INVESTIGATOR INITIATED TRIALS-COVBOOST

ICR ETHICS AND GCP FORUM 2022

PRESENTED BY:

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COMPANY DEVELOPMENT

Founded in 2009 by-primarily to support Academic Studies
Experience includes 12yrs+ in senior NHS positions and 15yrs + in academic/commercial clinical trials/CRO environment.
Previous experience allowed vision and direction for Company

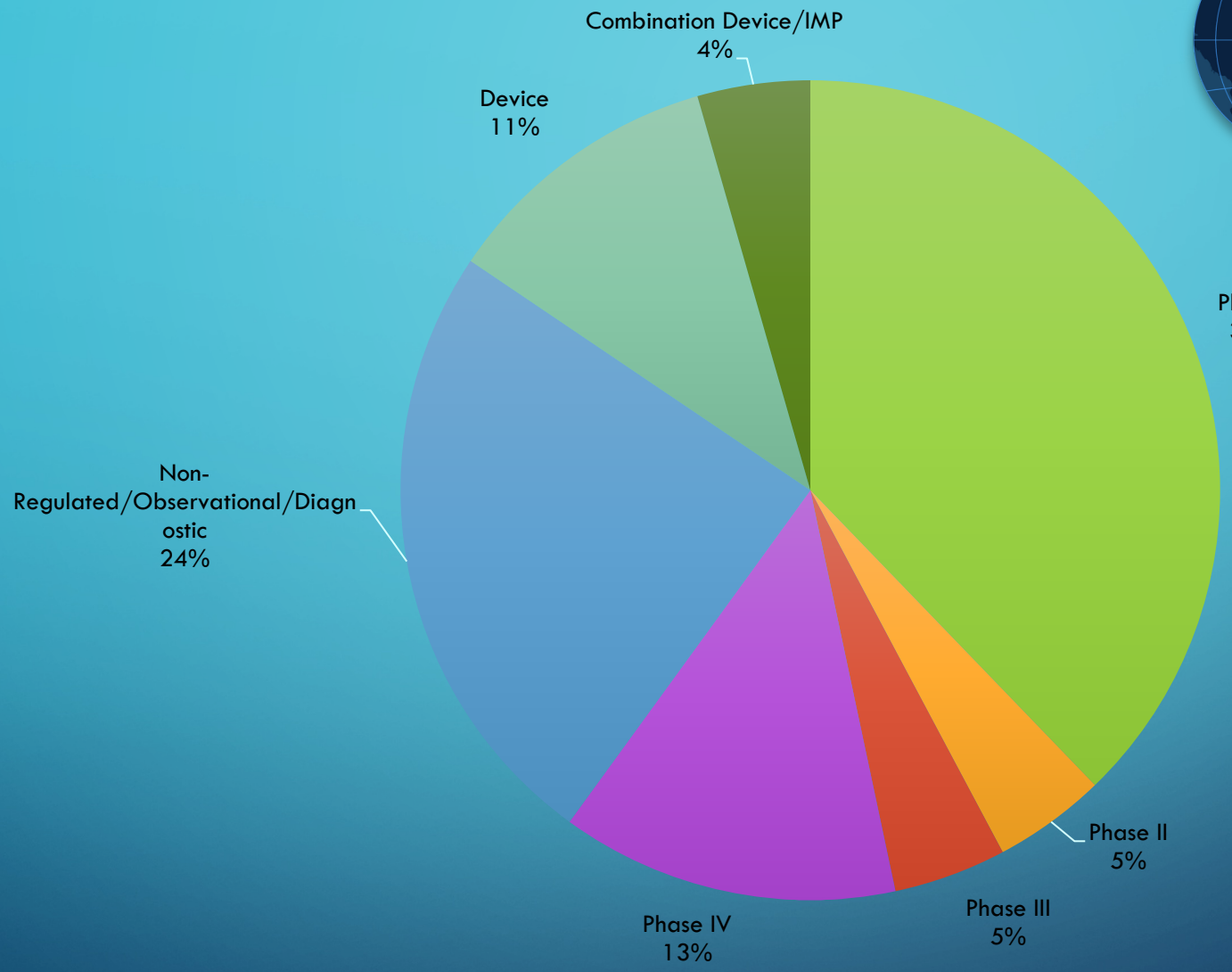
Since inception, PHARMExcel has organically grown

ISO 9001 compliant QMS-undergoing ISO accreditation

25+ staff and now undertakes clinical trials throughout the UK, Europe and ROW.

Still maintains a large portfolio of Investigator Initiated Trials (IITs)-this is at the heart of PHARMExcel

Phase Spread of Studies -Total studies Awarded -Mar 2022



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Includes Covid 19 Vaccine Trials

INVESTIGATOR INITIATED STUDIES-CHALLENGES-I

- **Inadequate Investigator Support**
  - Essential to survey the resources available at site, usually before the protocol is written-Look at what services are **ACTUALLY** required-set up R&R Matrix
  - Establish funding source (grant/commercial)
  - Establish type and Phase of trial (CTIMP, Device, Combination, Observational etc)
  - Establish IMP/Device requirements (licensed? CE marked?-Sourcing/Import/export/QP services
  - Establish Laboratory requirements (local vs central)
  - Establish territories, number of sites, number of participants required

Cost study based on above criteria

INVESTIGATOR INITIATED STUDIES-CHALLENGES-II

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- **Inadequate Design**
  - Ensure study has been appropriately powered-look at statistical resource/support-often not in place!
  - Ensure sites can actually recruit target numbers-undertake feasibility if appropriate-competing studies/experience in team
- **Inadequate Funding**
  - Clinical research is expensive! Resources required, legal and compliance risks etc
  - Industry support differs in many ways, usually in the form of funding, provision of product, or aid in study design and conduct -If industry provides support, the issues of intellectual property, data ownership, and publication rights become sensitive
  - If grant funded- often a cap/finding limited -doesn't always reflect requirements to run the study. A well-funded project is essential to successful completion.

INVESTIGATOR INITIATED STUDIES CHALLENGES-III

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- **Regulatory Burden**
  - Need to identify regulatory route-CTIMP, Device, Combined IMP/Device etc
  - Need to establish if UK only (MHRA, HRA/REC combined review) or if other Countries/Territories involved (EMA/FDA)
  - Is it Phase I? (HVs)-May be shorter approval timelines
  - Covid 19-was previously fast tracked. As of 1st March standard review times now apply (MHRA Covid 19 inbox no longer operational)

The above requires adequate risk assessments

VALUE ADDED

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We have extensive knowledge of the UK/EU research environment

We support/guide Investigators throughout the entire study

We work as a collaborator-Extension of existing teams

We are flexible and agile-we try not to say no!

We have dedicated personnel assigned to the study-try to assign therapeutic backgrounds

We are quality and process driven

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COVID -19 IMPACT

COVID-19-THE HURDLES AND OPPORTUNITIES

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- Staff suddenly home based-New policies and procedures-new ways to work
- All non Covid projects placed on hold-re-prioritise workloads
- Risk assessments and amendments required regarding delivery of projects
- Unable to send monitors/CRAs on site-remote/central working
- Covid trials started-Fast paced delivery

ADOPTING A NEW AGILE APPROACH TO CRO CLINICAL TRIAL MANAGEMENT

CASE STUDY

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- Funded by the Government through the National Institute for Health Research (NIHR) and the Vaccine Taskforce
- Phase II, Investigational Medicinal Product (IMP) study evaluating seven different COVID-19 vaccinations given as a third (booster) dose
- Recruiting participants who had previously received either two doses of BNT162b2 (Pfizer–BioNtech) or two doses of ChAdOx1 nCOV-19 (Oxford–AstraZeneca).

COV-BOOST
Evaluating COVID-19 vaccine boosters

THE BRIEF

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Data be made available to the Joint Committee on Vaccination and Immunisation (JCVI) by the end of July 2021

Allow the Government time to decide the policy strategy for an Autumn booster programme.

Short window of approximately 5 months to achieve.

We had to look to an alternative way of cross-party working from the usual CRO approach to ensure critical timelines would be met.

Our main end goal was to bring everyone together, working fast and efficiently, ensuring adherence to regulations, whilst maintaining the highest quality standards.

4 NEW AGILE STRATEGIES

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USE OF ONLINE PLATFORMS-WORKFORCE HOME-BASED-NUMEROUS SITES

ALL COVID STUDIES FAST TRACKED

ROLLING REGULATORY REVIEWS-INCREASED SCIENTIFIC/REGULATORY COLLABORATIONS

REMOTE AND CENTRAL MONITORING-RISK PROPORTIONATE

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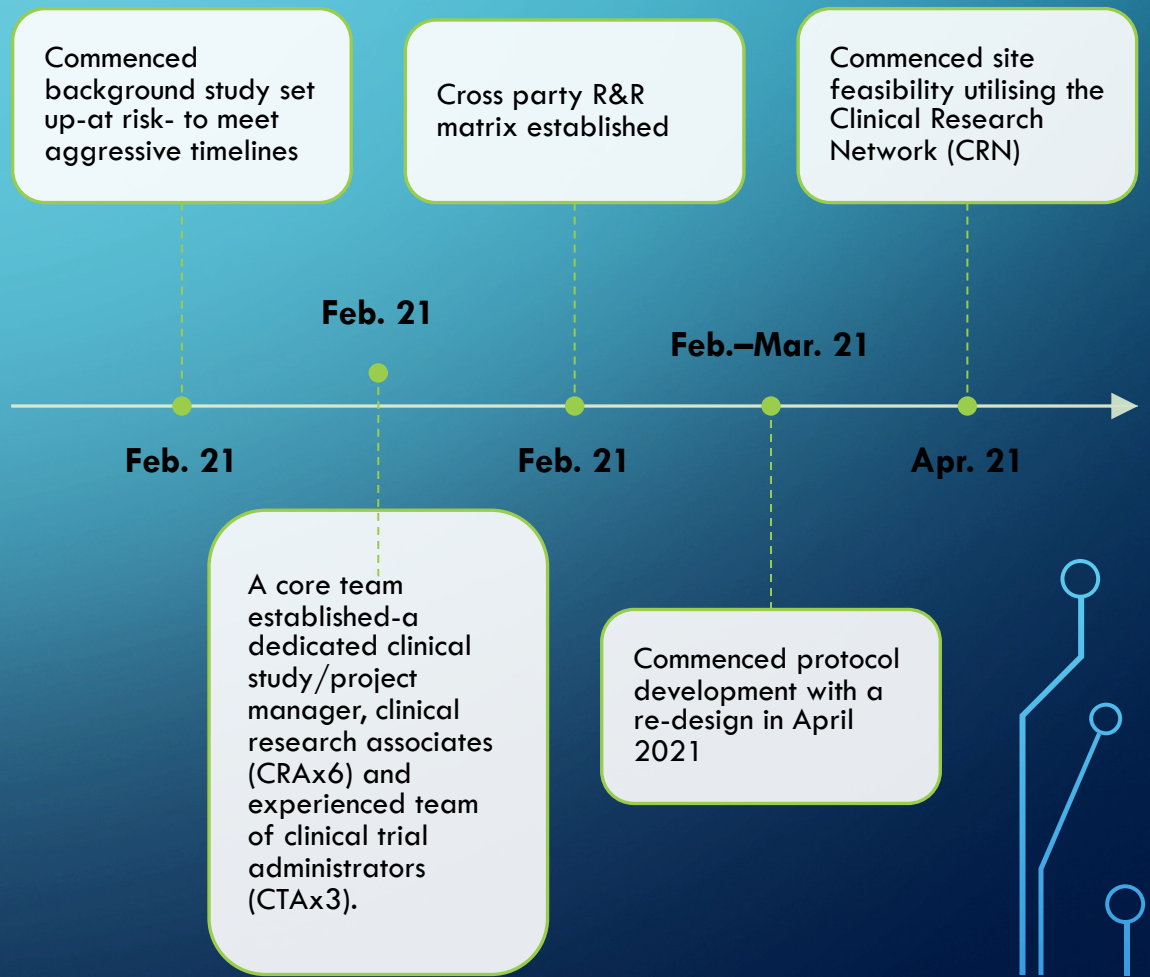
AN AGILE APPROACH



GROUP STRUCTURE

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Randomised 1:1:1:1

Group A
N=888

- 2 x ChAdOx1 N=444 → ChAdOx1 Novavax Novavax 50 Men ACWY
- 2 x BNT162b2 N=444 → ChAdOx1 Novavax Novavax 50 Men ACWY

Randomised 1:1:1:1:1

Group B
N=1110

- 2 x ChAdOx1 N=555 → BNT162b2 Valneva Valneva 50 Janssen Men ACWY
- 2 x BNT162b2 N=555 → BNT162b2 Valneva Valneva 50 Janssen Men ACWY

Randomised 1:1:1:1

Group C
N=888

- 2 x ChAdOx1 N=444 → Moderna Curevac Curevac 50 Men ACWY
- 2 x BNT162b2 N=444 → Moderna Curevac Curevac 50 Men ACWY

RECRUITMENT METHODS

- Press release went out Friday 21st May 0000 HRS – DHSC leading comms –LCRN support locally using localised materials
- NIHR vaccine volunteer database
- Email lists
- Website/Social media
- PIC Sites

Other approved methods

- Public places, including buses and trains
- Newspapers, Radio
- Direct mail-out using electoral roll

APPROVAL TIMELINES

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COV-BOOST
Evaluating COVID-19 vaccine boosters

- MHRA, REC and HRA rolling reviews
- Docs sent in final draft format and as they became available-reviewed in real time
- Feed back provided throughout process
- Fast track approvals-7 working days

Full submission -6th May 2021
REC approval-13th May 2021
MHRA/HRA approval 17th May 2021

NEW STUDY PROCESSES

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IMP-vaccine accountability logs/IMP management plans created for all groups

Safety plan and work instructions written-in line with Manufacturer Agreements-cross reporting

New SIV delivery methods

New activation processes-3 part activation

New Monitoring methods-risk based

Rolling reviews

New EDC trackers

New site working portals-exchange of information with sites

SITE SET UP

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SIVs commenced-18 sites over 5 days (20th-26th May)

Sites commenced rolling activations (20th May-8th June)

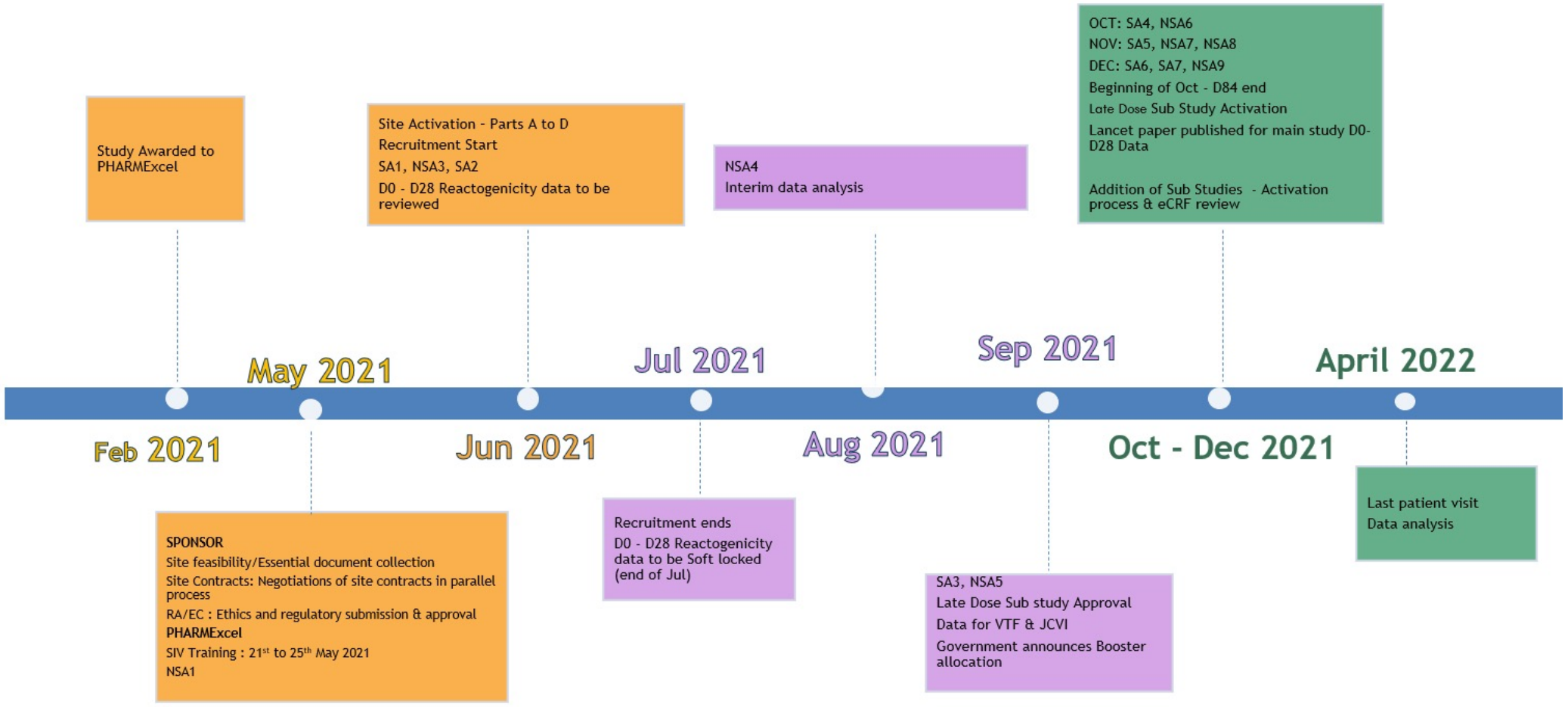
First site recruitment commenced 1st June 2021

Agile Monitoring –Real time data review

COV-BOOST
Evaluating COVID-19 vaccine boosters

Total 4-month- Study notification-1st patient recruited!

TIMELINE


Study Awarded to PHARMExcel
Site Activation - Parts A to D
Recruitment Start
SA1, NSA3, SA2
D0 - D28 Reactogenicity data to be reviewed
NSA4
Interim data analysis
OCT: SA4, NSA6
NOV: SA5, NSA7, NSA8
DEC: SA6, SA7, NSA9
Beginning of Oct - D84 end
Late Dose Sub Study Activation
Lancet paper published for main study D0-D28 Data
Addition of Sub Studies - Activation process & eCRF review
Feb 2021
May 2021
Jun 2021
Jul 2021
Aug 2021
Sep 2021
Oct - Dec 2021
April 2022
SPONSOR
Site feasibility/Essential document collection
Site Contracts: Negotiations of site contracts in parallel process
RA/EC : Ethics and regulatory submission & approval
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SIV Training : 21st to 25th May 2021
NSA1
Recruitment ends
D0 - D28 Reactogenicity data to be Soft locked (end of Jul)
SA3, NSA5
Late Dose Sub study Approval
Data for VTF & JCVI
Government announces Booster allocation
Last patient visit
Data analysis

STUDY ACTIVITY

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- Gathered, reviewed and Quality Controlled (QC) documentation throughout all stages- worked collaboratively with the Sponsor and the lead site's (UHS) project team
- Established a working portal (SharePoint) for each site, allowing quick and efficient exchange of, and access to, essential documents for the study
- The EDC was reviewed by the COVBoost CRA team as a rolling remote activity using a study-specific EDC tracker (independently devised and was approved and implemented for this trial)
- All participant's day 28 reactogenicity data had to be monitored, cleaned and analysed to ensure it was submitted to the Joint Committee on Vaccination and Immunisation (JCVI) by August
- Booster programme rolled out in Autumn 2021

KEY HURDLES EXPERIENCED

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- New PHARMExcel staff onboarding at time of study implementation
- Fast paced nature of study-multi site and 3000 participants-hit all our timelines
- Rolling data reviews -huge amount of data to review -prioritized data sets
- Slow EDC (REDCap) so issues with remote monitoring-time consuming!!
- Multiple Teams involved-so communication co-ordination was key-TMGs, Whatsapp
- New study processes required “bedding in”-undertook continual reviews

IMPROVED OUTCOMES-I

- From initial feasibility, essential document development, through to approvals (including further amendments), and all site activations **took four weeks, an unprecedented delivery time.**
- Adopting an agile/flexible way of working allowed PHARMExcel and all parties involved to create a responsive and effective performance across the study.
- Solid relationship with Sponsor, CI and R&D teams vital
- Able to capitalise on change quickly -virtual comms tools, weekly TMGs, rolling review and action cycles, remote and central monitoring, continual evaluation and improvement of processes –allowed results to be delivered within a very strict deadline.

CONCLUSION

- The sites have now completed recruitment for the main study
- PHARMExcel team continue to oversee the final stages of the main study with multiple additional sub studies
  - Control group-unblinding (666 participants)
  - Novavax (111 participants)
  - 4th Dose (210 participants)
  - Fractional Dose (961 participants)
  - Omicron Variant (414 participants)

All studies complete next year

Whilst it was certainly a challenge, this real-time example demonstrates what can be achieved through effective Sponsor-CRO-Site and Regulatory collaborations!


Do you have any Questions?