Faculty of Pharmaceutical Medicine

FPM Clinical Trials Resilience Survey

Final Report v1.0

15th December 2020

Contents

1 Executive summary

The COVID-19 pandemic has disrupted the lives and livelihoods of many of the members of the Faculty of Pharmaceutical Medicine (FPM). In the UK, within both the NHS and national economy resources were diverted in an attempt to manage the outbreak. This effort was mirrored across pharmaceutical medicine, with pharmaceutical companies and regulators pausing or postponing the start of many trials in other disease areas to focus on the hunt for therapies for COVID-19.

This refocusing in approach has been enormously challenging, but we have learnt a lot over the last few months, and the return to the non-pandemic clinical trial landscape in the 'new normal' could be very different.

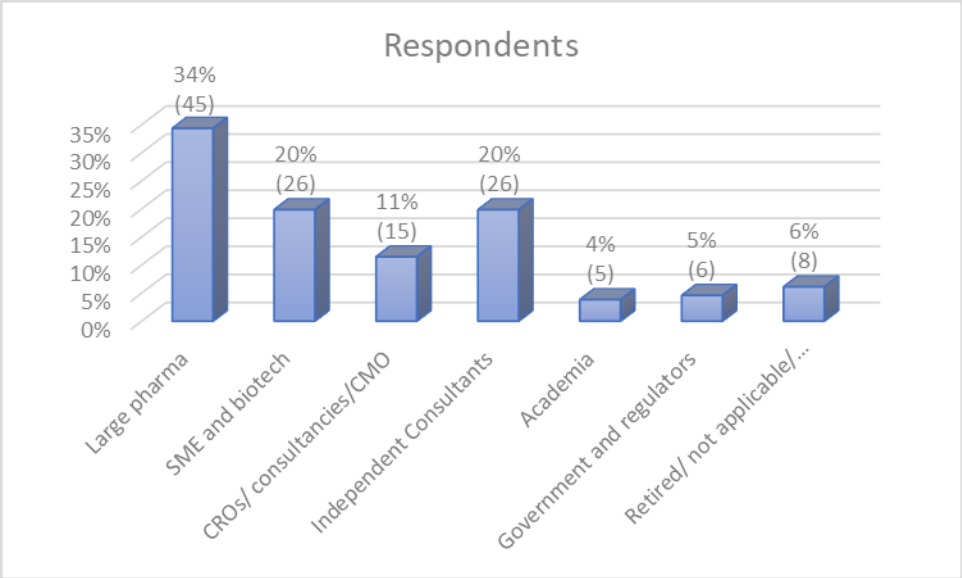
The FPM Clinical Trials Resilience Survey (Oct-Nov 2020) sought to understand these pressures and the adaptations that our members have experienced. We wanted to try to learn whether the COVID-19 pandemic has brought about permanent changes to pharmaceutical medicine and drug development and regulations that could or should now become integrated into 'normal' practice.

The results are illuminating and will help guide FPM and our external stakeholders as the current pandemic continues. The outputs from the survey may be relevant to maintaining effective systems during further COVID-19 waves, but also to future, as yet unknown, pandemics and global health challenges.

2 About the survey

- The 'Clinical Trials Resilience Survey' was run by FPM between the 22nd October and the 4th November 2020
- The survey was sent to all 1500+ members of FPM and was also made available to non-members to complete
- FPM members are medically qualified and employed within the pharmaceutical industry, biotechnology companies and contract research organisations, or the drug regulatory authorities
- 128 people responded, including 118 members and 10 non-members
- 75% (95) respondents were based in the UK / 9% (12) in USA / 9% (12) in Europe outside UK / 7% (9) from outside Europe and the USA
- The majority of respondents worked on clinical trials; 70% respondents stated they worked on clinical trials and drug development and 19% in clinical pharmacology and 11% did not record involvement in trials. Just over half worked in pharmaceutical companies and biotech companies and just under half in contract research organisations (CROs) / contract manufacturing organisations (CMOs) or as consultants

Table 1: Respondents' employers



3 Adaptions made to expedite treatments or vaccines for COVID-19

Over half the respondents (54%) reported that their organisation has been directly involved in developing treatments or vaccines for COVID-19.

3.1 Focus of clinical trial programmes

Those respondents that were involved in developing treatments or vaccines for COVID-19 reported on vaccine programmes, therapeutic antibodies, small molecules, stem cell treatments, palliative care and programmes for repurposing. Several respondents' COVID-19 drugs were being developed at the expense of other programmes being put on hold.

3.2 Innovative programme designs

- Adaptive programmes and trial designs
- Shortening of programmes with amalgamation of development phases with anticipation of early conditional approval or early access
- New biological modelling and digital tools
- Focus on epidemiological research as understanding of the disease emerged

Information from trial designs and the emerging epidemiology led to COVID-19 programmes having stratified approaches to patient selection, prospectively, retrospectively and adaptively and many amendments to trials and analyses.

The shortened and adapted timescales also brought resultant pressure on medicines production planning, which many respondents were also involved with.

3.3 Choice of Region in which to run COVID trials

The reason for choice of region for conducting studies was predominantly in countries with high prevalence of the disease. Some respondents reported that they only carried out trials in countries that allowed remote source data verification (SDV), or ones they were allowed to travel to, or where track and trace was already set up. Many reported studies were being conducted in the USA and several respondents reported, after receiving regulatory approval challenges, getting national health authority approval for allocation of study sites where national studies took precedence.

3.4 Regulatory Interactions and Approval for COVID 19 trials

Almost all respondents reported increased collaboration and expedited and rapid approvals of clinical trials by MHRA, FDA and other regulatory agencies. However, this was not unified globally, with variations in requirements/procedures, which has required a lot of flexibility. More virtual tools were used for the approval of trials.

Respondents commented on the benefits to all stakeholders of rolling review. This and the accelerated approval processes, and increased dialogue and communications with companies was much

appreciated. One respondent noted regulatory advice on how best to develop COVID-19 treatments was valuable, especially the recognition that COVID-19 specific endpoints were still evolving.

One respondent commented that they had to generate regulatory digest documents to address the large volume of information issued by competent authorities in Europe, which was not consistent.

3.5 Recruiting and Maintaining Patients in Covid-19 Trials

During the pandemic, many respondents reported challenges in recruiting and maintaining of patients in COVID-19 trials. A vaccine respondent reported the collaboration benefits of working with the vaccines task force.

Challenges in recruiting resulted from the variations in the incidence of the infection. Some suggested setting up many sites, others that they were constantly adapting trials to make it easier to recruit patients. Being able to recruit patients was inhibited both when there are fewer patients and when the infection was very common due to pressure on healthcare care facilities. The latter put extra pressure on the healthcare staff who could then not run trials. Respondents reported use of social media to recruit non-hospitalized patients, remote screening, remote consent and couriers for delivery of trial medicines for self-administration. Techniques for running studies included mobile phone apps data collection and virtual or home visits (as opposed to site visits) for check-ups. At least one respondent commented on competition from other trials. Though patients and healthy volunteers were generally willing to be involved, at certain times there was 'competition' for patients.

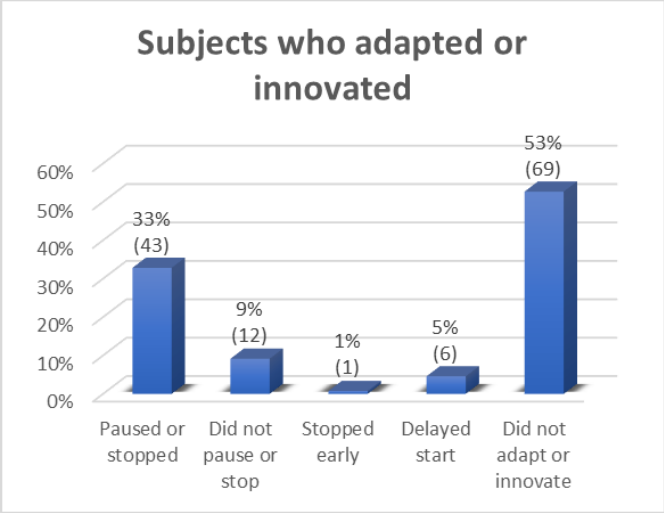
3.6 Changes in Trial Monitoring Including Patient Safety

The biggest practical adaptations made were in the use of remote monitoring for source data verification (SDV) and remote data collection, increased acceptance of flexibility of visit windows. Some reported adaption of protocols and standard operating procedures (SOPs) in order to do this. Increased use of video conferencing facilities with trial staff was also reported. However, one respondent felt a safe return to on-site visits was important and another that there should be a mix of remote and on-site monitoring. It was importantly noted, however, that some countries do not allow remote SDV and the on-site monitoring may be the solution for ultimately satisfying those regulatory authorities.

4 The impact on non-COVID-19 clinical research programmes

79% of all respondents reported that other clinical research programme activities in their organisation had been impacted by the pandemic.

4.1 Delays and adaptations



Inevitably, many respondents reported delays to trial programmes. One respondent working in a CRO noted that sponsors had shifted complete strategic focus and closed entire development programmes. Another CRO respondent reported the furlough of staff and refocusing on writing COVID risk assessments. Compounding factors were reported included delays in essential pre-clinical development and manufacturing. Lack of study feasibility visits resulted in preventing sites being set up and initiated and study start deferral was reported.

4.2 Sites and recruitment

Several respondents reported that not only were companies prioritising COVID-19 trials over non-COVID-19 trials but so too were hospitals and clinical trial infrastructure. This was reported as being a particular challenge in the UK, in which sites are not reopening. One respondent believed that the UK is losing trials to other European countries where they have started to reopen sites. Recruitment was impacted by hospital outpatient department closures, R&D trusts prioritising COVID-19 research and lack of allocation of research staff (presumably study co-ordinators). However, one respondent also noted such difficulties globally, that had slowed recruitment in USA, South Africa and Malaysia and Thailand.

4.3 Therapeutic areas

Therapeutic areas most affected that were mentioned included respiratory, dementia (not able to administer face to face questionnaires and not possible to do remotely) and oncology. Missed visits and tests, including MRI scans, were frequently reported and in one case delivery of trial supplies to patients was delayed. Lockdown, preventing mobility of volunteers and patients and quarantine restrictions on staff, resulted in an impact on all therapeutic trials and phase I studies. A couple of respondents reported patients dropping from studies as they were anxious take part (or attend hospitals). Another reported a large change in patients recruited distorting the trial population to much younger patients, dropping median age by seven years. Quality data was a concern of one of the respondents, due to delayed audits. All these factors may lead to challenges when it comes to registration dossiers for licensing and particularly on how to conduct and assess audits with so much missing data.

4.4 Practical considerations

Both hospital trials and Phase I units reported extensive use of antibody / PCR COVID-19 testing requirements for patients and staff involved in trials. Phase I units continued but have had to implement increased distancing between volunteers, thereby reducing the number of volunteers that can be treated at any one time. The need for spacing impacted the re-start or continuation of trials, as well as smaller numbers of patients who could be seen in wards and outpatient clinics.

Several respondents specifically reported increased costs in running trials. This may inhibit investment in future clinical research due to lack of funds. The increase in cost was also impacted at company and CRO level, where additional resource was focussed on rewriting procedures as a result of many regulatory guidances for both COVID, trial continuation and impact on outcome of trials.

5 What adaptations and innovations have been made for non COVID Trials

5.1 Design of Programmes

Over half the respondents to this question reported no change to the designs of their development programmes. Of the remaining respondents; one reported having to drop one of their intended indications, one stated they re-focused on trials of lower risk molecules only, not those for autoimmune diseases or immunomodulation drugs; several (5) reported switching programmes to use remote monitoring and virtual meetings; and three switched ongoing programmes to COVID indications. Programme design as opposed to individual trials was reported to include focus on risk mitigation and contingency plans.

5.2 Regulatory interactions and Approval and setting up and of trials

Almost half the respondents who responded to this question (62) interacted with regulators for non-COVID-19 trials during the pandemic. Most did not specify which agencies. Most of those responding reported virtual interactions and of those only four reported slowed interactions, all the others reported normal speed or rapid responses. Only one reported a discussion of putting a trial on hold, and that decision was taken in conjunction with the MHRA.

5.3 Recruiting and Maintaining Patients and Trial Amendments in Open Trials

Many changes were made to protocols and 27 (64%) of the 42 respondents who completed the part of the survey that related to sites that remained open made one or more amendments. A few recorded the adaptions as deviations. Approximately half of the respondents recorded successful interactions with the agencies, ABPI or NIHR.

Adaptions to recruiting and maintaining patients in the trials

Recruiting adaptions to study management	Resulted in protocol amendments
Alternative methods for data collection	
Phone "visits"	
Home visits	Yes
Video calls	
Shifting assessments to other hospitals (imaging or identifying closer sites for visits)	
Visit schedules disrupted	Yes
Altering drug dispensing	
longer periods dispensed	Some made amendments but a couple reported as protocol deviations
less direct observation of dosing	
delivery direct to patients at home	
Managing trial participants	No
Increased patient engagement	Sites managed outside of the protocol
Managing patient anxiety	
Managing local cancer pandemic guidance	
Trials units and staff	
Spacing for patients and staff	Amendments for use of COVID 19 screening
PPE kit	
COVID 19 screening pre screening	
Protocol amendments to cover all changes	Yes
Targeting healthy volunteers on furlough increased recruitment	No

5.4 Quality Issues

Remote monitoring and SDV was reported by 32 of the respondents and two reported successful remote audits. Little detail was provided as to how the data was remotely audited, but some respondents wanted to go back on site. It was also reported that remote monitoring is not allowed in some countries and other approaches were taken, i.e. home visits, use of testing, PPE and performing the monitoring at an alternative site.

5.5 Continuation

Despite these challenges, many sponsors were able to keep non-COVID-19 trials running throughout the UK lockdown and the pandemic. Some that were initially paused have since re-started and there are plans to gradually recommence an increasing number, as understanding of the logistics required grows.

6 The impact of the pandemic on SOPs for clinical programmes and trial design

Almost half of respondents (48%) reported that the pandemic had impacted their organisation's standard operating procedures (SOPs) for clinical programmes and trial design and brought about variations to their Good Clinical Practice.

A significant portion of those responding survey were already considering permanent changes to SOPs. We asked them to group their response to different categories.

6.1 Development programming and funding

General standard operating procedures (SOPs) have been written for issues such as global health security planning and re-prioritisation of programmes at global level. These SOPs extended to PPE, general hygiene and screening. Some respondents noted that the pandemic had impacted costs and the ability to raise money, sometimes easier and sometimes more difficult. The extension and adaptation of trials could also mean the companies might run out of money to complete the trials.

6.2 Protocol writing, novel trial design and standard phrases developed

Two respondents reported that they have now added COVID-19 wording to their protocol template. This included screening and restriction of entry to trials of vulnerable patients into the protocols and writing altered adverse event and serious adverse event (AE/SAE) collection language. Some are setting up procedures going forward for digital protocols and routine digital consent.

It was also noted in this section that new protocols need to be managed to protect against the number of protocol deviations. This was suggested to include flexibility of visit windows, remote visits, ensuring only essential data is captured, remote data collections from mobile devices and possibility to deliver trial supplies directly to patients.

One respondent raised the issue of robustness of innovative trial design for decision making, such as sensitivity in the adaptive designs.

In writing protocols, the impact on understanding disease epidemiology was also reported to be important, as the consequences on trial populations in non-COVID-19 trials where the number of elderly and frail as a percentage of patients dropped markedly. Thus, future protocols will consider this.

6.3 Impact on primary endpoints, estimands and Statistical Analysis Plans

Protocol deviations, especially non-collection of endpoint data (especially primary), were considered for changes to procedures, such that this would be protected and managed. Estimands are the definitions of how endpoint variables are handled, a critical new requirement by ICH at the beginning of the study. They are required to be provided for early statistical analysis plans (SAPs). In a situation where there are many adaptions to the protocols during the study, the SAPs will also need adjustments. How to handle

missing data was reported by several respondents and one said their organisation was defining business critical data for monitoring, to prioritise on which variables to focus on. It was noted that some have implemented procedures for recording detailed reasons for missing data, such that they can understanding the impact in the analysis and explain this. The potential impact on estimands of all the changes in the pandemic was noted by one respondent, whose organisation implemented a continuing ongoing statistical review in future trials. Primary endpoints in a new disease like COVID-19 have been really challenging to agree across different agencies, in spite of some guidance being made available.

6.4 Choice of countries in which to run clinical trials

The majority of respondents to this question altered choice of country for trial sites during the pandemic. Only three of the 21 respondents who answered the question reported that they had not altered the countries in which they ran their trials due to the pandemic.

6.5 Trial operational procedures, set up, monitoring, safety, close out etc

There was detailed guidance from the regulatory agencies at the beginning of pandemic and three respondents clearly stated procedures were changed accordingly. Of all the 28 respondents who completed this section, all reported changes to procedures. COVID-19 precautions and risk mitigation were built into procedures, as they were into protocols.

Many respondents reported looking at how they could do full remote monitoring. None reported the detail of how this might be done although one reported more centralised monitoring, another planning to use remote site tours and another developed a process around remote monitoring assessment.

In one case SOP deviations were made to allow remote sponsor oversight, monitoring and SDV/SDR. One respondent reported a strong shift to risk-based monitoring (many pharmaceutical companies have espoused this for some years). Another was involved in writing procedures for remote audits and another reported conducting remote audits. Procedures for outpatient trials have been challenging to adapt. Solutions included; use of video conferencing, courier delivery, digital assessments; and inclusion and engagement of carers in study visits as well as patients.

6.6 Practical issues during pandemics

Practical issues and adaptations that were highlighted, including: one respondent reporting a shift from patients to using healthy volunteers. With healthy volunteers there was more constant contact with volunteers when not in the clinic with the option to admit earlier and stay longer leading to additional cost, however. Additional costs to keep one oncology study ongoing were reported where they were paying for patients' safe transportation and housing of relatives. If patients need accommodating overnight, cancer centres prefer to keep them at the centre rather than having them in a hotel to reduce COVID-19 risk. There was reported by another respondent reduced capacity in-house due to bed spacing so adaptations had to be put in place to permit 'outpatient' procedures (with patients shielding at home [with compensation included], private travel).

7 External examples of successful adjustments to clinical research & development

This section was for comments from the respondents on activities they had learnt about and had appreciated, but were not involved in.

7.1 Collaboration

Most of the research and development community were thought to be more collaborative, which was strongly welcomed. Some respondents were frustrated by a lack of overall unified and global leadership, that transcends country politics. Something that the pharmaceutical industry is used to through ICH. EFPIA support of increased collaboration across pharma/ academic/ regulators/ government bodies e.g. AZ/GSK/University of Cambridge lighthouse lab was thought to have been valuable.

7.2 Impact of new levels of use of communication and other technology

The impact of internal ability to have many more meetings working from home expanded speed and geographic extension of working. One respondent stated that working relationships were even tighter than in the past with project team colleagues, some of which based in California and in Japan. The international collaborative working effort one the team led them to submit a novel treatment ahead of schedule to EMA.

7.3 Communication and open access of emerging data to allow adaption of studies

On line guidelines were mentioned (Standard of Care, Regulatory), Webinar sessions from academia, colleges, pharma, CROs and trade associations facilitating problem solving and adapting protocols development. It was also reported that the Faculty of Pharmaceutical Medicine has “done a fantastic job in keeping us informed”. The British Pharmacological Society webinar on investigating the pharmacology of drugs in a pandemic was considered valuable before the next pandemic for understanding re-purposing of drugs. The regular publication of data both UK patient data and nationally co-ordinated international data such as OPENSafely study of risk factors, ICNARC audit reports and of course ISARIC, strongly facilitated the underpinning of research programmes internationally. Generally, regulators were more flexible and shared information about guidelines and practice and gave support to each other.

7.4 Innovative programmes and study designs

The RECOVERY and AGILE platforms and Synairgen studies were mentioned and the resulting data from RECOVERY on dexamethasone. A comment on the ability to utilising minimal data and trial participation from many hospital sites. It was noted that COVID-19 development programs, aided by regulatory flexibility, learned to run at record speed, without compromising safety.

COVID-free hospitals for oncology patients to maintain treatment trialled in the Netherlands were mentioned, where oncology trials were switched there and allowed to continue. Several oncology trials in the USA adapted well to running trials remotely, and patients responded well to this. It avoids some of the long distances patients have to travel to be in trials. It was noted by one respondent that other EU

countries have been much faster than the UK to get back up to full recruitment and studies being fully open and stated that UK needs to learn from this and ensure this is a key aspect in subsequent waves.

7.5 Regulatory agency activities in the pandemic

Accelerated regulatory review and approval processes, new access to MHRA advice, as well as emergency authorisations, were all welcomed. This also included accelerated paediatric investigation plan (PIP) assessments. Some welcomed the centrally co-ordinated approach on trial prioritisation in countries in Europe but in other sections of the survey some felt this slowed down initiation of high-quality research, driving companies to conduct research in other countries. The simplification of protocols allowed by global regulators allowed more remote oversight and standardised company letters could help for those involved and then flexibility in managing investigator requests.

The pandemic has also highlighted the need to ensure that SOPs are designed to include the most appropriate and appropriately diverse group of trial participants. The frail and elderly and BAME communities have been even more under-represented than previously. The inclusion / exclusion criteria for trials may need to be re-examined, to ensure they are fit for purpose.

8 Building resilience for the future

> Most respondents (78%) stated that at least some of the changes to clinical programme design and operational practice brought about by the pandemic could be integrated into best practice moving forward and help to build resilience against potential further global pandemics and health challenges.

8.1 R&D strategy

It was suggested that the pharmaceutical and biotech industries need stronger strategic senior engagement with CEOs and Medical Directors of hospitals, not just the local Principal Investigator and R&D department (who the members of FPM normally interact with), to build advocacy for the importance of commercial research. To emphasise the importance of clinical research at this time of the UK leaving the EU is important to all stakeholders. A thriving industry in the UK brings benefit to all.

One respondent thought that more clinical trial sites for non-COVID-19 trials need to have comprehensive business continuity plans and service level agreements, in the eventuality of another pandemic or other disasters.

It was suggested that more UK involvement in trials would benefit more Site Management Organisation (SMO) sites. This could be in the form of one hospital or GP practice, with a PI acting as a hub and distributing trial activities to other hospitals or GP practices, which could act as buffer when hospitals and GPs are overloaded. In this regard the NIHR as the overall broker could facilitate when using its staff in the Clinical Research Networks.

In the pandemic most trials were, from a national perspective, overseen by the NIHR and it was felt that it could have been valuable to have more decentralised trials. A second suggestion was that increased devolved trial models should make these more resilient to future pandemics or other disruption.

One respondent said that the NHS needs to be much better equipped and protected with PPE and frequent testing. COVID-19 (or any other contagious disease) free areas in hospitals need to be established to give subjects the confidence to come for appointments and forms of safe transport to appointments need to be created. This would mean existing non-COVID-19 trials would have a better chance of trials of continuing.

It was noted that the global pandemic preparedness deviated substantially from our historical ‘best practice’. It is becoming apparent that virology drug development has not been prioritised to an appropriate extent in the decade since last flu pandemic. This is a global issue and very few general antivirals, such as SNG001, have been brought into development. Support for general antivirals in drug development, rather than only vaccines, is required moving forward.

There is a perception that smaller companies with innovative products may have been overlooked by NIHR and other government funds, and that support was given to larger and often less innovative companies. It is easy to understand due the need for outside funding by the bigger companies, but could limit innovation at a time when many of the aspects of the disease had never been seen before and so

presenting major scientific challenges. Other funding risks induced by COVID-19 include a diversion of funding from major charitable and academic funding bodies, which will have an impact on non-COVID-19 programmes.

Clear guidance and improved communications from the NHS and NIHR on a strategy for the restart of clinical trials and on which types of trials should be prioritized was requested. The non-COVID-19 trials that have been heavily impacted were not prioritized. One respondent suggested to ensure better remote eMR access across all NHS trusts should be a standard. Consideration of flexibility around standard of care procedures/tests to be performed by local GPs/hospitals where possible were thought to be something that might be helpful both in and outside clinical trials.

There was a request to engage with key external stakeholders (mainly governmental) to ensure that political leaders are educated appropriately in statistics and data interpretation and more importantly that the UK plans properly for future pandemics and has appropriate infrastructure, systems and processes in pace to deal with any situation that may arise.

Improving collaboration with government agencies worldwide on international healthcare initiatives would be helpful especially for big multicentre studies, whilst also helping in the integration of data, digital, diagnostic and pharmaceutical companies. The aim would be to achieve more global collaborations, with harmonized and joined effort in future clinical programmes.

8.2 Programme and Trial design and Protocols

Several respondents commented on the need for more flexibility in all the company sponsored protocols that can be maintained during a crisis. The practicalities of this flexibility should be considered carefully in an early Statistical Analysis Plan. It might also drive the ability to make amendments effectively without damaging the robustness of the evaluation

There was a suggestion that standards may have dropped and there should be no pandemic research exceptions for robustness of clinical research. This might include setting standards and encouraging mandatory minimal clinical and biomarkers data sets for obligatory databasing and analysis. It was implied it was needed for both non-trial databasing as well as trial databases.

The practical implementation of remote monitoring was reported to very difficult in the EU. Ways to have this done more easily would really help. More ability to use remote technology for patients and for monitoring. The building in of COVID-19-type precautions into future protocols should become standard practice. It was commented that regulatory validation of apps would be of value and help with the validation of remote tools, especially the preservation of confidentiality and consent. Clinical research in general should move away from on-site monitoring of patient trial records and acceptable alternatives should be considered.

One message should focus on resilience for all those who work in drug clinical development programs, particularly in the infectious disease area, where antibiotic resistance and largescale infections will likely occur again at any time. Start a new way of thinking based in actual vaccine development requirements and ensuring all studies are appropriately powered with valid end points.

Several respondents suggested there should be examples of contingency plans for people to refer to and hopefully implement as they set up and run clinical trials. This would be better than individuals having to come up with fresh plans in isolation. It would then mean that waves of COVID-19 or other pandemics have as little effect on clinical research as possible. It was overall suggested that we need to build events like the current pandemic into our risk planning and generally improve our use of tools that can easily be adapted for remote use.

8.3 Drug safety

Important points were made about drug safety and pharmacovigilance (PV). In drug safety it was pointed out that COVID pandemics likely changed adverse events reporting patterns (less reporting, distribution of types of reports changed). This may have a substantial effect in practices such as data mining for signal detection. There is potential that some risk mitigation activities may have undergone changes, as some may be difficult to implement or keep at this time. These changes of risk mitigation actions may, in turn, also change the incidence of adverse events linked to the risks these actions target. The overall impact is now difficult to predict, but it is still something to keep in mind when conducting routine and additional PV activities in the future, post-pandemic.

8.4 How FPM can help?

Respondents generally saw FPM's role as an important educator, provider of key information, and a leader in supporting national and international policy initiatives for ever improving standards of research. It also offered a forum for sharing experience via discussions and symposia. It was suggested that FPM could follow on from this survey with the issue of a 'best practice' guidance document with an accompanying educational programme.

FPM should continue to provide expert advice and analysis on all aspects of the pandemic related to drug and vaccine research and development in their communications. In addition, it was suggested that FPM could organise more educational and eventually training sessions on 'learnings from COVID-19 pandemic', or similar.

FPM could also pursue consideration of strong support for development of guidance for wider use of E-consent, remote and virtual site visits, and remote monitoring of study data. This might also be useful to organise presentations from developers of software who provide remote assessments support.

Significant early warning scanning by FPM could potentially also warn clinical developers in advance about anything that could have a significant impact on clinical trials in the future. It was suggested that there needs to be an increased number of clinicians capable to undertake and plan first into human (FIH)/patient studies – the FPM FIH training programme should be expanded and promoted. Well-being and mental support during and after COVID for FPM members was considered important, particularly for the trainees.

8.5 Employers comment

This comment was from one employer will resonate with both private and public sector employers and managers. "We found our staff very resilient and inventive, and eager to overcome what seemed on the

face of things to be an almost impossible working situation. Some of the changes we have made are really helpful in or outside a pandemic". It reminds us of the importance of awareness of staff safety requirements, as well as improved knowledge of the impact of future global health challenges.

9 Summary

We are very grateful to those who gave their time to complete the survey. The data and information gathered will help FPM and external stakeholders learn and develop and innovate in their plans and procedures. We hope that if/when a similar pandemic transpires the global community will be even better placed to combat that threat.

Risk planning for pandemics needs to be reviewed and updated for all activities related to clinical trials and pharmaceutical medicine. Much of what has come out of the pandemic will improve research and collaboration. Regulators and sponsors need to discuss future flexibility around all research procedures. Adoption of tools that can easily be adapted for remote use e.g. e-consent and remote monitoring / approval of apps to support trials should be encouraged, validated and enabled.

In order to embed resilience into the healthcare system, it is recommended that post-COVID-19, there must be more of a focus of attention and funding on infection, including targeted and non-targeted virologics, vaccines, antibiotics and antifungals. Also, a reminder that infection is the commonest respiratory disease and killer. This will allow us to be better prepared for the inevitable emergence of resistant pathogens whether they be virus, bacteria or fungi. Future pandemics will happen, but we must not ignore the regular significant mortality of seasonal disease patterns.

Small companies with innovative products and ideas should not be overlooked and should be engaged and incentivised to participate in collaborations and joint programmes.

A lack of relevant pharmaceutical medicine & medicines development expertise in decision-making positions within key stakeholders should be considered and this could help inform a re-prioritisation of clinical trial programmes at a global level, both within individual organisations and in collaboration. This would support a consolidated shift to global health security programming.

10 Recommendations

Throughout this report we have attempted to summarise and analyse the data we obtained, and here we make recommendations for four overarching groups:

1. **National organisations responsible for clinical research coordination and infrastructure**

- Centralised public sector bodies are encouraged to embrace all skill sets across professional groups related to vaccine and drug development, including those from industry
- Stronger links should be developed between industry, NIHR, Government, regulators and the medical directors of hospitals to ensure all trials are pandemic resilient
- There should be a research focus and associated funding on developing technology and safe standards for the remote conduct, monitoring and audit of clinical trials
- During a pandemic, regulators and national agencies should prioritise trial applications on a case-by-case basis, based on the broad public health benefit, transparency is key in this process
- During a pandemic, where appropriate, all stakeholders should develop communications to patients to inform, education and help to reduce anxiety regarding participation in new and ongoing trials
- A centralised system for the prioritisation of trials and the allocation of patients should be considered
- A national strategy for re-start of clinical trials should be developed.
- Consideration should be given to site management organisation through NIHR, to allow shifting of site visits or such things as taking biopsies, where the overload in one hospital exceeds another

2. **Regulatory agencies**

- Regulatory agencies around the world should share best practice and learnings from the COVID-19 pandemic
- Regulatory agencies should continue to implement rolling review and new methods of early access
- Rapid approval and both managing multiple trial amendments should be incorporated into a pandemic plan
- Guidance should be considered for the evaluation of evidence from the multiple adaptions to clinical trials, such as missing data, gaps and adherence to medication, distortion of patient populations, alterations to adverse events reported etc
- Global guidance should be developed for unified approaches to remote SDV and audits
- Virtual interactions should be maintained

3. Pharmaceutical companies, academic centres, medical research charities and clinical trial investigators

- All trial sponsors should take stock and examine how best to incorporate events like the current pandemic into risk planning, not only to protect research but also the patient and volunteer participants
- Regular updating of risk management strategies would help resilience in the future
- Consideration of regular statistical review of trials to account for changes in conduct, endpoints, patients populations and such issues as missing data
- Sponsors should re-examine all existing relevant SOPs and incorporate the many aspects of changes that occur in a pandemic
- Sponsors should incorporate routine changes to protocol writing to allow for pandemic type events, which might include digital protocols, remote set up, monitoring, reporting and quality management, and encourage more flexible interactions with trial participants
- Where appropriate, sponsors and investigators should share best practice in the amendments and contingency plans they made to trial protocols and SOPs
- Improvement and efficiency of clinical trials has been seen and should be continued, such as innovation of virtual trials, more digital technology, more interactions with the public through social media
- Further efficiencies already stimulated in ICH, such as minimising collection of data and focusing on estimand variables, should be considered
- Consideration should be given to the amount of distortion there may be to health economic endpoints
- Protocols should be written to include the most appropriate patient population possible, inclusive of all communities and age-groups

4. Education and training bodies and patient organisations

- FPM should drive understanding, guidance and research and education in best practice for the issues such as e-consent, remote conduct of trials, remote monitoring and audits.
- FPM should enhance the well-being and mental health support it offers its members
- The sector should work together to increase training of clinicians to perform first into human trials
- Patient organisations, including the Patient Information Forum and the NIHR Centre for Engagement & Dissemination, should consider how to support patients in trials with information and advice during future pandemics