



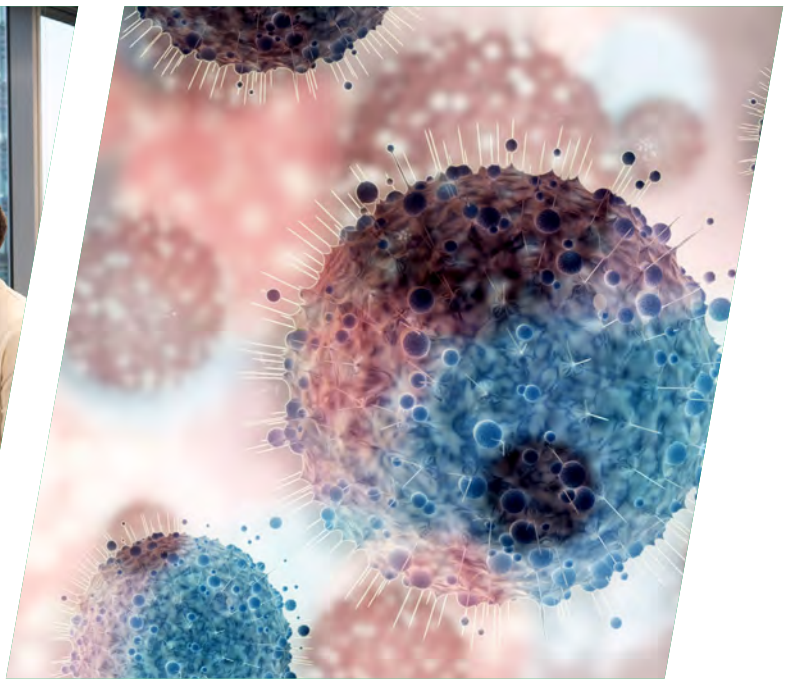

hVIVO

Advancing Infectious Disease Vaccine Development

End-to-End Global Solutions for Early-Phase & Human Challenge Trials

Contents

Foreword by Dr Andrew Catchpole, Chief Scientific Officer, hVIVO

Progress in respiratory virus research rarely comes from a single breakthrough. It comes from the steady accumulation of better tools, clearer data, and more integrated ways of working. The past few years have shown how quickly the field can move when scientific innovation is paired with operational discipline, and this collection reflects that momentum.

Across the industry, teams are rethinking how earlyphase development should work — how to stabilise samples more effectively, how to streamline outpatient workflows, how to generate data that is both scientifically rigorous and immediately useful for regulatory decision-making. These are not abstract improvements; they are practical shifts that shorten timelines and strengthen the evidence base behind new vaccines and therapeutics.

A consistent theme running through all of this is the value of early regulatory engagement. When development programmes are aligned with regulatory expectations from the outset, the path forward becomes clearer, risks are reduced, and critical decisions can be made with greater confidence. In infectious disease, where timing matters, and publichealth needs evolve quickly, that alignment is essential.

This lookbook brings together perspectives from across the development continuum — formulation, laboratory science, clinical operations, and controlled human infection models. Each contribution highlights a different aspect of how modern vaccine and antiviral development can be made more efficient, more predictable, and more resilient.

For researchers, developers, and clinical leaders working to advance the next generation of infectiousdisease solutions, the message is simple: when scientific insight and operational excellence work together, progress accelerates. The tools and approaches outlined here are part of that acceleration.

Andrew first studied virology at the University of Warwick before undertaking postgraduate research for a DPhil in influenza replication at Oxford University. Since then, he has applied his scientific expertise in a commercial environment.

After working as part of a multidisciplinary R&D team developing nuclear medicine research instruments at GE Healthcare, he then returned to the field of virology to join hVIVO, an industry-leading service provider of human viral challenge studies (controlled human infection studies).

Andrew is now recognised as an expert in human viral challenge studies, having played major roles in the development of influenza, RSV, HRV, and SARS-CoV-2 challenge models at hVIVO. He has overseen the design and execution of a variety of antiviral, immunomodulator, and vaccine product efficacy studies.

As Chief Scientific Officer, Andrew leads scientific strategy for the company. A major part of his role is to provide scientific consultancy, both internally and externally, to hVIVO's customers and collaborators on challenge study design, laboratory sample analysis, and data interpretation, as well as overseeing the company's challenge agent production activities.

Inside the hMPV surge: Why vaccine development is accelerating

The current landscape regarding hMPV infections around the world is perplexing.

In early January 2025, hMPV (or human metapneumovirus) appeared in news feeds almost daily, following reports of a substantial surge of infections in China.

These reports triggered a wave of articles across news outlets, some featuring inflammatory headlines and others adopting a more balanced tone. When taken out of context, reports that cases have doubled within a week in the USA can sound alarming, but this virus is known to circulate during winter and spring. Such patterns are not unusual and are expected for hMPV and other seasonal respiratory viruses.

Fear of the unknown

Among virologists, hMPV has long been understood to be a critical respiratory pathogen, well before it hit the headline news in 2025. Despite the COVID pandemic creating many so-called "armchair virologists", it is fair to say that, before January, hMPV was not a commonly known name. In fact, much of the general public had never heard of hMPV.

Images of hospitals overwhelmed by virus infections naturally revive recent memories from the early stages of the COVID pandemic. Combined with the unfamiliar name of the virus, this may explain the concern that has been raised across news outlets and online.

Welcome clarification

In response to the swarm of media surrounding hMPV, the WHO clarified its exact understanding of the situation in China. The organisation explained that the "surge" of hMPV infections was, in fact, within normal and anticipated levels for this time of year.

During Dr. Harris' statement, emphasis was placed on the fact that the majority of new respiratory infections in China were still being caused by seasonal influenza rather than hMPV. This served as a reminder that the flu continues to represent a greater burden, with struggling healthcare systems most impacted due to hospitalisation rates.

Increased public awareness helps fuel research

Nevertheless, hMPV remains a significant pathogen, and its increased media attention is not unwelcome. Greater awareness of viruses that continue to cause substantial human disease and suffering is undoubtedly beneficial; increased awareness often leads to increased research funding and, ultimately, enhanced medical countermeasures.

While hMPV is already well recognised within the scientific community, it is not nearly as extensively studied as influenza or RSV (Respiratory Syncytial Virus), either in academia or in industrial vaccine and treatment development. This is perhaps unsurprising given that hMPV was only discovered in 2001, far more recently than RSV or influenza, which have been known about for much longer.

Moreover, the *Pneumoviridae* virus family, which includes both RSV and hMPV, was long considered highly challenging in effective vaccine development. This perception began to shift with the discovery of the importance of the pre-fusion formation of RSV's F protein as the appropriate vaccine target.

Vaccines designed to elicit antibodies specifically targeting the pre-fusion formation of virus' F protein, known as the pre-F vaccines, have fundamentally transformed the field and demonstrated that effective vaccines are achievable.

Challenge studies de-risk vaccine development

Developing a vaccine based on any completely new construct or scientific strategy always carries risks, especially with respect to achieving the desired protective effect. Human viral challenge models have long been regarded as an ideal method for mitigating the risk of costly large-scale vaccine trial failure.

This is because they involve the direct inoculation of healthy study participants with the virus of interest, allowing vaccine efficacy to be directly tested in a highly controlled environment and requiring far fewer study participants than traditional trials. hVIVO is proud of its major role in bringing the world's first effective RSV vaccines to market through the use of its RSV challenge model.

The model provided the first-ever demonstration of vaccine efficacy in humans for RSV pre-F vaccines. This discovery led to the assessment of several RSV pre-F vaccines using the model, and the successful proof-of-concept outcomes from these challenge studies were instrumental in accelerating RSV vaccines to market.

RSV vaccine success fuels hMPV vaccine development

Recently, the success of RSV vaccines has led several biotech and pharma RSV research teams to shift their focus to hMPV. As a result, multiple promising hMPV vaccines are now in the development pipeline.

However, most have not yet reached the development stage of efficacy testing in humans, and none have yet demonstrated efficacy in preventing or substantially reducing the burden of hMPV disease.

High hopes for the hMPV challenge model

Following this trend of RSV vaccine research teams transitioning to working on hMPV, hVIVO has leveraged its challenge model development expertise over the past year to develop an hMPV challenge model, culminating in a challenge study in mid-2025.

The study was extremely successful, showing that an effective hMPV challenge model could be established with sufficient infection rates observed and, as anticipated, under safe and controlled conditions. The hMPV challenge model is anticipated to help accelerate hMPV vaccine development, just as the RSV model did for RSV vaccines, ultimately helping to control this important global pathogen and save lives.

The science powering the next wave of respiratory vaccines

As respiratory vaccines continue to place a substantial strain on healthcare systems worldwide, vaccine development has entered a new era.

This article examines the history of respiratory virus vaccines, how modified mRNA (modRNA) technology may overcome the limitations of existing vaccines, and the development of universal vaccines for influenza, COVID-19, and other viruses.

In addition, the paper outlines the crucial role human challenge trials will play in accelerating vaccine development and producing high-quality data. With its advanced facilities, profound scientific expertise, and a strong track record, hVIVO is uniquely positioned to support customers in navigating this new landscape and efficiently deliver cutting-edge vaccines to market.

1. modRNA vaccines are redefining respiratory virus prevention

A new era of vaccine development has been ushered in thanks to the success of modRNA vaccines during the COVID-19 pandemic.

Their capability for rapid design to target emerging strains, scalable manufacturing methods, and potential to enable universal protection (e.g. against all influenza strains) position them as a transformative platform for preventing respiratory viruses.

2. Human challenge trials can accelerate vaccine development

Conventional vaccine field trials are slow, expensive, and frequently produce low-quality data. In contrast, human challenge trials reduce time and expenses while generating robust viral load and symptomology data.

Another key advantage over field trials is the ability to evaluate efficacy against low-circulation virus strains, which frequently lead to seasonal vaccine mismatch and variable effectiveness.

3. hVIVO will be at the forefront of vaccine clinical development

hVIVO is a leader in vaccine and anti-viral clinical development due to its extensive experience and tailored quarantine site. Its human challenge models allow products to “succeed fast or fail fast,” substantially minimising risks and expenses.

Respiratory viruses remain a significant global health threat, challenging both public health systems and vaccine developers. This article examines the changing landscape of respiratory viral infection prevention, including the shortcomings of conventional vaccine platforms and the potential of modified messenger RNA (modRNA) technology.

It also highlights the transformative impact of human challenge trials and explains how hVIVO’s specialist capabilities and expanded infrastructure position it at the forefront of vaccine development by accelerating trial results, generating high-quality data, and minimising risk and expenses.

The global burden of respiratory viral infection

In 2025, respiratory viruses continued to pose significant challenges to global public health. Their tendency to mutate enables frequent immune evasion and high cross-species and human-human transmissibility which, coupled with their seasonality, has complicated the development of vaccines that provide broad (i.e., covering many or all strains of a virus) and lasting protection.

The need for annual vaccine updates creates a continuous economic burden while vaccine strain match remains unreliable.

Influenza viruses exemplify these challenges.

Although current vaccines prevent millions of cases each year (around 9.8 million in the United States alone for the 2024/2025 season), Influenza causes approximately one billion cases (including three to five million severe cases) of illness and between 290,000 and 650,000 global deaths annually.[1,2]

Influenza viruses continually evade both acquired and vaccine-induced immunity through antigenic drift and occasional rapid antigenic shift.[3] This requires constant surveillance and annual vaccine reformulation to counter prevalent and newly emerging strains.

Seasonal infection patterns, driven by climate, host behavior, and co-circulation with other respiratory pathogens, further complicate prediction and preparedness.[4]

The World Health Organisation (WHO) Global Influenza Surveillance and Response System (GISRS) was founded in 1952 and now operates with networks across 130 WHO member states.[5] GISRS holds biannual meetings, typically in February and September for the Northern and Southern hemispheres, respectively.

During these meetings, experts review epidemiological data, genetic and antigenic properties, and vaccine effectiveness before providing recommendations for strains to include in upcoming seasonal vaccines.

In February 2025, the latest recommendations for the Northern hemisphere were released.[6] Regulatory authorities, including the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), can modify which strains are included in their region, according to local epidemiological data.

Despite seasonal adjustments, emerging mutations frequently result in vaccine mismatch, leading to significant variability in influenza vaccine effectiveness by year and by region . Since the 2004/2005 season, influenza vaccine efficacy estimates in the United States have ranged from 10% to 60%.[7]

History of respiratory virus vaccines

Until the recent emergence of modRNA vaccines, most respiratory virus vaccines have been either live attenuated vaccines (LAVs), where a live virus with reduced virulence is used to stimulate an immune response, or inactivated virus vaccines.

LAVs have been used since World War II and remain common today due to the stronger and more durable immunity they induce. More recently, intranasal administration (e.g., AstraZeneca's "Fluenz" influenza vaccine) has proven extremely useful for vaccinating children. Disadvantages of LAVs include contraindications in pregnant and immunocompromised individuals, and the risk of mutations into more virulent strains.

Inactivated virus vaccines involve administering all or part (e.g. split virions) of an inactivated or dead virus. The antigens from the inactivated virus cause a different and potentially weaker immune response than LAVs, often requiring several doses or the addition of adjuvants. Inactivated virus vaccines, including Sanofi's quadrivalent influenza vaccine, are still used today due to their strong safety profile.

Both LAVs and inactivated virus vaccines work by introducing all or part of a virus to stimulate an immune response. Historically, these vaccines were manufactured in egg-based production procedures, which carried the risk of supply chain issues. Egg-adaptation changes to the viruses are also known to increase vaccine mismatch and reduce effectiveness.[8]

To address these challenges, cell-based (i.e. grown in a cell culture) vaccines emerged, offering faster and larger-scale manufacturing methods and allowing more efficient responses to emerging strains and potential pandemics.

Genetically engineered recombinant influenza vaccines entered the market in 2013. These vaccines are produced by synthesising synthetic viral DNA (in the case of influenza, the DNA encoding the haemaggluttinin [HA] protein) and inserting (recombining) it into the genome of the host virus. The host is then cultured to generate large quantities of the target protein, which is purified and formulated into the vaccine. Recombinant vaccines offer additional production efficiencies and have been demonstrated to trigger stronger immune responses than both egg- and cell-based vaccines.[9]

The arrival of modRNA vaccines

modRNA technology offers a significant opportunity for the development of new vaccines against influenza and other respiratory viruses. In contrast to conventional vaccines, which introduce viral antigens directly to stimulate an immune response, synthetic modRNA is delivered and then translated by the host cells to produce the viral antigen(s) encoded by the modRNA. The antigen(s) produced may then stimulate both humoral and cell-mediated immune responses.

Although modRNA has been studied as a therapeutic platform since the late 1980s, early development was limited by poor stability and undesirable innate immunogenicity through the activation of toll-like receptors.[10]

Breakthroughs in nucleoside modification in the early 2000s, (specifically, the development of pseudouridine, an analogue of uridine) enhanced modRNA stability and decreased these unwanted immunogenic effects.[11]

The COVID-19 pandemic dramatically accelerated the approval of the first modRNA vaccines, highlighting their distinct advantages over conventional vaccine platforms: rapid development and scalable manufacturing. Once SARS-CoV-2 had been sequenced, researchers already working on modRNA rapidly designed SARS-CoV-2 vaccine candidates, and clinical trials began within months.

Within only one year of the virus' identification, the FDA/EMA authorised the emergency/conditional use of two mRNA vaccines (developed by BioNTech/Pfizer and Moderna). The cell-free production process of modRNA vaccines could be rapidly scaled up to address the huge demand created by the pandemic.

Initially, the modRNA vaccines, based on wild-type SARS-CoV-2 (Wuhan-Hu-1), demonstrated approximately 95% efficacy in reducing symptomatic COVID-19. As novel SARS-CoV-2 strains emerged, protection against severe disease remained high; however, overall vaccine efficacy began to decline.

To counter dominant strains, formulations have undergone regular updates. The WHO Technical Advisory Group on COVID-19 Vaccine Composition has recommended both bivalent and monovalent vaccines in the years since.

The future of respiratory virus vaccines

The remarkable success of modRNA vaccines against SARS-CoV-2, prompted the rapid development of other modRNA vaccines. Last year, the FDA approved mRESVIA, a modRNA vaccine encoding the respiratory syncytial virus [RSV] fusion [F] protein, for use in adults aged 60 years and older. modRNA vaccines for cytomegalovirus and Epstein-Barr virus are also in the early stages of development.

modRNA technology offers an opportunity for the development of universal vaccines (i.e., a vaccine that protects against all strains of a virus) by targeting conserved antigens (e.g., the HA stem, instead of the variable head). Universal modRNA vaccines for influenza and coronavirus, as well as a combined influenza and SARS-CoV-2 candidate, are currently under investigation in Phase 3 studies, with hopes for approval next year.

If universal modRNA vaccines prove effective against influenza and coronavirus variants, the 2020s could be defined as a new era in vaccine development. Eliminating the need for seasonal vaccine reformation, combined with the inherent production advantages of modRNA vaccines, could significantly reduce the economic burden of these diseases.

Universal vaccines have the potential to eradicate certain diseases in humans or at least eliminate their incidence in vaccinated populations. However, modRNA vaccines are not without drawbacks. Challenges include increased reactogenicity and shorter immunity duration compared with other vaccine types. Current ultra-cold storage requirements complicate distribution; manufacturers will no doubt concentrate on enhancing storage conditions to enable easier, cheaper, and more ubiquitous distribution.

Accelerating vaccine development with human challenge models

At this pivotal time for vaccines, clinical development strategies must be optimised and up to date with the latest advances. Conventional vaccine field trials, which involve vaccinating large cohorts of participants and observing them over extended periods, can be an expensive and inefficient gamble for vaccine candidates.

These studies also suffer from low-quality data outputs (e.g. using proxy endpoints of influenza-like illness rather than more specific and comprehensive viral load assessments). Field trials struggle to evaluate efficacy against low-circulation strains, and the seasonality of respiratory viruses prevents adequate assessment of efficacy before vaccines are deployed.

Human challenge trials (HCTs), also known as controlled human infection models (CHIMs), involve the deliberate exposure of participants to the pathogen being studied with or without a test treatment or vaccine. Participants are monitored in a controlled environment during the predicted course of disease to evaluate infection rates, viral load, and symptomology.

The origins of HCTs date back to 1796, when Edward Jenner inoculated a young patient with cowpox. The patient later demonstrated immunity to smallpox, which causes more severe disease than cowpox, and the experiment ultimately laid the foundation for the concept of vaccines.

Since then, HCTs have advanced substantially, adapting to contemporary ethical standards and regulations. They have contributed to the development of vaccines for diseases such as influenza, dengue, norovirus, malaria, cholera, typhoid, and RSV. HCTs deliver rapid and more comprehensive results.

By controlling study conditions, variability is reduced, and interference from other pathogens is avoided, enabling more accurate virological and immunological assessments. This allows for smaller sample sizes compared to conventional field studies, reducing both the cost and risk of early-stage vaccine development.

hVIVO's human challenge trials

hVIVO has an unmatched history in conducting HCTs. After conducting its first HCT in 2001, the company opened its first dedicated quarantine facility and associated laboratories in 2011. Renewed interest in HCTs during the COVID-19 pandemic led the company to expand its facilities in 2021, including an HCT in 36 participants to characterise SARS-CoV-2.

Overall, hVIVO has challenged more than 5,000 participants with respiratory viruses and other pathogens. The company has established human challenge models for contemporaneous influenza A and B, RSV A and B, hMPV, human rhinovirus, and SARS-CoV-2. Its integrated specialist virology lab has validated qualitative and quantitative assays for each of these viruses, enabling seamless operations throughout their studies.

Last year, recent growth resulted in the opening of a flagship quarantine and lab site in Canary Wharf, London. The 50-bed quarantine site is certified to handle pathogens as high as biosafety level 3 (BSL3) and can support multiple pathogens simultaneously. hVIVO has the facilities and expertise to lead the way in this new era of vaccine innovation.

HCTs conducted by hVIVO can generate high-quality data efficiently, enabling vaccine and therapeutic candidates to succeed fast or fail fast. In addition, the company's timely results could support innovations in seasonal vaccine assessment and subsequent development. hVIVO can develop models and assays for rare virus strains, which will be indispensable for the evaluation and approval of universal vaccines.

hVIVO's expanded clinical trial and consultancy offering

Canary Wharf's on-site pharmacy, IMP facilities, and outpatient unit, together with hVIVO's dedicated project management and clinical teams, are primed and ready to accelerate vaccine and antiviral development. hVIVO's comprehensive participant database supports the rapid recruitment of healthy participants, including older populations, as well as patients with asthma or COPD.

In 2020, Venn Life Sciences, a specialist consultancy in early-phase clinical development, joined the hVIVO Group. Venn's highly respected team of consultants has experience covering preclinical development, CMC, pharmacokinetics, statistics and methodology, data management, medical writing, quality assurance, and regulatory affairs. Close collaboration between Venn and hVIVO's clinical site teams ensures that clinical trials are executed to the highest scientific and regulatory standards.

In January 2025, hVIVO acquired CRS, an early-phase clinical research organisation headquartered in Germany. This acquisition allowed hVIVO to use two clinical trial units and accompanying expert teams to expand its overall site offering into the EU. The sites specialise in first-in-human studies and complex pharmacokinetic and pharmacodynamic studies in patients with renal or hepatic impairment.

hVIVO's presence in Germany will enable clients to benefit from the recent proposals by the German Federal Ministry of Health for new Standard Contractual Clauses (SCs). These SCs will substantially reduce Clinical Trial Agreement (CTA) review times once finalised.

With a cutting-edge quarantine site, advanced laboratories, and an expanded site and service offerings, hVIVO is undoubtedly well-positioned to support the development of vaccines and antiviral therapeutics. Experts provide guidance throughout the entire product lifecycle, from feasibility through to the full execution of Phase 1 to 3 trials.

While human challenge models can enhance the efficiency of the key early phases in vaccine programs, hVIVO's expanded capacity can be utilised to carry out field trials, which will remain essential for generating longer-term and robust safety data and for pathogens unsuitable for challenge trials.

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Building scalable formulations through process optimisation

The understanding of a "successful" study drug can vary greatly; for example, a study drug in the pharmaceutical field may be clinically effective, but potentially too expensive to manufacture at scale viably.

Drug development often progresses from one phase to the next without considering long-term feasibility, such as scalability, cost-effectiveness, and market access. Sustainable success is assured by implementing future-proof strategies from the outset.

In a recent interview with Erik Gout, Director of Chemistry, Manufacturing, and Controls (CMC), and Azra Gholami, CMC Consultant at hVIVO looked to explore these issues further.

These two experts shared their expertise in process optimisation and formulation development, emphasising the importance of considering long-term implications beyond the development phase to ensure sustained success.

hVIVO's consultancy boasts extensive expertise in biologics and small molecules, each of which necessitates the implementation of a distinct optimisation approach.

Biologics development is broken down into upstream and downstream processes, with the upstream process generally defining the cell line before Phase 1. This is rarely changed after it has been defined, because modifications may require a total redesign of the downstream purification. The discussion here focuses on small molecules.

Ensuring scalability via optimisation and formulation development

Phase 1 clinical development must focus on the evaluation of drug safety, generally done using a basic or no formulation. Small molecule formulation tends not to be optimised, however, and the drug substance's synthesis route may still be under development.

The feasibility of the drug substance process and formulation must also be assessed for use in future Phase 3 and commercial production. This is done when transitioning from Phase 1 to Phase 2, and it is essential to optimise both the drug substance and the drug product at this stage, while also considering the final formulation and process.

Erik stresses that it is vital to align development with long-term goals, advising clients to consider both scalability and the cost of goods at an early development stage.

"It's not just about reaching the next phase," he states. "Early decisions should assess whether the formulation can scale effectively."

He continues, "Key considerations include cost-efficient excipients, adaptable production processes that allow for Contract Development and Manufacturing Organisations (CDMOs) changes, and standardised methods to support a smooth transfer to commercial manufacturing."

"For (bio)pharmaceutical clients using separate CDMOs for drug substance and drug product, hVIVO can manage both to ensure alignment. We offer consultancy on decision-making, testing, process control, risk management, and logistics."

"While CDMOs have scientific expertise, hVIVO bridges knowledge gaps — like stability differences — by facilitating information exchange. We guide stability testing to ensure shelf life and help define critical manufacturing parameters through scalable process controls and risk management."

The importance of mitigating risks

“Our most important key services include process troubleshooting and risk management,” explains Azra. “From the outset, we proactively identify and mitigate risks associated with the manufacturing process. Mitigating risks of unstable products can be achieved through process control and selecting the right packaging material.”

“The choice of packaging — whether opting for cost-effective or more specialised materials — can significantly impact the cost of goods during commercial production. Similarly, transport conditions, like storage at 5°C or lower versus room temperature, play a critical role. Storage at room temperature will generally be more cost-effective in the long run. Ultimately, the goal is to minimise unnecessary complexities while optimising for cost efficiency and quality.”

Balancing perfect versus the real world

A gap often exists between what can be achieved technically and what is commercially feasible. A balance must be struck between innovation and feasibility in order to ensure longterm success. (Bio)Pharmaceutical companies are advised to take a strategic view from the outset, focusing on commercial outcomes rather than solely short-term goals. Aligning early informed decisions with long-term objectives will significantly improve the likelihood of achieving sustainable success.

(Bio)Pharmaceutical companies are advised to take a strategic view from the outset, focusing on commercial outcomes rather than solely short-term goals. Aligning early informed decisions with long-term objectives will significantly improve the likelihood of achieving sustainable success.

Venn offers expert guidance on process optimisation and formulation development, supporting its clients in identifying potential obstacles in future development phases while maintaining a clear focus on the overall commercial goal. For example, this includes evaluating storage conditions, transport, and associated costs.

Regulatory strategy as a competitive advantage in modern drug development

Written by Vi Stuart, Regulatory Consultant, and Ronald Ullers, Senior Consultant CMC - Regulatory Affairs at hVIVO

Regulatory affairs have long been regarded as a necessary hurdle in drug development, with drug developers routinely required to ensure compliance by preparing dossiers and managing submissions via complicated national and international frameworks.

That perception is outdated, however, as regulatory strategy now represents a source of competitive advantage rather than mere compliance. Regulatory expertise can de-risk programs, accelerate timelines, and even improve a compound's commercial value when it is integrated into drug development planning at an early stage.

Regulatory experts at hVIVO have seen this transformation firsthand, with their extensive experience across human challenge studies, early-phase clinical trials, and complex therapeutic areas highlighting that regulatory affairs are no longer solely confined to the back room.

Rather, regulatory affairs are key to influencing policy, shaping development pathways, and ensuring that innovative and vital treatments reach patients as quickly as possible.

Ensuring both compliance and acceleration

Compliance remains the foundation of any work related to regulatory affairs, because no program can progress without robust documentation, including CTAs, INDs, eCTDs, and GxP validation.

Acceleration is assured by embedding a well-designed regulatory strategy from the outset. For example, beginning with a Target Product Profile (TPP) and a specifically tailored regulatory roadmap allows sponsors to align on population, indication, and endpoints prior to committing any major resources.

Employing such a proactive approach ensures the avoidance of potentially expensive missteps while maintaining developmental focus on the defined end goal.

hVIVO emphasises that the importance of a regulatory strategy is not simply a static checklist. Rather, this strategy must be a living plan that is adaptable to both commercial realities and scientific progress.

The early involvement of regulatory experts ensures that sponsors are clear on what is acceptable to regulatory agencies, what is realistically feasible, and how best to position their specific product for success.

Expedited pathways as strategic assets

Regulatory designations such as EMA PRIME, FDA Fast Track, and orphan status are more than just badges of honor. These strategic assets help accelerate development and enhance commercial value, with smaller biotechs leveraging them to attract partners and investors, and larger pharmaceutical companies using them to reduce their products' time to market.

The team of regulatory consultants at hVIVO has guided sponsors through these regulatory pathways, helping them secure designations that transform a program's trajectory.

A universal flu vaccine application for the EMA PRIME scheme provides a useful example of how a combination of these expedited pathways and an appropriate regulatory strategy can directly impact both commercial outcomes and scientific progress.

The importance of relationships and influence

Regulatory success depends on more than just technical expertise, however. Relationships with sponsors, agencies, and policymakers are also key to a program's success, and hVIVO's experienced consultants have extensive experience preparing briefing packages, rehearsing meetings, and managing interactions with regulators to improve the likelihood of a positive outcome.

hVIVO's team understands that simplicity and clarity are essential, especially when working with agencies that operate under tight review timelines.

Human challenge studies highlight the importance of this point because acceptance of these models varies, as they are not currently fully codified in regulatory guidance. hVIVO's teams have helped challenge models to become more widely accepted by directly engaging regulators, clearly explaining the science, and lobbying for greater and wider inclusion in guidance.

This approach is a notable example of regulatory strategy in action: influencing policy and creating pathways for innovation that would otherwise be blocked by building trust and rapport with regulators.

Human challenge studies: A case study in strategy

Challenge models may be considered less rigorous than field trials, but they offer vital proof-of-concept data that is key to de-risking subsequent development and accelerating antiviral and vaccine programs.

Regulatory strategy makes challenge studies acceptable, and hVIVO's experts have secured regulatory confidence by positioning them as controlled, scientifically robust, and ethical, and by aligning endpoints with field trial triggers where applicable.

This increased acceptance must continue to broaden into the future, expanding into later phases, patient populations, and new therapeutic areas. This will require a robust combination of scientific excellence and regulatory advocacy, but it remains a clear example of how strategy elevates compliance into competitive advantage.

Integration across the hVIVO group

Its integrated approach is another of hVIVO's key strengths. The company's regulatory services operate seamlessly across non-clinical, clinical, and CMC.

Senior experts undertake the work, supported by a network of specialists across the group, ensuring delivery is never delegated to less experienced or junior team members.

Sponsors benefit from end-to-end support thanks to this breadth and depth, ranging from marketing authorisation dossiers to consultancy and operational support for IND-enabling toxicology packages.

Integration also ensures quality and consistency across the development lifecycle. Sponsors benefit from cross-functional expertise, whether in cardiometabolic research, respiratory or infectious diseases, or complex combination products. This rare holistic approach affords sponsors a genuine competitive advantage.

Strategy as partnership

Regulatory strategy continues to evolve, with this evolving landscape being reshaped by early adaptive designs, real-world evidence, and master protocols such as umbrella and platform protocols.

Agencies are increasingly open to innovative approaches, but only when sponsors present them clearly and convincingly. The role of regulatory affairs has also evolved and is now as much about negotiation and communication as it is about comprehensive documentation.

Partnership is the future, regulators are increasingly encouraging dialogue, sponsors are seeking greater acceleration, and experienced service providers are required to serve as the bridge between. The right combination of technical expertise and relational skill is key to regulatory professionals' ability to shape policy, influence guidance, and accelerate innovation.

Conclusion

Regulatory affairs are no longer the hurdle that they were historically considered to be; rather, they can become a lever for credibility, speed, and commercial success with the right strategy.

Compliance is imperative, but competitive advantage stems from acceleration. Strong relationships, expedited pathways, and integrated expertise all help to ensure a regulatory strategy that drives innovation rather than simply satisfying requirements.

hVIVO understands that regulatory strategy is essential, making the difference between success and delay, or confidence and uncertainty. Sponsors opting to partner with experienced regulatory experts will do more than meet obligations; they will gain a competitive edge in the race to provide improved therapies to patients.

About the authors

Ronald Ullers, Senior Consultant Regulatory Affairs CMC. Ronald holds a Ph.D. in molecular microbiology and brings 18+ years of experience in the biopharmaceutical industry. He specialises in regulatory affairs with a focus on chemistry, manufacturing, and control (CMC) for a diverse range of biotech products, vaccines, ATMP's and small molecules.

Vi Stuart, Regulatory Affairs Consultant. Vi is a seasoned global regulatory affairs leader having 25+ years of experience across Roche, Eisai, GSK, Cancer Research UK, and Paraxel specialising in respiratory and oncology therapy areas. She is a passionate advocate for regulatory innovation, including decentralised trials, real-world evidence, and digital endpoints.

From assay design to translational impact

Written by Chris Forsdyke, Head of Laboratory Services, and Elisa Masat, Principal Development Scientist.

When considering assays, routine lab tests often come to mind — boxes to tick, datasets to generate. But assays are more than that. They are the building blocks and architecture that underscore translational research.

Without them, research lacks both structure and validity. With them, it is possible to design programs that are resilient, scalable, and ready to flourish into novel therapeutic domains.

Why assays require early planning

Rather than being add-ons, assays are the means by which biological processes are converted to data that is meaningful and measurable. As a result, they should be considered at the beginning of the study design.

When integrated into frameworks early on, they can shape downstream analytical strategies, providing consistency throughout different developmental phases, spanning pre-clinical to late-stage clinical.

In doing so, they give sponsors confidence that data generated will endure over time. A one-off test may answer a short-term question, however, a validated assay becomes infrastructure and can support a program for years to come.

Expertise in infectious disease

hVIVO's lab expertise is ideal for infectious and respiratory diseases. They built platforms that support human challenge research, vaccine development, and antiviral testing. That includes investing in molecular biology, immunology, and microbiology capabilities, and building teams committed to developing and validating assays.

With the passage of time, those building blocks became a foundation that can be used over and over in a portfolio of research.

Expanding the architecture

Today, these foundations are expanding. hVIVO has added digital PCR, Ligand binding assay diversity, multiplexing, and next-generation sequencing, as well as robotics and automation, all while extending its capabilities in both microbiology and cell culture. These platforms enable work with smaller sample volumes, elevated throughput, and more flexibility.

They also open possibilities for novel indications ranging from oncology and metabolic disease to cardiovascular research and gene therapy. The same architectural approach is applicable — develop the assays, validate them, and then use them as infrastructure to aid long-term development.

From infectious disease to more general translational science

hVIVO is excited about the agility this gives sponsors. They can combine platforms, adjust assays for specific development stages, and adapt to novel therapeutic domains.

Whether for neutralising antibody assessments in vaccine research, creating biomarker panels in oncology, or microbial propagation for antibacterial programs, the underlying principle remains the same: assays provide the framework that binds the science together.

Closing thought

Assays are architecture, not just tests. They form the foundations upon which translational research can be built, providing the framework that enables innovation to scale across indications and phases.

By treating assays like building blocks, hVIVO creates infrastructure that supports sponsors from the early discovery phase to clinical development - ultimately helping in the provision of better therapies to patients.

About the authors

Elisa Masat (PhD) is Principal Scientist at hVIVO. Leading a dedicated research and development team of eight scientists, researching, building, qualifying, and validating platforms in diverse technical domains. An expert in Immunology, Elisa has worked in other roles at hVIVO and at Charles River.

Chris Forsdyke is head of Laboratory Operations at hVIVO. He leads the transformation of hVIVO lab operations and efforts to scale its lab infrastructure and teams to serve users in preclinical through to clinical trials. Previously, Chris has held positions in Biotech and Pharma at companies including Lonza, Covance, and PPD.

The role of specialty laboratories in infectious disease research

Specialty laboratories provide advanced capabilities beyond routine diagnostics, positioning them at the forefront of infectious disease research and development.

The strength of these laboratories lies in their potential to provide a multifaceted approach, integrating molecular, virology, and immunology techniques to deliver comprehensive insights for antiviral drug discovery, vaccine development, and translational research.

Cell culture is a key foundation for drug screening, viral propagation, and physiologically relevant modelling, complementing immunological and genomic analyses. This ensures high specificity, sensitivity, and reproducibility, allowing their users to perform accurate immune profiling, pathogen detection, and functional characterisation.

Benefits of a multi-faceted approach

Single-modality testing is typically unable to capture the complexity of infectious diseases due to pathogens' capacity for rapid evolution. Specialty labs combine viral infectivity assays, genomic analysis, immune response profiling, and cell culture systems to:

- Enhance diagnostic yield and reduce turnaround times
- Support regulatory-compliant workflows for clinical trials
- Facilitate real-time surveillance and outbreak response
- Power innovation in therapeutic and vaccine development via the development of physiologically relevant models

Core pillars and techniques

Molecular and genomics

This suite of tools is ideally suited to biomarker discovery, vaccine research, diagnostics development, and Phase I—III clinical trials. Techniques include:

- qPCR & ddPCR for the quantification of gene expression and viral load
- Next-Generation Sequencing (NGS) for whole genome sequencing, microbiome analysis, and variant calling
- Multi-pathogen screening via advanced platforms such as GenMark® ePlex® , and BioFire®
- Biomarker profiling for translational research and diagnostics

Virology

This suite of tools is suitable for research on respiratory pathogens, antiviral drug development, and emerging infectious disease programs.

Techniques include:

- Viral quantification via TCID50, Plaque Assays, and Focus Forming Assays (FFA)
- Antiviral screening via drug potency assays (IC50/IC90)
- Antibody functionality via neutralisation and ligand binding assays
- Resistance monitoring via NGS

Immunology

The suite of tools is ideally suited to vaccine development, infectious disease research, immunogenicity studies, and cardiometabolic biomarker analysis. Techniques include:

- Protein and antibody quantification via ELISA
- Antigen-specific T cell analysis via ELISpot
- Immune signaling via Multiplex cytokine profiling
- Functional antibody activity via neutralisation assays
- PBMC isolation and immune repertoire sequencing

Cell culture

These types of tools are suitable for a wide range of applications, including viral infectivity and neutralisation assays, vaccine candidate evaluation aligned with relevant regulatory guidelines, and mechanistic studies of host-pathogen interactions; as well as antiviral drug screening and cytotoxicity testing, and neutralising antibody assessments and biological potency measurements.

Techniques include:

- Establishing appropriate cell lines like MDCK, HEK293, CHO, and Vero. These cell lines are cultured under strict conditions and employed in critical steps such as cell-based assays and respiratory virus propagation.
- Immunogenicity and host-pathogen interaction studies via primary human PBMCs
- Two-dimensional and three-dimensional culture models for physiologically relevant assays
- Lab-scale bioreactors for scale-up and cell culture, as appropriate

Advantages of working with a multifaceted specialty laboratory

There are several tangible benefits to working with a specialty laboratory that offers multifaceted capabilities.

For example, the laboratory can provide comprehensive insights across pathogen detection, infectivity, and immune response, as well as help to expedite drug and vaccine development.

Defensible, high-quality data is available for regulatory submissions, with global standardisation made possible via powerful automation and LIMS integration.

Specialty laboratories like hVIVO will continue to be at the forefront of innovation, integrating these diverse and highly beneficial technologies into validated workflow designs to better ensure resilience against evolving pathogens.

Ensuring success in outpatient vaccine trials

hVIVO has recently used its expertise in challenge studies to support a large outpatient vaccine trial in healthy volunteers.

Study requirements and objectives

A biotech company based in the United States aimed to undertake a large-scale outpatient vaccine study involving approximately 5,000 healthy participants in the US and UK.

hVIVO's goal as part of this work was to recruit around 1,000 participants in the UK prior to the beginning of the influenza season. A 26-week influenza-like illness follow-up was then performed.

Dosing was to be completed before the influenza season began, making use of the later onset of the influenza season in the UK versus the US to better align with the client's timelines.

The US-based biotech company was already operating in the US. hVIVO was contracted as the exclusive UK-based site due to its potential for improved efficiency in both operations and time.

Timelines for this study were challenging. Recruitment was scheduled to start in September 2024, with hVIVO promptly completing the feasibility assessment as soon as the protocol was delivered in early June 2024.

Operational execution

The study's success is attributed to the close collaboration between the sponsor, internal hVIVO teams (including laboratory staff, pharmacy, recruitment teams, and site personnel), and an external team of clinical research associates (CRAs) that were embedded with the sponsor.

These CRAs worked on site to ensure close cooperation between hVIVO staff and sponsors. Flexibility was essential, prompting the team to optimise clinic hours (including weekends) and deliver extended dosing sessions in order to maximise the number of dosed participants.

Clinical process optimisation

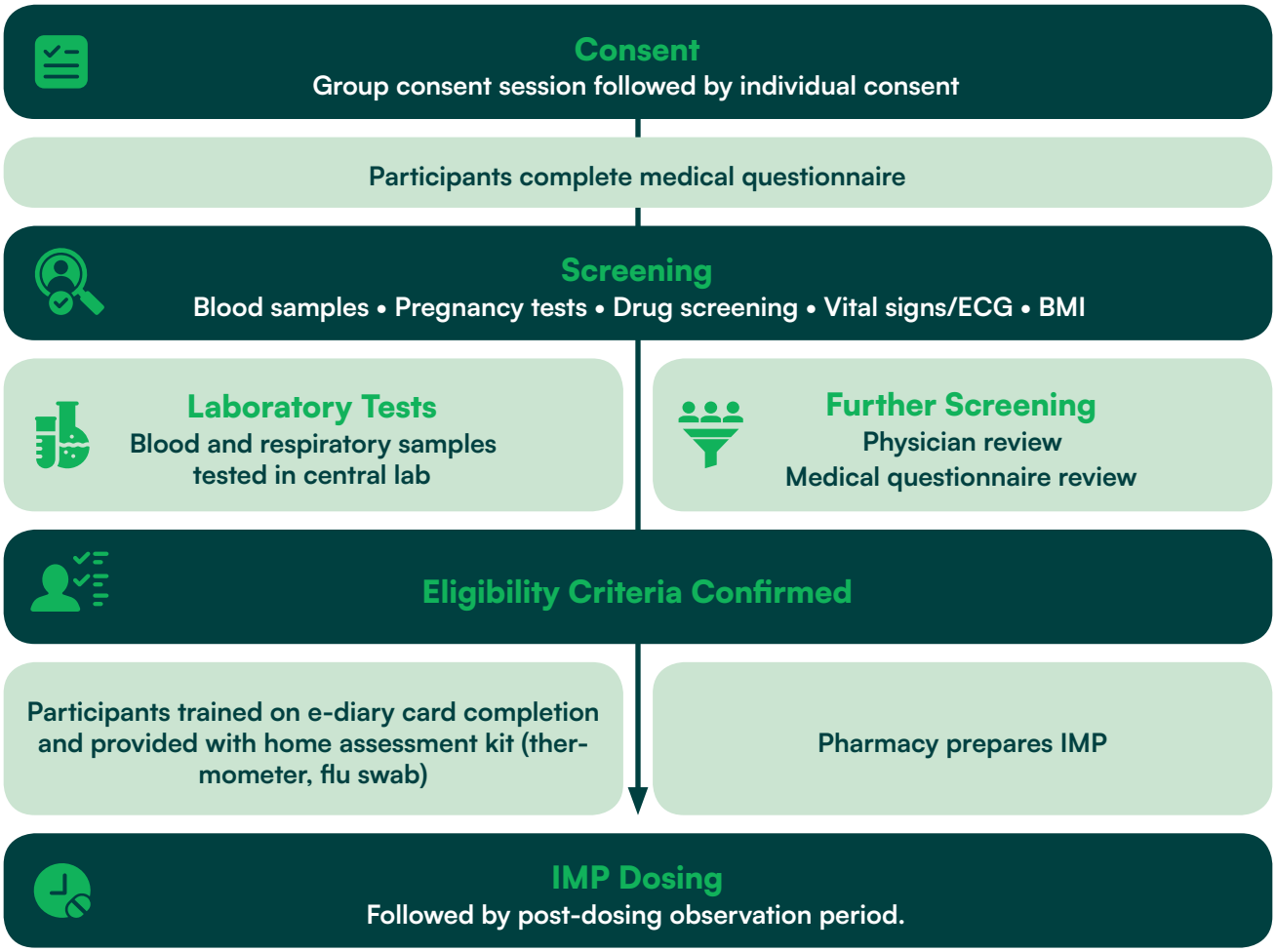
The team sought to dose 20 participants per session, but constant adjustments were needed to optimise efficiency in response to the unpredictable turnout of participants.

hVIVO implemented three dosing sessions per day (for example, 7:30 AM, 10:30 AM, and 1:30 PM) to accommodate varying numbers of participants, with each session staffed by at least seven clinical study support (CSS) personnel, five doctors, three nurses, and one phlebotomist.

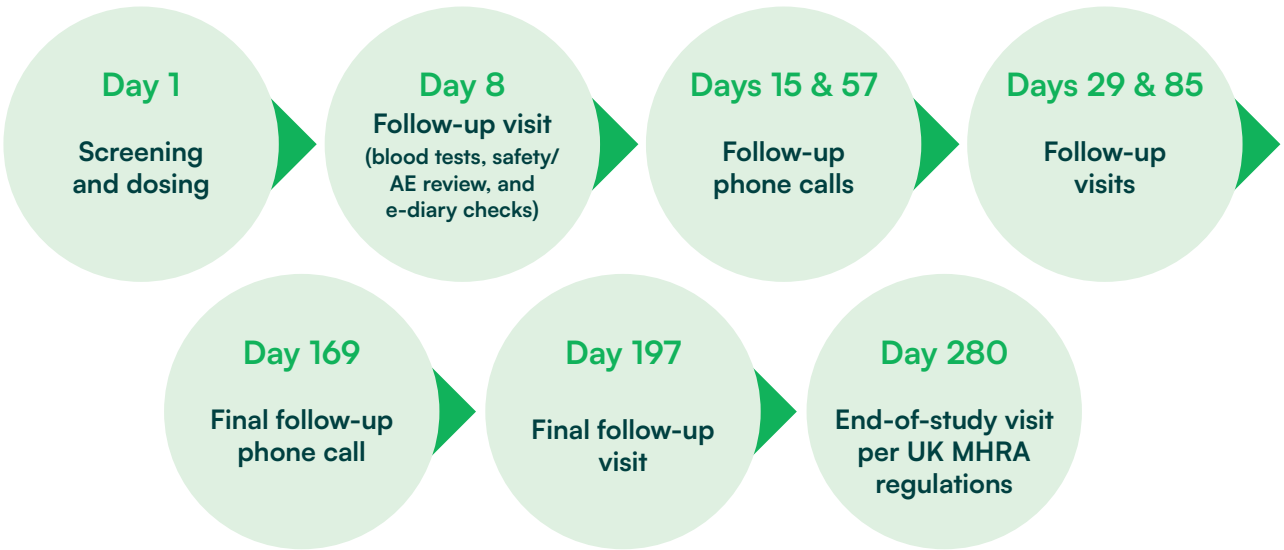
Dry runs were conducted to optimise facility utilisation prior to commencing the actual study. This proved crucial in ensuring a smooth operational flow on treatment days. The clinical administration team was required to effectively manage casebooks, paperwork filing, consent verification, and coordinate triggered assessments in instances where participants experienced acute respiratory infections.

The enrolment team was responsible for coordinating follow-up visits to maintain participant engagement, while the data management team ensured that all source data was transferred into the sponsor's electronic data capture system.

Screening and dosing process flow



Study schedule flowchart



Challenges and solutions

hVIVO's proactive approach and expert knowledge enabled potential issues to be resolved before they adversely affected the study's success.

These issues included unpredictable participant turnout, which could range from as few as 1 to 2 participants to as many as 43 participants per session. Real-time staffing adjustments were necessary to manage this effectively.

Dry runs also helped to ensure efficient use of space, manage the large workflow, and minimise overlap between screening and dosing teams. Snacks were provided to help keep participants engaged, mitigate waiting times, and prevent participant dropouts.

hVIVO's team of specialist virology scientists, its facilities, and its versatile services proved invaluable in running this vaccine study. The company's expertise in collecting, managing, and analysing specialist virology samples was key to ensuring the acquisition of robust and comprehensive study data.

Scientific advice was provided on updating laboratory protocols at all study sites to ensure optimal sample preservation, and guidance was offered on the IMP and blinding process.

hVIVO's integrated clinical trial site and laboratory services allowed for a seamless and efficient process throughout the entirety of the study.

Its extensive experience in managing challenge trials also allowed data to be modeled, with resource allocation, necessary staffing levels, and recruitment run rates all predicted to effectively deliver on expectations and proactively address challenges.

Processes were also monitored, measured, and adjusted where necessary, allowing the delivery of highly agile services.

Key metrics and achievements

hVIVO screened an average of 170 participants and dosed approximately 130 participants per week. More than 1,100 participants were screened in just over six weeks, with 817 participants (74%) successfully dosed, with follow-up completed later on in 2025.

Approximately 40% of participants who failed screening were excluded due to self-reported medical history, 25% due to factors such as out-of-range ECG, body mass index, or vital signs, and 15% due to positive drug tests.

Conclusion

hVIVO's extensive expertise in virology and clinical operations allowed this trial to be executed seamlessly, despite the significant challenges associated with the project.

hVIVO successfully dosed 817 subjects in just over six weeks, representing an extraordinary achievement considering the unpredictable nature of participant turnout and the study's complexity.

The team's ability to rapidly optimise resources, adapt to fluctuating numbers, and ensure high-quality clinical execution was fundamental to its success in meeting the trial's ambitious aims.

This outcome successfully showcases hVIVO's position as a premier clinical research site in the UK, highlighting its capacity to recruit for and effectively manage large-scale vaccine studies efficiently.

The capacity to screen, dose, and follow up on such a significant number of participants within a limited timescale is a testament to hVIVO's agile methodology, operational excellence, and deep scientific expertise.

The company's combination of expert scientists, clinicians, and clinical trial staff, its integrated site and lab facilities, and its impressive participant capacity can help to expedite the development of a wide range of vaccine and antiviral products.

Streamlining RSV clinical trial sample workflows

The analysis of samples containing Respiratory Syncytial Virus (RSV) in clinical trials is notoriously challenging due to the virus's inherent instability.

hVIVO's proprietary Stabilisation Transport Matrix (STM) has been designed to meet this challenge, enabling RSV transport and stabilisation in an array of clinical sample types, including nasopharyngeal swab and nasal wash samples.

The new STM from hVIVO has already achieved several notable milestones:

It has the capacity to maintain RSV viral RNA copies and RSV infectious titers at a dynamic range of up to eight hours at room temperature, affording clinical sites increased flexibility prior to sample processing.

It is able to maintain RSV viral RNA copies and RSV infectious titers at a dynamic range up to five weeks at -20°C, enabling the bulk shipments of samples and affording clinical trial sites increased flexibility in terms of their cryostorage requirements.

The new STM is also able to maintain RSV viral RNA copies and RSV infectious titers at a dynamic range up to nine months at -80°C, facilitating the testing of larger batches of clinical trial samples.

The matrix maintains stability and effectiveness at room temperature for up to nine months, facilitating the long-term storage of clinical trial collection kits and ensuring the minimal number of kit shipments at each site, as well as their tracking.

hVIVO's STM affords its users increased operational flexibility in terms of RSV clinical sample collection and storage without the loss of viral infectivity. These powerful capabilities make this new STM an ideal choice for both RSV clinical trials and challenge studies.