Friday, 11 October 2024

INSIGHTS

Healthcare Newsweekly For You

CONTENT *(Highlights)*

A-601, Marathon Innova, Opp. Peninsula Corporate Park, Off Ganpatrao Kadam Marg, Lower Parel (W), Mumbai 400 013, India.

Tel.:+91-22-6673 6800,
Fax: 91-22-66399727
web: www.sidvim.com

UPCOMING EVENTS

Webinar

Human Errors in GMP Manufacturing and Laboratory Processes Identification, Correction and Prevention - Latest FDA Regulatory Requirements & Most Common GMP Issues Caused by Human Error

23 October 2024, Online

Learning Benefits:

- Identify why human error is often designated the root cause of deviations and discrepancies.
- Identify why your CAPA's are less effective than you hoped.
- Understand why human error is not the real cause of the deficiencies and deviations.
- How to probe further to identify the causes or contributing factors that really cause the problems you are seeing.
- How to develop a true CAPA for these problems.
- Develop an efficient and effective CAPA system to remedy the ingrained problems.
- Identification and prevention of human error during data entry.
- Most common GMP issues caused by human error during laboratory and manufacturing processes.

Regulations that will be Covered:

Each country has its own specific set of regulations. Below are examples of regulations that are applicable:

- Code of Federal Regulations 21 sections 210, 211 for Biological products and Drugs and 600 series for Biologicals in addition for USA.
- Health Canada regulations for pharmaceutical and biotechnology products including appropriate annexes such as 1, 2, 3, 18.
- EMA Eudralex Volumes 1, 2, 3, 4, 9 for Drugs and Biologics in EU.
- International Conference on Harmonisation Quality Series Q1 through Q10 for USA, EU, Japan and other countries.

Register Now

DEALS/ FUNDING

GEMMABio secures $100M partnership with health ministry to bring rare disease gene therapies to Brazil

Fierce Biotech, 8 October 2024

GEMMABio, one of two new companies spun out of the now-folded Gene Therapy Program at the University of Pennsylvania, has announced its first major step in improving global access to rare disease gene therapies.

The Philadelphia-based biotech, founded and run by Jim Wilson, M.D., Ph.D., will receive up to $100 million from the Oswaldo Cruz Foundation (Fiocruz) for clinical research and manufacturing, the firm said in an Oct. 8 release. Fiocruz is a public health research institution that is part of Brazil's Ministry of Health.

"By combining our resources and knowledge, this collaboration represents a major advancement in making gene therapies accessible to more patients quickly and at a fraction of the typical cost," Wilson, who is president and CEO of GEMMABio, said in the release. "We are optimistic that this deal will serve as a global example for expanding access to advanced medical therapies as well as pursuing non-traditional ways to capitalize biotech companies."

https://www.fiercebiotech.com/biotech/gemmabio-secures-100m-partnership-health-ministry-bring-rare-disease-gene-therapies-brazil

★★★★★★

Lilly, insitro Enter Strategic Agreements for Metabolic Diseases

Contract Pharma, 10 October 2024

Will support insitro's IND-enabling studies for first set of pipeline programs from its machine learning platform.

Insitro, a machine learning-enabled drug discovery and development company, entered three strategic agreements with Lilly focused on advancing potential new medicines for metabolic diseases, including metabolic dysfunction-associated steatotic liver disease (MASLD), based on targets identified using insitro's AI/ML-based platform.

Current therapies for metabolic diseases primarily manage symptoms without addressing root causes. This collaboration aims to shift this paradigm by combining insitro's machine learning platforms, particularly directed at early biology discovery, with Lilly's expertise in drug delivery and metabolic disease biology.

Under the first two agreements, insitro has an option to in-license clinical stage, ternary N-acetylgalactosamine (GalNAc) delivery technology from Lilly that it will combine with two different small interfering ribonucleic acid (siRNA) molecules discovered and developed by insitro, each specifically directed toward a different target in the liver.

https://www.contractpharma.com/contents/view_breaking-news/2024-10-09/lilly-insitro-enter-strategic-agreements-for-metabolic-diseases/

★★★★★★

Seizure-spotting headset maker Ceribell seeks $101M Nasdaq IPO

Fierce Medtech, 7 October 2024

Ceribell, the maker of a portable, brain-reading headset for emergency seizure care, aims to go public on the Nasdaq through a $101 million IPO.

The former Fierce 15 winner has priced some 6.7 million shares in the range of $14 to $16, for a proposed total market value of about $505.4 million, according to Renaissance Capital. The company plans to list under the ticker "CBLL."

While seizures are most commonly associated with epilepsy, they can also be triggered by traumatic brain injuries, strokes, cardiac arrest and sepsis, among other conditions—including without any convulsive or physical symptoms.

Ceribell's disposable, point-of-care electroencephalography platform, including its artificial intelligence-powered detection algorithms, help track hidden brain activity and deliver a definitive diagnosis.

https://www.fiercebiotech.com/medtech/seizure-spotting-headset-maker-ceribell-seeks-101m-nasdaq-ipo

★★★★★★

MARAbio raises $19M to develop an antibody blood test for autoimmune-related autism

Fierce Medtech, 7 October 2024

A startup that aims to deliver a blood test to identify a biomarker linked with a specific subtype of autism—and then potentially develop early behavioral interventions and treatments—has raised $19 million to kick-start its operations.

MARAbio derived its name from a particular pattern of antibodies carried by the child's mother, which research has shown can react with eight different proteins found in the

developing brain. Maternal autoantibody-related autism, or MARA, has been associated with about 20% of all diagnoses of autism spectrum disorder.

Based on research licensed from the University of California, Davis, the Salt Lake City-based company has said that certain patterns of the autoantibodies may also be able to predict the severity of autism compared to other combinations.

https://www.fiercebiotech.com/medtech/marabio-raises-19m-develop-antibody-blood-test-autoimmune-related-autism

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Amneal Pharma to invest Rs 1,600 crore in Gujarat to make GLP-1 drugs

Business Standard, 8 October 2024

Nasdaq-listed Amneal Pharmaceuticals, which already operates multiple manufacturing facilities in Gujarat, is further investing up to Rs 1,680 crore ($200 million) over the next four to five years for peptide synthesis and advanced sterile fill-finish manufacturing.

The company said on Tuesday that it will build two new manufacturing facilities in Ahmedabad with a total investment of $150–200 million. The company will develop and supply a portfolio of next-generation branded medicines for metabolic diseases and obesity, including GLP-1 and amylin receptor agonists, in collaboration with Mets.

https://www.business-standard.com/companies/news/amneal-pharma-to-invest-rs-1-600-crore-in-gujarat-to-make-glp-1-drugs-124100800890_1.html

★★★★★★

Biologicals startup BioPrime raises $6M in Series A round

Your story, 8 October 2024

This investment marks Belgium-based Edaphon's first in Asia. BioPrime will use the funds to expand research in the crop protection segment, focusing on the co-development of novel biofungicides and bioinsecticides.

BioPrime, a startup in the biologicals space, said it has raised $6 million in a Series A round, led by Edaphon, with equal participation from existing investors Omnivore and Inflexor. This investment marks Belgium-based Edaphon's first investment in Asia. BioPrime will use the capital to expand research in the crop protection segment, focusing on the co-development of novel biofungicides and bioinsecticides. Biologicals startup BioPrime raises $6M in Series A round | YourStory

★★★★★★

Aptar Pharma Acquires Device Technology Assets of SipNose

Aptar.com, 9 October 2024

Acquiring SipNose's assets will further expand Aptar Pharma's intranasal drug delivery portfolio

Aptar Pharma, a global leader in drug delivery systems, services and active material science solutions, today announces that it has acquired all device technology assets from the proprietary portfolio of SipNose Nasal Delivery Systems, a company focused on intranasal delivery platforms for local, systemic and central nervous system indications.

SipNose offers a variety of devices that are designed and adapted to fit a wide range of therapies and offer the opportunity to precisely target areas of the nasal cavity to enable enhanced systemic, local or even direct-to-brain delivery.

https://aptar.com/news-events/aptar-pharma-acquires-device-technology-assets-of-sipnose/

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KKR weighing block deal option to monetise JB Pharma stake

Hindu Business line, 7 October 2024

The $2 billion deal has been in the making for several months, and only a few drug manufacturers had a look in, as the deal value was high

With discussions to sell stake in JB Chemicals and Pharmaceuticals running into a wall over valuation and pricing, private equity firm KKR is understood to be weighing the prospect of exiting through market sales, via the block deal windows of Indian exchanges, sources said The $2 billion deal has been in the making for several months, and only a few drug manufacturers had a look in, as the deal value was high. At one time, it looked as if Torrent Pharmaceuticals, the company with which KKR originally initiated dialogues, would walk away with the PE firm's 54 per cent stake.

https://www.thehindubusinessline.com/news/kkr-weighing-block-deal-option-to-monetise-jb-pharma-stake/article68728886.ece

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MSD ventures into fibroblast therapies with $1.9bn deal with Mestag

Pharmaceutical technology, 9 October 2024

The deal allows MSD to license one or more therapies against inflammatory diseases developed using the UK biotech's fibroblast platform.

MSD (Merck & Co) has signed a license and collaboration agreement with Mestag Therapeutics to develop new fibroblast therapies for inflammatory diseases – a deal potentially worth $1.9bn The companies did not disclose the particulars of the deal, noting that the agreement allows MSD the option to get exclusive development and marketing licences to "a prespecified number of potential targets." The UK-based biotech in return will receive an upfront payment, and access fees and will be in line to receive option fees and "downstream payments".

https://www.pharmaceutical-technology.com/news/msd-ventures-into-fibroblast-therapies-with-1-9bn-deal-with-mestag/

★★★★★★

Board of Fortis Healthcare approves NCD issuance of Rs 1550 cr

Business standard, 10 October 2024

The Board of Fortis Healthcare at its meeting held on 09 October 2024 has approved the issuance of listed, senior, secured, rated, redeemable Non-Convertible Debenture (NCDs) aggregating for a value of up to Rs 1550 crore having a face value of Rs. 1,00,000 on private placement basis to the eligible investors.

https://www.business-standard.com/markets/capital-market-news/board-of-fortis-healthcare-approves-ncd-issuance-of-rs-1550-cr-124101000221_1.html

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PHARMA AND BIOLOGICS

SMALL MOLECULE

TIFR study uses psychedelic drug to trace neuron that can reduce anxiety

EThealthworld, 6 October 2024

A team at the Tata Institute of Fundamental Research (TIFR) in Mumbai have steer a first-of-its-kind study to come out of India, using a psychedelic to identify a neuron that can activate the ventral hippocampus in the brain—which processes emotional information and regulates stress—in a manner that could alleviate anxiety. https://health.economictimes.indiatimes.com/news/pharma/research-development/tifr-study-uses-psychedelic-drug-to-trace-neuron-that-can-reduce-anxiety/113979186

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Pii Introduces Accelevate Early Development Platform

ContractPharma, 10 October 2024

Accelerates the preparation of IND submissions, allowing pharmaceutical companies to reach IND readiness in 100 days for aseptic products.

Pharmaceutics International Inc. (Pii), a provider of pharmaceutical development and manufacturing services, has launched its Accelevate Early Development Platform, which is designed to accelerate the preparation of Investigational New Drug (IND) submissions, offering small to mid-sized pharmaceutical companies the ability to reach IND readiness in 100 days for aseptic products.

The Accelevate platform addresses a critical need in the pharmaceutical industry, where the pressure to reduce time-to-market has become increasingly pronounced, particularly for smaller companies that lack the internal resources to navigate the complexities of early-stage development. Accelevate offers an innovative approach, integrating Pii's advanced technology, regulatory expertise, and project management capabilities to deliver a seamless, efficient path from molecule identification to IND submission. https://www.contractpharma.com/contents/view_breaking-news/2024-10-09/pii-introduces-accelevate-early-development-platform/?widget=listSection

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Future of oral small molecule drugs – addressing potential in multiple sclerosis

Europeanpharmaceuticalreview, 3 October 2024

Advances in selectivity, safety, and patient convenience, oral small molecule drugs continue to be a key focus in drug development. Here, Dr Andreas Muehler and Daniel Vitt, PhD, the co-founders of Immunic Therapeutics, discuss the potential of Vidofludimus calcium as a breakthrough treatment for autoimmune diseases.

https://www.europeanpharmaceuticalreview.com/article/234618/future-of-oral-small-molecule-drugs-addressing-potential-in-multiple-sclerosis/

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AstraZeneca Expands Cardiovascular Disease Prospects, Paying $100M for Oral Way to Drug Lp(a)

Medcitynews, 7 October 2024

Cardiovascular disease drugs in development intended to reduce lipoprotein (a) are mostly injectable medications, though Eli Lilly has both oral and injectable drugs in the

clinic. AstraZeneca aims to hit that key protein target with an oral small molecule licensed from CSPC Pharmaceutical Group.

While drugs are available that reduce levels of lipoprotein (a), a protein associated with cardiovascular disease, no currently available therapies target this protein directly. Several companies are in various stages of clinical development with drugs that could tackle this protein, and AstraZeneca is paying $100 million to license a preclinical drug giving it a contender in the chase.

https://medcitynews.com/2024/10/astrazeneca-cardiovascular-disease-lipoprotein-a-cspc-lpa-azn/

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LARGE MOLECULE

The Positive Topline Results From Phase III Study of UCB/Biogen's Dapirolizumab Pegol Brings a Ray of Hope in Systemic Lupus Erythematosus Therapeutic Space | DelveInsight

Themalaysianreserve, 8 October 2024

UCB and Biogen reported encouraging topline findings from the Phase III PHOENYCS GO trial, which assessed dapirolizumab pegol, a novel Fc-free anti-CD40L drug candidate, in individuals with moderate-to-severe SLE. The promising outcomes with dapirolizumab pegol signify significant advancements in creating treatments that can enhance the quality of life for individuals with lupus, a condition that continues to have considerable unmet medical needs, particularly impacting women.

LAS VEGAS, Oct. 7, 2024 /PRNewswire/ — Systemic lupus erythematosus is a long-lasting autoimmune disorder that can impact various areas of the body. Lupus arises when the immune system, typically responsible for defending against infections and illnesses, mistakenly targets the body's own tissues. This misguided response leads to inflammation and, in some instances, lasting damage to tissues, potentially affecting a wide range of organs including the skin, joints, heart, lungs, kidneys, blood cells, and brain.

The Positive Topline Results From Phase III Study of UCB/Biogen's Dapirolizumab Pegol Brings a Ray of Hope in Systemic Lupus Erythematosus Therapeutic Space | DelveInsight - The Malaysian Reserve

★★★★★★

Lonza completes acquisition of large-scale biologics site from Roche

Pharmaceutical manufacturer, 3 October 2024

Lonza announced it has completed its acquisition of the Genentech large-scale biologics manufacturing site in Vacaville, California (US) from Roche for USD 1.2 billion.

The acquisition extends Lonza's US Biologics footprint with a significant presence on the West Coast, complementing its existing global manufacturing network.

The products previously manufactured at the site will now be supplied by Lonza to Roche with committed minimum volumes over the medium term, phasing out over time as the site transitions to serve alternative customers.

https://pharmaceuticalmanufacturer.media/pharma-manufacturing-news/latest-pharmaceutical-manufacturing-news/lonza-completes-acquisition-biologics-site-roche/

★★★★★★

Recipharm invests in sterile development capabilities

Pharmaceutical manufacturer, 4 October 2024

Recipharm is expanding its pharmaceutical development capabilities through targeted investments and the integration of advanced technologies.

The new investments bolsters its services for early- and late- stage product development in oral solid dosage (OSD), sterile fill & finish (SFF) and complement existing development capabilities.

Significant investments include a development lab for sterile formulations for small molecules in Bengaluru, the installation of a GMP VarioSys line for pre-filled syringes at Wasserburg and a GMP LAB+ equipment at Kaysersberg.

https://pharmaceuticalmanufacturer.media/pharma-manufacturing-news/pharma-finance-and-investment-news/recipharm-invests-in-sterile-development-capabilities/

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REGULATORS AND REGULATORY ACTIONS

Pfizer, BioNTech win bid to invalidate CureVac's UK COVID vaccine patents

Reuters, 8 October 2024

Pfizer and its German partner BioNTech on Tuesday won their attempt to invalidate two of rival CureVac's patents at London's High Court.

Pfizer and BioNTech had filed their lawsuit in September 2022 over patents relating to messenger RNA (mRNA) technology, which underpins Pfizer and BioNTech's COVID-19 vaccine.

Tuesday's ruling relates to the London leg of Pfizer, BioNTech and CureVac's global legal battle, which also involves litigation in the United States and Germany.

https://www.reuters.com/business/healthcare-pharmaceuticals/pfizer-biontech-win-bid-invalidate-curevacs-uk-covid-vaccine-patents-2024-10-08/

★★★★★★

Danco to seek FDA nod for use of abortion drug in miscarriages, WSJ reports

Reuters, 8 October 2024

Danco Laboratories plans to ask the U.S. Food and Drug Administration to approve its abortion pill regimen for management of miscarriages, the Wall Street Journal reported on Tuesday.

Danco is preparing scientific data and taking other steps to file for expanded approval of the treatment called Mifeprex, the WSJ reported, citing people familiar with the matter.

Mifeprex was approved by the FDA in 2000 for medication abortion, which accounts for more than half of all medical termination of pregnancies in the U.S.

https://www.reuters.com/business/healthcare-pharmaceuticals/danco-lab-seek-expanded-use-abortion-pill-manage-miscarriages-wsj-reports-2024-10-08/

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GSK agrees to settle about 80,000 Zantac lawsuits for up to $2.2 bln

Reuters, 10 October 2024

GSK has agreed to pay up to $2.2 billion to settle most lawsuits in U.S. state courts claiming that a discontinued version of the heartburn drug Zantac caused cancer, the company announced on Wednesday.

The agreement with 10 plaintiffs' law firms resolves about 80,000 cases, or 93% of cases pending against the British drugmaker in state courts nationwide, the company said. GSK also said it would pay $70 million to settle a related whistleblower lawsuit filed by a Connecticut laboratory.

https://www.reuters.com/legal/gsk-reaches-up-22-billion-settlement-zantac-us-state-court-cases-2024-10-09/

US FDA declines to approve Zealand's drug for low blood sugar in infants

ET Pharma, 9 October 2024

The Food and Drug Administration (FDA) in its so-called "complete response letter " cited the timing of a third-party manufacturing facility reinspection for the decision, the company said. The letter, however, did not mention any concerns about the clinical data package or safety of the drug, dasiglucagon.

https://pharma.economictimes.indiatimes.com/news/drug-approvals-and-launches/us-fda-declines-to-approve-zealands-drug-for-low-blood-sugar-in-infants/114071653?utm_source=top_news&utm_medium=sectionListing

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Alembic Pharma rises after oncology facility completes US FDA audit with 'zero' observations

Business standard, 8 October 2024

Alembic Pharmaceuticals added 2.50% to Rs 1277.65 after the company announced the successful completion of the United States Food and Drug Administration (US FDA) inspection for its oncology formulation facility located at Panelav, Gujarat.

The US FDA had conducted an inspection at the company's oncology (injectable and oral solid) formulation facility from 7 October 2024 to 8 October 2024.

"The inspection was successfully completed without any Form 483 observation," the company said in a statement. Alembic Pharmaceuticals is in the business of development, manufacturing, and marketing of pharmaceutical products, i.e. formulations and active pharmaceutical ingredients.

https://www.business-standard.com/markets/capital-market-news/alembic-pharma-rises-after-oncology-facility-completes-us-fda-audit-with-zero-observations-124100900178_1.html

★★★★★★

UK firm GSK to pay $2.2bn over Zantac cancer claims

BCC, 10 October 2024

UK pharmaceutical giant GSK says it will pay as much as $2.2bn (£1.68bn) to settle thousands of cases in US courts over claims that a discontinued version of its heartburn drug Zantac caused cancer.

The firm announced that it had reached agreements with 10 law firms who represent around 80,000 claimants. The settlements account for 93% of all cases.

GSK will also pay $70m to resolve a whistleblower complaint by a laboratory that alleged the drugmaker defrauded the US government by concealing Zantac's cancer risks.

GSK did not admit wrongdoing in any of the cases.

https://www.bbc.com/news/articles/c62r5nn94d7o

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FDA declines to approve Zealand Pharma's hypoglycaemia therapy in infants

Pharmaceutical technology, 9 October 2024

The regulator sought additional analyses from existing continuous glucose monitoring data collected during Phase III trials.

The US Food and Drug Administration (FDA) has issued a complete response letter (CRL) to Zealand Pharma, declining the approval of dasiglucagon for the treatment and prevention of hypoglycaemia in infants with congenital hyperinsulinism (CHI).

The CRL, which pertains to Part 1 of the new drug application (NDA) for patients aged seven days and older, cites the need for a reinspection at a third-party manufacturing facility. This regulatory decision is linked to the timing of a reinspection at a contract manufacturing site that concluded in August/September 2024.

https://www.pharmaceutical-technology.com/news/fda-zealand-hypoglycemia-therapy/

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Glenmark Life Sciences to rebrand as Alivus Life Sciences, shares in green

Hindu business line, 9 October 2024

The rebranding, which includes alterations to the company's Memorandum of Association and Articles of Association, is subject to shareholder approval via postal ballot and necessary regulatory clearances. Glenmark Life Sciences Limited announced plans to change its name to Alivus Life Sciences Limited, following its acquisition by Nirma Limited. The company's Board of Directors approved the name change on October 8, 2024, through a circular resolution.

https://www.thehindubusinessline.com/markets/stock-markets/glenmark-life-sciences-to-rebrand-as-alivus-life-sciences-shares-in-green/article68735665.ece

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Government allows cough syrup export without testing for top market

Pharmatutor, 9 October 2024

The manufacturers are exporting the Cough Syrup to USA, UK, Canada, EU, Japan, Australia, Singapore, Republic of Korea and Switzerland, the requirement of testing from the laboratories may be waived off, in view of approval granted by these countries regulatory agencies for plants or section engaged in manufacturing and export of Cough Syrup, said in a notification by DGFT.

It is further mentioned in a notification that if Cough Syrup is manufactured in a plant/section approved by the regulatory agencies for above mentioned countries for any product, such Cough Syrup shall be permitted to be exported to any country without testing as mandated.

https://www.pharmatutor.org/pharma-news/2024/government-allows-cough-syrup-export-without-testing-for-top-market

MEDTECH

FDA amplifies Medtronic recall of MiniMed insulin pumps over shortened battery life

Fierce Medtech, 8 October 2024

Medtronic has been notifying users of its MiniMed insulin pumps to be aware of potentially shortened battery lives and to heed the devices' low-power warnings and alerts. Now, the FDA has elevated the efforts into a Class I recall, the agency's most serious category, following reports of dangerously high blood sugar levels.

The medtech giant first began reaching out to people with diabetes and healthcare providers about the issue in late July. The company said its analysis found that dropping or bumping the MiniMed 600 and 700 series pumps could damage the internal electric hardware, and then cause the battery to drain more quickly—ultimately increasing the risk of the pump stopping or slowing the delivery of insulin sooner than expected.

Medtronic said that, between January 2023 to September of this year, it has received 170 reports of hyperglycemia, or blood sugar readings over 400 mg/dL, as well as 11 cases of diabetic ketoacidosis.

https://www.fiercebiotech.com/medtech/fda-amplifies-medtronic-recall-minimed-insulin-pumps-over-shortened-battery-life

★★★★★★

Illumina launches compact, low-cost gene sequencing devices

Reuters, 10 October 2024

Medical equipment maker Illumina announced on Wednesday its new series of smaller, low-cost benchtop gene sequencers, to make sequencing accessible to more research and testing labs.

New generation sequencers, like Illumina's MiSeq devices, help determine the sequence of DNA or RNA to study genetic variation associated with diseases and diagnose rare genetic conditions.

Unlike Illumina's NovaSeq X devices — which are as large as a Xerox copier and designed for in-depth sequencing — the new MiSeq i100 systems can be placed on benchtops, allowing smaller labs, which typically outsource gene sequencing, to have these capabilities in-house.

https://www.reuters.com/business/healthcare-pharmaceuticals/illumina-launches-compact-low-cost-gene-sequencing-devices-2024-10-09/

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INTERESTING MEDICAL NEWS

Oral Epilepsy Drug Eases Symptoms of OSA

Medscape, Heidi Splete, September 23, 2024

An epilepsy drug sold in Europe as Ospolot and also known as sulthiame showed promise in reducing sleep disordered breathing and other symptoms of obstructive sleep apnea (OSA), based on data from nearly 300 individuals presented in a late-breaking study at the European Respiratory Society Congress 2024.

"Current therapies are mechanical and based on the notion of an airway splint," said presenting author Jan Hedner, MD, professor of respiratory medicine at Sahlgrenska University Hospital and the University of Gothenburg, Gothenburg, Sweden, in an interview. "In other words, applying an airflow at elevated pressure (continuous positive airway pressure) or advancing the jaw with a dental device," he said. "Adherence to this type of therapy is limited. In the case of continuous positive airway pressure (CPAP), it is < 50% after 3-4 years of therapy," he added. Therefore, there is a need for a better tolerated therapy, such as a drug, and possibly a combination of mechanical and pharmaceutical therapies, he told *Medscape Medical News*.

The use of medication has emerged as a viable option for OSA, with a high rate of compliance and acceptable safety profile, Hedner said in his presentation.

"Modified carbonic anhydrase activity may be a pathophysiological mechanism in OSA," said Hedner. Sulthiame, a carbonic anhydrase inhibitor, showed safety and effectiveness for improving OSA in a previous phase 2b trial, he said.

In the current study, the researchers sought to determine the most effective dose of sulthiame for patients with OSA. They randomized 298 adults with OSA who could not accept or tolerate oral splints or CPAP to 100 mg, 200 mg, or 300 mg of sulthiame daily (74, 74, and 75 patients, respectively) or placebo (75 patients).

The mean age of the patients was 56 years, 26.2% were women, and the average apnea/hypopnea index (AHI3a, defined as apnea/hypopnea with ≥ 3% O2 desaturation) at baseline was 29 n/h. Patients were treated at centers in Spain, France, Belgium, Germany, and the Czech Republic. Baseline demographics and clinical characteristics were similar among the treatment groups.

The primary endpoint was the change in AHI3a from baseline to 15 weeks, and significant changes occurred in patients who received the 100 mg, 200 mg, and 300 mg doses, with decreases of 17.8%, 34.8%, and 39.9%, respectively.

Peak efficacy occurred in the range of 200-300 mg and was similar for patients with moderate or severe OSA, Hedner said in his presentation.

Notably, in a post hoc analysis, apnea improved by 47.1% at a 300 mg dose when the AHI4 measure (apnea/hypopnea with ≥ 4% O2 desaturation) was used in a placebo-adjusted dose-dependent reduction, the researchers wrote. The changes in AHI4 from baseline in this analysis also were significant for 200 mg and 100 mg doses (36.8% and 26.2%, respectively).

Patients underwent polysomnography at baseline and at weeks 4 and 12.

Mean overnight oxygen saturation also improved significantly from baseline with doses of 200 mg and 300 mg compared with placebo ($P < .0001$ for both).

In addition, scores on the Epworth Sleepiness Scale (ESS) improved from baseline to week 15 in all dosage groups, and the subgroup of patients with ESS scores of ≥ 11 at baseline showed even greater improvement in ESS, Hedner said in his presentation.

Total arousal index and sleep quality also improved from baseline compared with placebo, and no clinically relevant reduction in REM sleep was noted, Hedner added.

Treatment-emergent adverse events were in line with the known safety profile of sulthiame and included paresthesia, headache, fatigue, and nausea; these were mainly moderate and dose-dependent, with no evidence of cardiovascular safety issues, he said.

Although the study results were not surprising given previous research, the investigators were pleased with the potency of the therapy, Hedner told *Medscape Medical News*. "We are also happy about potential added values such as a blood pressure lowering effect, which is beneficial in this group of patients; however, we need to further study these mechanisms in detail," he noted.

The study findings were limited by the relatively small scale, and larger studies on long-term efficacy and tolerability are also needed, Hedner told *Medscape Medical News*.

"The current study was a dose-finding study, and we now have useful information on most suitable dose," he said.

However, the results support sulthiame as an effective, well tolerated, and promising novel candidate for drug therapy in patients with OSA, worthy of phase 3 studies, Hedner said.

Oral Option Could Be Game-Changer, But Not Yet

The gold standard of treatment for OSA is a CPAP machine, but the effectiveness is limited by patient tolerance, said Q. Afifa Shamim-Uzzaman, MD, an associate professor and a sleep medicine specialist at the University of Michigan, Ann Arbor, Michigan, in an interview.

"Presently, there are no effective pharmacological treatments for OSA — having a pill that treats OSA would be a total game changer and huge advance for the treatment of OSA and the field of sleep medicine," said Shamim-Uzzaman, who was not involved in the study. "More patients may be able to obtain treatment for OSA and thereby reduce the potential complications of untreated OSA," she said.

"Carbonic anhydrase inhibitors such as acetazolamide and sulthiame have been studied with limited success for the treatment of other forms of sleep disordered breathing such as central sleep apnea (CSA) but have shown less efficacy for OSA and are presently not recommended in the treatment of OSA by the American Academy of Sleep Medicine," Shamim-Uzzaman told *Medscape Medical News*.

Recently, emerging evidence about different phenotypes of OSA suggests that nonanatomic features (such as high loop gain) may play a role in patients with OSA, not only in those with CSA, she said. Whether carbonic anhydrase inhibitors could play a greater role in treating sleep apnea in patients with predominantly nonanatomic pathophysiologic traits remains to be seen, she emphasized.

The sulthiame data are promising, but more research is needed, Shamim-Uzzaman said. Although patients in the highest dose group showed a reduction in AHI of nearly 40%,

they still would have moderate OSA, and the OSA did not appear to decrease to a normal range in any of the treatment groups, she noted.

"More research is needed to identify which types of patients would be responders to this form of therapy, to understand if these effects are maintained long term (beyond 15 weeks), to evaluate patient-centered outcomes, especially in different sleep apnea subgroups (such as phenotypes with high loop gain vs those without), and to assess interactions with other therapies," she said.

The study was supported by manufacturer Desitin.

Hedner disclosed serving as a consultant to AstraZeneca, Bayer, CereusScience, Jazz Pharmaceuticals, MSD, Weinmann GmbH, Desitin, SomnoMed, and Itamar Medical; serving on the speakers' bureau for Almirall, AstraZeneca, Jazz Pharmaceuticals, ResMed, Philips Respironics, and Weinmann; and receiving grants or research support from Bayer, ResMed, Philips Respironics, and SomnoMed. He also disclosed shared ownership of intellectual property related to sleep apnea therapy.

Shamim-Uzzaman had no financial conflicts to disclose.

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Sugar May Drive Dementia, German Medical Societies Warn

Medscape Ute Eppinger, July 26, 2024

On World Brain Day (July 22, 2024), the German Society of Neurology (DGN) and the German Brain Foundation pointed out that too much sugar can harm the brain. The current results of the Global Burden of Diseases study shows that stroke and dementia are among the top 10 causes of death. A healthy, active lifestyle with sufficient exercise and sleep, along with the avoidance of harmful substances like alcohol, nicotine, or excessive sugar, protects the brain.

"Of course, the dose makes the poison as the brain, being the body's powerhouse, needs glucose to function," said Dr Frank Erbguth, president of the German Brain Foundation, in a press release from DGN and the German Brain Foundation. "However, with a permanent increase in blood sugar levels due to too many, too lavish meals and constant snacking on the side, we overload the system and fuel the development of neurologic diseases, particularly dementia and stroke."

The per capita consumption of sugar was 33.2 kg in 2021/2022, which is almost twice the recommended amount. The German Nutrition Society recommends that no more than 10% of energy come from sugar. With a goal of 2000 kilocalories, that's 50 g per day, or

18 kg per year. This total includes not only added sugar but also naturally occurring sugar, such as in fruits, honey, or juices.

What's the Mechanism?

High blood sugar levels damage brain blood vessels and promote deposits on the vessel walls, thus reducing blood flow and nutrient supply to brain cells. This process can cause various limitations, as well as vascular dementia.

In Germany, around 250,000 people are diagnosed with dementia annually, and 15%-25% have vascular dementia. That proportion represents between 40,000 and 60,000 new cases each year.

In addition, glycosaminoglycans, which are complex sugar molecules, can directly impair cognition. They affect the function of synapses between nerve cells and, thus, affect neuronal plasticity. Experimental data presented at the 2023 American Chemical Society Congress have shown this phenomenon.

Twenty years ago, a study provided evidence that a diet high in fat and sugar disrupts neuronal plasticity and can impair the function of the hippocampus in the long term. A recent meta-analysis confirms these findings: Although mental performance improves at 2-12 hours after sugar consumption, sustained sugar intake can permanently damage cognitive function.

Diabetes mellitus can indirectly cause brain damage. Since the 1990s, it has been known that patients with type 2 diabetes have a significantly higher risk for dementia. It is suspected that glucose metabolism is also disrupted in neurons, thus contributing to the development of Alzheimer's disease. Insulin also plays a role in the formation of Alzheimer's plaques.

The Max Planck Institute for Metabolism Research demonstrated last year that regular consumption of high-sugar and high-fat foods can change the brain. This leads to an increased craving for high-sugar and high-fat foods, which in turn promotes the development of obesity and type 2 diabetes.

Reduce Sugar Consumption

DGN and the German Brain Foundation advise minimizing sugar consumption. This process is often challenging, as even a small dose of sugar can trigger the gut to send signals to the brain via the vagus nerve, thus causing a strong craving for more sugar. "This could be the reason why some people quickly eat a whole chocolate bar after just one piece," said Erbguth. In addition, dopamine, a "feel-good hormone," is released in the brain when consuming sugar, thus leading to a desire for more.

"It is wise to break free from this cycle by largely avoiding sugar," said Dr Peter Berlit, secretary general and spokesperson for DGN. "The effort is worth it, as 40% of all dementia cases and 90% of all strokes are preventable, with many of them linked to industrial sugar," said Berlit. DGN and the German Brain Foundation support the call for a tax on particularly sugary beverages. They also point out that foods like yogurt or tomato ketchup contain sugar, and alcohol can also significantly raise blood sugar levels.

This story was translated from the Medscape German edition using several editorial tools, including AI, as part of the process. Human editors reviewed this content before publication.

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