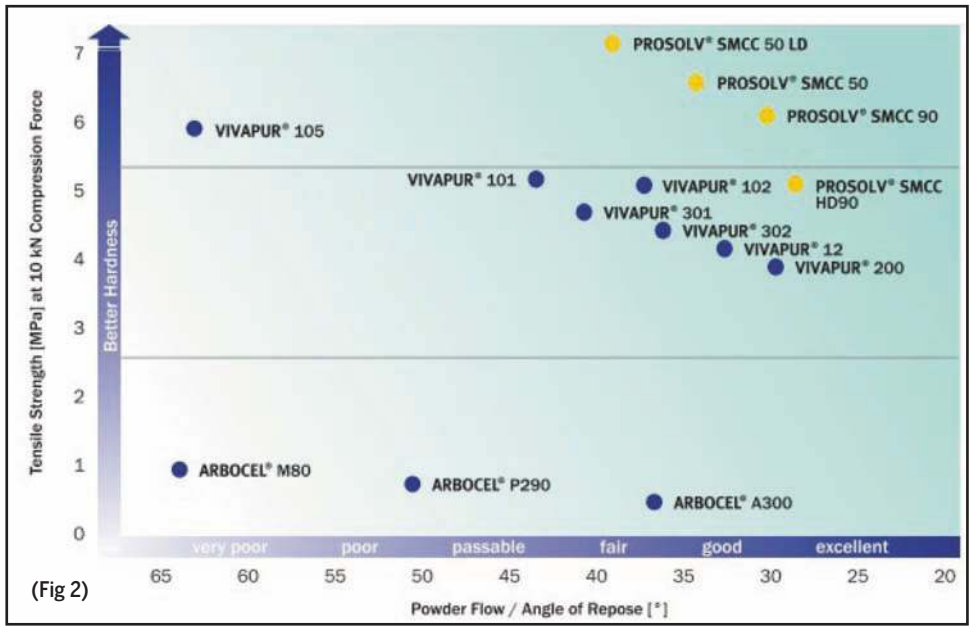
PROSOLV® SMCC is 30-50 per cent more compactible than MCC *(Fig 1)*. Therefore, the same hardness as observed with MCC tablets can be achieved with less compaction force *(Fig 2)*. This results in more porous tablets which enable faster disintegration and more complete drug dissolution.

PROSOLV® SMCC also has approximately five times the surface area of MCC, which in terms of blend quality, promotes better blending, homogeneity, dispersion, and overall content uniformity *(Fig 3)*.

Below image compares tablets made with PROSOLV® SMCC 90 (left) and MCC+CSD (right). Blue pigment was added to the blending as a demonstration of content uniformity. In this example, PROSOLV® SMCC 90 promotes interactive blending and clearly creates a more uniform blend *(Fig 4)*.



(Fig 1)



(Fig 2)

Effects of PROSOLV® technology

Silicification of MCC reduces the cohesiveness of the powder bed. Consequently, it has much better powder flowability than traditional MCC grades of the same particle size leading to more manufacturing output via high speed tableting. Compared to traditional MCC, the unique surface structure of PROSOLV® SMCC enables excellent blend homogeneity and content uniformity even for low-dose micronised Active Pharmaceutical Ingredient (API).

Benefits of using PROSOLV® SMCC

- PROSOLV® SMCC has superior flow and allows dust-free handling
- Improves compressibility and helps in rapid formulation development
- Improved compactability is achieved leading to more robust tablets
- Provides hard compacts in

roller compaction
- ◆ Can be used for sticky, hygroscopic and compression-sensitive API
- ◆ Excellent content uniformity in potent API can be achieved
- ◆ As co-processed, has good solubility characteristics for insoluble API
- ◆ Frequently used in multi-unit particulates (MUPS) formulations
- ◆ Provides smaller tablet sizes as fewer excipients are needed at lower usage levels

Formulation examples using PROSOLV® SMCC technology

A) Low-dose API formulation study:

A client was making a generic low-dose levothyroxine product but was having content uniformity problems. The original product was made with a MCC/lactose wet granulation process. In an attempt to improve content uniformity, the company tried a direct compression blend with MCC 102 with little improvement.

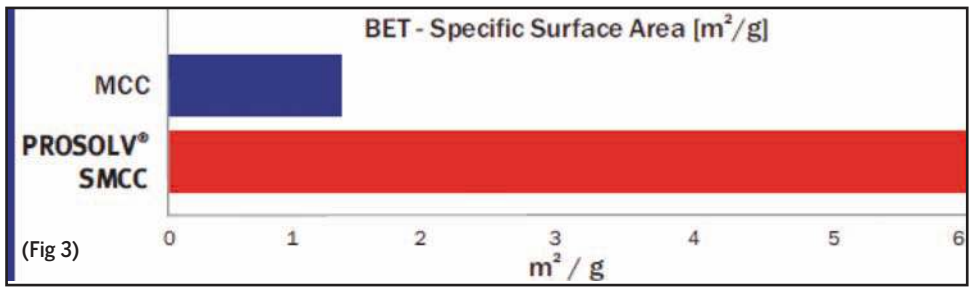
The client then tried a direct compression blend with PROSOLV® SMCC 90 and saw immediate improvement in content uniformity. To achieve even better results, the company made a pre-blend with 15 per cent of PROSOLV SMCC 90 and geometrically blended it with the bulk of PROSOLV® SMCC. The content uniformity further improved and so did the % RSD.

Going a step further, the client took the same pre-blend of API with PROSOLV® SMCC 90 of the requirement. They then blended it with PROSOLV® SMCC 50 and PROSOLV® SMCC 90 (50 per cent each) to try and minimise the disparities which exist between the particle size of API and excipients. By using that formula and direct compression process, achieved excellent content uniformity and % RSD of 0.08-0.1 per cent *(Table 1)*.

B) Reducing tablet size for a higher drug load

1) Formulation Challenge: The 19 active formulation, including herbal constituents, required large amounts of both MCC and DCP to achieve workable compactability, yet still exhibited significant segregation, low content uniformity and poor flow. The resulting tablet also exceeded target size due to multiple components and large amount of excipients.

2) Formulation results: After formulating with PROSOLV® SMCC, the need for Dicalcium phosphate was eliminated. Compactability, segregation and content uniformity were improved and tablet weight was reduced by 33 per cent. Finally, due to improved flow characteristics and consolidated blending, tableting speed and production efficiency both were increased *(Table 2)*.



(Fig 3)

(Fig 4)

Grade	Functionality
PROSOLV® SMCC 50 LD	Best in class filler
PROSOLV® SMCC 50 LD	Formulas in which optimal compaction and decent flow are required
PROSOLV® SMCC 90	Formulas in which a balance of flow and compaction are required
PROSOLV® SMCC HD 90	Formulas in which optimal flow and consolidation are required. This grade shows the best disintegration time
PROSOLV® SMCC 90 LM	Equivalent to PROSOLV SMCC 90 with lower moisture content (<3%)

(Table 1)

Formula	Process	% RSD
Original product	MCC/Lactose wet granulation	-8.0%
MCC blend	Direct compression blend with PH 102	5-8.0%
PROSOLV® blend	Direct compression blend with PROSOLV® SMCC 90	2-2.5%
PROSOLV® pre-blend	Pre-blend with 15% of SMCC 90 requirement	0.8-1.0%
PROSOLV® mixed grade pre-blend	Pre-blend with 15% of PROSOLV® SMCC 90 requirement; titrated with 50/50 PROSOLV® SMCC 90 and PROSOLV® SMCC 50	0.08-0.1%

(Table 2)

MCC/DCP formulation	PROSOLV® SMCC formulation
20% MCC 20% DCP	7 % PROSOLV SMCC 90 No DCP required
Low compactability	Exceptional tablet hardness Hardness 90-120 N Friability 0.08%
Excessive tablet weight > 1800 mg	Target weight achieved < 1300 mg
Low bulk density, Active with poor flow	Consolidated powder blend with excellent flow
Significant segregation of active Fine particles seen floating on top of blend	Non- segregating formulation Separation of fine particles reduced < 2 % RSD in tablet weight

Conclusion

PROSOLV® SMCC can be used by formulators to address challenges which occur due to conventional granulation processes. It serves as a multifunctional excipient enabling fast and simpler formulation development which is hassle-free with proven benefits.

References

1) Sherwood, B. E., Hunter, E. A., Staniforth J. N. (1996) Silicified microcrystalline cellulose (SMCC): a new class of high functionality binders for direct tableting. Proc. AAPS Conf. PT 6164
2) Staniforth, J. N., Tobyn, M. J. (1996) towards a new class of high functionality tablet binders. III: Physical characteristics and particle morphology of silicified microcrystalline cellulose (SMCC). Proc. AAPS Conf. PT6162
3) Sherwood, B. E., Becker, J. W. (1998) a new class of high functionality excipients: silicified microcrystalline cellulose. Pharm. Tech. 22: 78-88
4) Tobyn, M. J., McCarthy, G. P., Staniforth, J. N., Edge, S. (1998) Physicochemical comparison between microcrystalline cellulose and silicified microcrystalline cellulose. Int. J.Pharm. 169: 183-194
5) B. van Veena, G.K. Bolhuisb, Y.S. Wub, K. Zuurmanb, H.W. Frijlinkb (2005) Compaction mechanism and tablet strength of unlubricated and lubricated (silicified) microcrystalline cellulose. Eur. J. Pharmaceutics & Biopharmaceutics. 133-134

For more details, contact:
Suyesh.kale@jrsindia.com

ACRYCOAT® Methacrylic Acid Copolymer
Enteric coating | Film coating | Sustained release
Taste masking | Moisture barrier coating

COLORCOAT™ Ready-to-use Coating System
Film coating | Enteric coating | Moisture barrier coating
Transparent coating | Flavour coating

ACRYPOL® Carbomer
Thickening agent | Suspending agent | Emulsifying agent
Topical application | Oral care application

KYRON™ Taste Masking & Super Disintegrant
Taste masking of drug | Suspension | Dry syrup
Chewable tablets | Mouth dissolving tablets

ACRYSOL™ Castor Oil Derivative
Vitamin solubilizer | API solubilizer | Cream emulsifier
Oil & Perfume solubilizer | Dissolution improver

ACRYFLOW™ Stearate Derivatives
Tablet Lubricant | Sustained release

NUTRACOAT™ Natural Coating System
Sustained release | Moisture barrier coating | Taste masking

COREL PHARMA CHEM

the next generation polymer technologist...

Corel House, Opp. Bhagwat Petrol Pump, Gota, S.G. Highway, Ahmedabad - 382 481, Gujarat, INDIA
Tele.: +91-8000880011 / 22 / 33
E-mail: corel@corelpharmachem.com, marketing@corelpharmachem.com, www.corelpharmachem.com

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