IQVIA CONSUMER HEALTH

White Paper

Subject Recruitment for the Consumerization of Clinical Trials in Asia Pacific

In a COVID-19 climate, there has been a huge shift in clinical trial management. Bespoke subject recruitment is a fundamental step to bring a trial to a prospective participant.

IN COLLABORATION WITH

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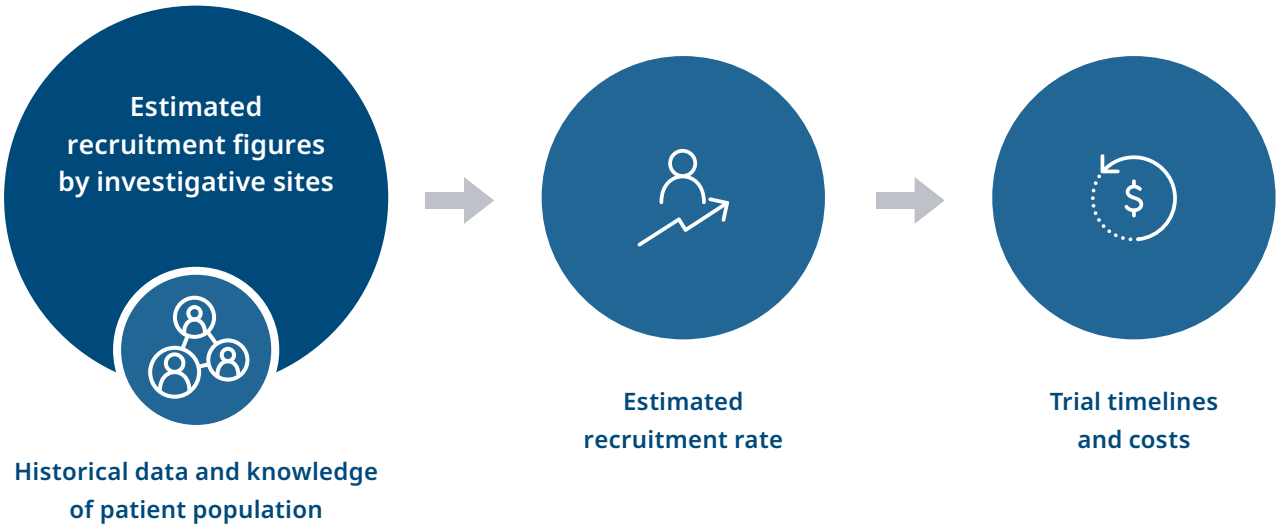
Introduction

Clinical trial enrollment in the era of COVID-19 will not be easy and needs to change. In Asia Pacific (APAC), increased competition for subjects and more stringent eligibility criteria coupled with highly differentiated regulatory frameworks are making it more challenging to solely depend on traditional, site-led recruitment models. Beyond the population immediately accessible to investigators, there is a growing need to reach out to subjects unknown to sites. Recruitment methodology such as Direct-to-Patient (DTP) recruitment can address that unmet need.

Subject recruitment for clinical trials in APAC has in the past been primarily driven by investigative sites. Using historical data and knowledge of their patient population, sites would estimate the number of subjects that they expect to recruit for clinical trials.

The estimated recruitment figures were a key data point in the site selection process and were also used to derive an estimated recruitment rate, which would guide project timelines and inevitably, this is directly correlated with the cost of trial conduct.
(See Figure below)

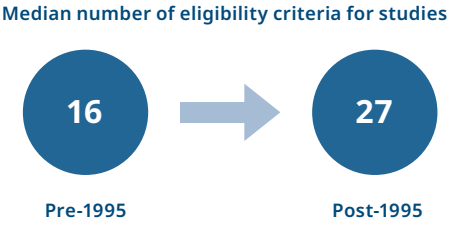


The site-led model of study recruitment has faced severe challenges with increased clinical trials complexities, and smaller eligible patient pool. There are two major challenges that sites face that are beyond their control in today's competitive environment.

1. Competition for subjects has increased. This is partly a consequence of the increased number of clinical trials taking place in APAC. In 2020, amid the coronavirus pandemic, sponsors registered 12,484 studies on the Chinese Clinical Trial Registry.[1] That represented an increase of 54% over 2019 and a jump of 101% compared to 2018.

The increase is even greater in some therapeutic areas, creating intense competition for the same target population or subject pool.

2. Inclusion/exclusion criteria that dictate subject participation have become more stringent and complex. An analysis of oncology clinical trials found the median number of eligibility criteria was 16 for studies started between 1986 and 1995.[2] Twenty years later, the median number of eligibility criteria rose to 27.



Increasingly, sites include patients in their enrollment forecasts based on a high-level understanding of the study, only to later learn they are ineligible for reasons such as the presence of comorbidities.

While sites in APAC still enroll faster than in other regions, increased competition for subjects and increasingly stringent eligibility criteria have made recruitment harder than in the past.[3] Sponsors cannot depend solely on sites to enroll subjects any more. A new approach capable of reaching out to more subjects is needed for studies to meet their enrollment targets.

What is DTP recruitment?

Forward-thinking sponsors and Clinical Research Organizations (CROs) have identified Direct-to-Patient (DTP) recruitment as a method to supplement site-based subject recruitment. DTP is a methodology that identifies and engages with potential clinical trial subjects through multi-channel marketing campaigns. Notably, DTP uncovers subjects who are hidden to established investigative sites, for example those who are treated for a chronic disease at a community hospital or are looking for self-treatment options at pharmacies with little clinical trial exposure.

Social media is one of the channels used for DTP enrollment campaigns. By targeting a specific subject profile, sponsors and CROs can use social media platforms to reach individuals who may be eligible for a clinical trial directly. Online outreach can be combined with on-site support to maximize the impact of DTP campaigns.

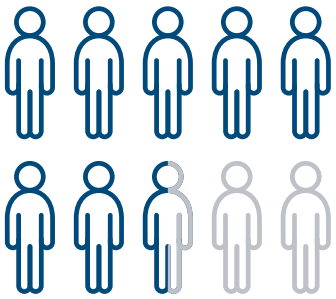
However, regulations surrounding DTP recruitment vary significantly across countries. For instance, South Korea has guidelines that discourage the use of Social Network Services to broadcast information on clinical trials, which can limit the reach of recruitment campaigns based on traditional media.

The pandemic-driven rise of DTP in APAC

The COVID-19 pandemic has altered the pathways that subjects take to seek treatment, renewing interest in engaging subjects directly. In the past, approaching subjects directly to create awareness about clinical trials has had its fair share of challenges, primarily because of apprehension towards how there may be less control of digital content. The COVID-19 pandemic has changed the dynamic. With lock-downs, travel advisory and social distancing measures implemented, the number of subjects visiting hospitals for non-essential consultation reduced greatly.
Even as restrictions eased, patients stayed away from hospitals due to fear of COVID-19 exposure.

These behaviour changes forced sponsors to review their subject recruitment strategy and in some cases, study design of clinical trials.

The surging interest in decentralized clinical trials reflects our current and future reality. Sponsors, CROs and research sites will need to work closely to augment recruitment strategy by engaging with subjects unknown to sites.



75%
of respondents in one survey said COVID-19 increased their use of decentralized clinical trials.[4]

Engaging with subjects directly through the use of digital channels and guiding them through pre-screening, screening, informed consent, and randomization is a perfect fit for the post-COVID-19 environment.

Exploring the potential of DTP techniques

Sponsors were able to rapidly adopt DTP in 2020 because of pioneering work done in the last few years to validate the approach, as is exemplified by IQVIA's journey. IQVIA's DTP journey from early ideas to well-validated approach can be described through a series of clinical trials, starting with a feminine hygiene (Pharmacy OTC product) study in 2016.

Clinical Trial Educators (CTEs) are an on-the-ground resource primarily focused on patient recruitment at a site level. CTEs visit sites more frequently than clinical research associates and work closely with investigators and all other key stakeholders at sites, including study coordinator, nurses, pharmacist etc. to address barrier to recruitment. Specific CTE tasks include the mapping of patient pathways and provision of guidance to site staff. The role is relatively new to APAC but is well-established and accepted in the US and Europe.

Case study 1

Feminine care clinical trial in Thailand

A feasibility study identified Thailand as high potential to contribute to subject recruitment because of the large number of subjects treated for recurring Urinary tract infections.

However, the reality was a stark contrast with few subjects qualifying for randomization as they were unable to produce documented medical reports as evidence of disease recurrence.

Analyzing the problem

To properly analyze the root cause of poor enrollment, a Clinical Trial Educator (CTE) from IQVIA worked closely with the research sites to analyze the problem.

Insights

The analysis revealed key consumer insights that women in Thailand view feminine health issues as a private matter and shy away from consulting doctors or visiting hospitals.

Many prefer to first self-medicate with over-the-counter (OTC) remedies. The site-patient interactions that typically facilitate recruitment simply were not taking place to generate enrollment.

Developing a targeted solution

Working with a local agency, IQVIA developed a multi-channel clinical trial marketing campaign that engaged directly with women in Thailand.

The campaign featured

- Clinical trial advertisements that were adapted with Thai cultural nuances
- A website that explained the risks of failing to get proper medical attention for bacterial vaginosis.

To drive traffic to the website, IQVIA ran multi-channel marketing campaigns on forum boards and Facebook groups followed by Thai women in the targeted age group.

The Facebook adverts geo-targeted women residing in the vicinity of the investigative sites, inviting them to register their interest to participate in the study.

Conclusion

The DTP campaign was a successful proof of concept, driving increased participant interest in the clinical trial within a month.

This was an early validation of the techniques and support needed to mobilize DTP in APAC, paving the way for more ambitious deployments of digital and other technologies to enroll study subjects.

Demonstrating the resilience of DTP amid the pandemic

The lessons from the feminine care clinical trial shaped how IQVIA responded to sponsors needing support in Phase III with challenging patient groups, as was the case in a Phase III clinical trial that needed to enroll well-controlled asthma patients in China.

The trial faced a lack of interest from patients due to the availability of other treatment options, strict eligibility criteria that were not in-line with local clinical practice, and competition from other clinical trials targeting the same patient population.

Case study 2

Clinical trial on asthma patients in China

To address the identified recruitment barriers, IQVIA deployed CTEs to step-up on protocol training. That provided an opportunity for CTEs to address concerns raised by investigators. Consequently, site-specific action plans were developed to resolve issues impacting recruitment.

Analyzing the problem

Analysis of the barriers to enrollment led to further refinements that increased the focus on physicians based very close to the sites who had previously collaborated with the study investigators.

IQVIA identified that sub-investigators as more likely to take the time to discuss the value of the study with the CTE and ultimately to refer their patients.

Insights

The iterative changes to the enrollment strategy increased the screening and randomization rates at most sites. Overall, the randomization rate increased more than 90% following the implementation of the changes.

What has changed?

In a pre-COVID-19 scenario that would be the end of the story. However, the asthma clinical trial was still active when the pandemic began in China. Restrictions imposed in response to COVID-19 hit all clinical trials but the asthma study was particularly affected.

The biggest challenge

China assigned respiratory physicians to the management of COVID-19 patients, thereby investigators were not available to lead the trial.

The impact

The physicians ultimately returned to their pre-pandemic roles but the disruption could have caused them to drop out of the clinical trial, either because they were no longer contactable or interested in the study.

Developing a solution

When the physicians returned to their hospitals, IQVIA arranged multiple online livestreams aimed at investigators and referring physicians to get the study enrolling quickly again. The CTE mitigated that risk by maintaining relationships with the physicians throughout the pandemic via the WeChat platform or telephone.

Conclusion

The events helped to re-engage physicians and restart the subject referral process, accelerating trial timeline and mitigating some of the disruption caused by the pandemic.

Validating the strength of DTP to dramatically improve enrollment

The experience gained through years of exploration and refinement of DTP techniques came together in a Phase III clinical trial sponsored by GlaxoSmithKline Consumer Healthcare (GSKCH) in China.

Featured case study

GlaxoSmithKline Consumer Healthcare (GSKCH)
Topical pain relief clinical trial in China

The situation

Developing the initial strategy

Identifying early barriers to recruitment

Adapting to a fast-changing environment

Pivotal study for a new high strength formulation of Voltaren

GSKCH initiated the study to compare the effect of the topical pain relief gel Voltaren 2%, a new high strength version of a marketed product. Ankle sprain, an acute pain incident, was chosen as the target indication in the belief it offered the highest probability of success and a faster route to market than chronic conditions.

Ankle sprain chosen as target indication

Acute and self-limiting nature of condition posed significant enrollment challenges

As mild-to-moderate ankle sprains are common, a large pool of potential subjects was expected. However, the acute and self-limiting nature of this condition posed significant enrollment challenges, as did the need for subjects to be randomized within 24 hours of their injury and before taking any confounding treatments. Recruitment fell behind target initially.

Recruitment fell behind target initially

IQVIA assessed consumer behavior

To revitalize recruitment, IQVIA assessed consumer behavior, confirming the assumption that only a small fraction of subjects with mild to moderate ankle sprains seek medical care for the condition. Most people preferred traditional medicines and other self medication options available over-the-counter in pharmacies.

Developing the initial strategy

Assessment of online behavior of ankle sprain patients to propose a digital strategy

Working together, IQVIA and GSKCH zoomed in on finding potential subjects at events or venues with a higher incidence of ankle sprains, such as jogging parks and construction sites. IQVIA also assessed the likely online behavior of ankle sprain patients to propose a complementary digital strategy.

The digital campaign targeted people who searched online for ankle sprain treatments

The digital campaign targeted people who searched online for ankle sprain treatments. The goal was to generate traction and awareness of the trial through multiple applications to engage potential participants and direct them to the study website.

Adverts pushed through multiple applications to direct potential participants to study website

Despite being new to digital campaigns in clinical trials, GSKCH embraced the approach from IQVIA that featured data on the potential outreach to subjects via online platforms.

The digital campaign generated significant online activity

Early on the digital campaign generated significant online activity. However, the high click-through rate failed to translate into potential subjects presenting at sites. In total only 12 phone calls were logged. Eight of them were eligible to participate in the study but none of them went on to enroll.

High click-through rate but failed to translate into potential subjects

Assessment to understand the missed connections in online to offline process

IQVIA's clinical research associates (CRAs) spoke to investigators to understand the missed connections in the online to offline process. The discussions revealed the orthopedic physicians who were expected to enroll patients were unable to cope with the volume of incoming calls that in some cases interrupted their schedule, leading them to disengage.

Orthopedic physicians unable to cope with volume of calls

Call center to take the burden off investigators

One way to mitigate these dropped or missed enrollments was via a call center to take the burden off investigators and provide potential participants with a basic consultation prior to first site visit. However, to bring recruitment back on track, there was a need to pivot to other offline strategies.

Still a need to pivot to other strategies

Adapting to a fast-changing environment

Unable to target large sporting events due to COVID-19 pandemic

In early 2020, attempts to re-energize the clinical trial were hindered by Chinese New Year and the start of the COVID-19 pandemic. Plans to target large sporting events due to take place at the start of 2020 were canceled and the study itself was put on hold for three months. This new challenge gave IQVIA and GSKCH the chance to design a new enrollment plan tailored to the pandemic environment.

The chance to design a new enrollment plan tailored to the pandemic environment

A Healthcare Professional (HCP) such as physician/pharmacist, referral scheme supported by CTEs was implemented to ensure ankle sprain subjects were made aware of the clinical trial even if they initially went to a location other than an investigator site for treatment.

Creation of a HCP referral scheme

IQVIA and GSKCH jointly discussed the HCP referral scheme keeping in mind consumer behavior and self-care pathway for ankle sprain subjects in Chinese cities. The approach was relatively new in China but lessons learnt from prior successes boosted the team's confidence.

The CTE mapped site-specific subject pathways, expanded each site's referral networks, engaged site staff to identify hidden patients

Based on those experiences, the CTE mapped site-specific subject pathways, expanded each site's referral networks, engaged site staff to identify hidden patients, and activated key stakeholders involved in the ankle sprain treatment pathway.

HCP referral scheme uncovered potential subjects who visited ER with ankle sprains

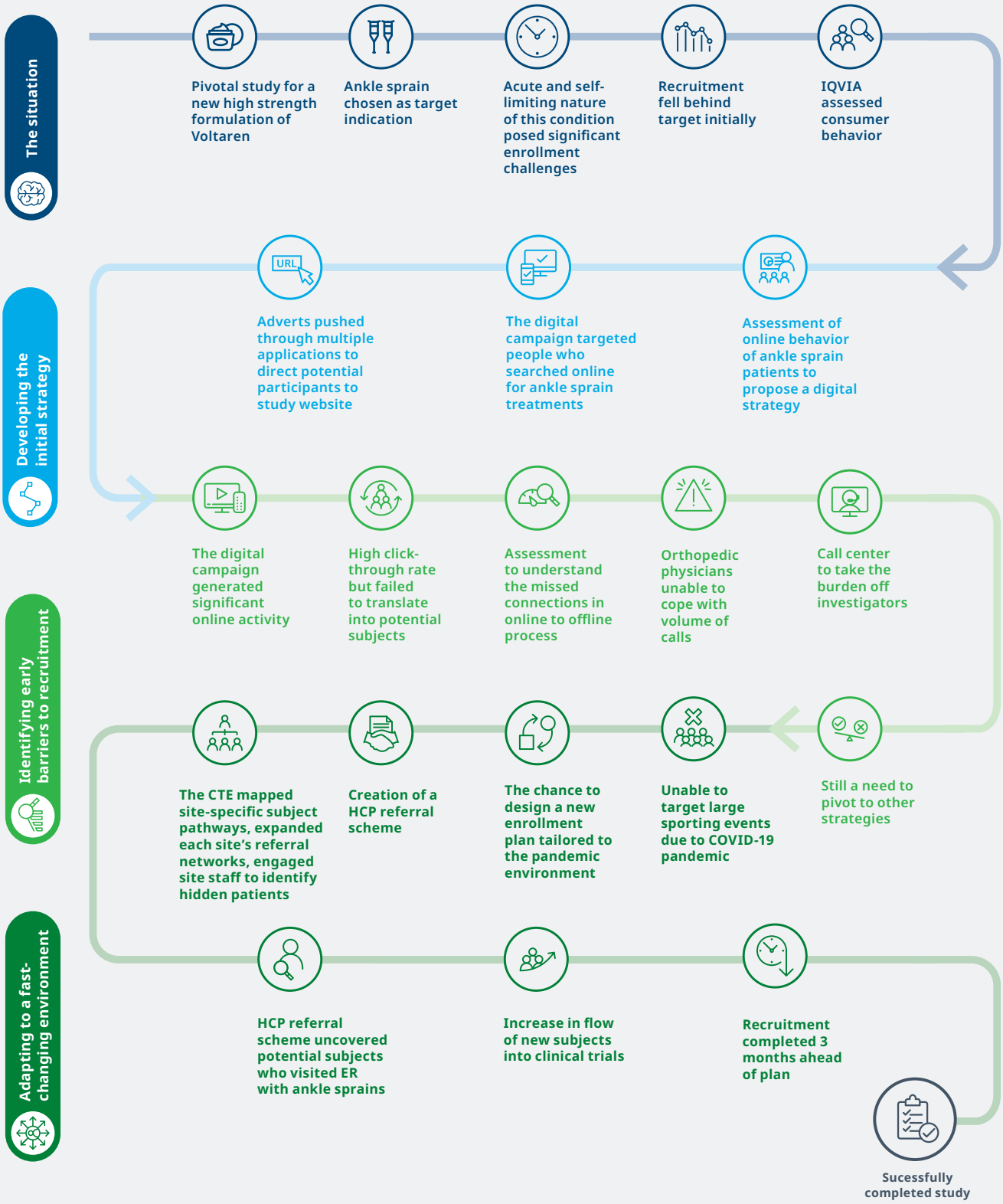
THE HCP referral plan when rolled out, uncovered potential subjects who visited emergency rooms (ER) with ankle sprains. Historically, ERs are not typically chosen as a department for trials. However, the IQVIA CTEs built relationships with the orthopedic physicians in ERs and were successful in mapping a referral network linking ERs with the research sites.

Increase in flow of new subjects into clinical trials

This was a turning point for direct referrals and recruitment rates increased across all participating sites by building a strong referral pathway for subjects that would otherwise be missed. The end result was meeting the enrollment target three months ahead of schedule and completing subject visits in a challenging year.

Recruitment completed 3 months ahead of plan

Overview of GSKCH Topical pain relief clinical trial in China



Study challenge:

Stringent eligibility criteria, low subject interest, limited outreach channel and impact of COVID-19 have been identified to be the key barriers to recruit subjects for this study on a topical pain relief medication that is available OTC.

Solution:

To address the recruitment barriers identified, a multi-pronged approach was devised, focusing on expanding the subject pool by mapping referral networks around and at the investigational sites.

Result:

The recruitment strategy that capitalized on optimizing the potential of referral networks contributed more than 80% of subjects randomized which was instrumental in supporting the study achieve its last patient in 3 months ahead of target.

Lessons learnt for future success

The journey of the OTC and self care trials, from significant early difficulties to the later resounding success, demonstrated clear lessons about strategies in different situations. Digital enrollment has proven highly effective in some studies. However, in addition, programs that support subject touchpoints, such as call centers, also play a vital role. The experience suggests the whole workflow of digital channels to reach potential participants should be carefully designed for the journey.

The successful application of the HCP referral plan to the topical pain relief clinical trial and multiple other studies shows the broad utility of the approach. The experience also showed us that there are several complex factors at play from changing subject behavior and pathways, external environment in the post COVID-19 world and role of HCPs in the self-care and healthcare space, all of which need to be distilled into a bespoke strategy for success.

Conclusion

APAC is often viewed as slower to adopt new approaches to clinical development than Europe and the US, in part because the regulatory landscape is more fragmented than in those regions. Fragmentation is still a barrier to adoption of new approaches in APAC but the pandemic has driven regulators to consider new ways of working and given sponsors and CROs a chance to validate novel techniques.

COVID-19 brought changes to clinical trial dynamics, accelerating the rise of decentralized virtual and hybrid clinical trials and increasing the need for bespoke, tailored approaches to subject recruitment.

The case studies provide a deep perspective of the on-ground realities in the post-pandemic world and a foundation for the strategies that will enable sponsors to thrive in the new environment. By building on the lessons of those studies, sponsors will be able to deploy bespoke solutions that are truly subject and consumer-centered, and improve the experience of key stakeholders in a trial.

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About IQVIA Asia Pacific

IQVIA (NYSE:IQV) is a leading global provider of advanced analytics, technology solutions, and clinical research services to the life sciences industry. IQVIA creates intelligent connections across all aspects of healthcare through its analytics, transformative technology, big data resources and extensive domain expertise. IQVIA Connected Intelligence™ delivers powerful insights with speed and agility — enabling customers to accelerate the clinical development and commercialization of innovative medical treatments that improve healthcare outcomes for patients. With approximately 70,000 employees, IQVIA conducts operations in more than 100 countries.

With regional headquarters in Singapore and offices in 15 countries, IQVIA Asia Pacific provides technology-enabled services and solutions to meet the growing and rapidly changing needs of clients, both local and multinational, operating in Asia Pacific. IQVIA is committed to advancing healthcare by offering evidence-based insights and deep domain expertise in thought leadership, with the aim of improving understanding and accelerating innovation within the healthcare ecosystem.

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Swapna leads the Consumer health clinical strategy for Asia Pacific, across multiple categories particularly OTC and Nutrition. Her role involves engaging client R&D stakeholders for clinical studies linked to new product development, registration and claims substantiation. She has 12 years of in-market and regional experience spanning new business strategy, product lifecycle management, strategic marketing and post M&A commercial integration in Consumer Health, Pharma, Biologicals and Telecom in Europe and Asia. She brings with her Consumer health category expertise in VMS, OTC, Topicals, brand extension and innovation in Europe and Asia with leading CH MNCs such as Sanofi, Novartis and GSK Consumer Health. Swapna holds an MBA in New Market Development from HEC Paris, France. She has a BSc. Microbiology, Genetics and Chemistry with a Post graduate diploma in Bioinformatics.

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With thanks to the GSK Consumer Health team for their contribution and collaboration in the development of this white paper.

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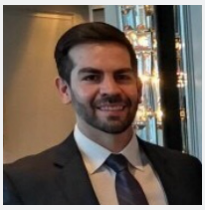

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