Commercial Clinical Operations Group (cCOG)

Date: Tuesday 5th June 2019
Time: 10:30 – 16:15
Location: Novo Nordisk Ltd, 3 City Place Beehive Ring Road Gatwick, RH6 0PA
Chair: Jose Vicente-Garcia (GSK)
Minutes: Charlotte McIntosh (MSD)

Guests:

Lorraine Fincham	Commercial Research Initiative Manager, NIHR
Lydia Vitolo	Industry Manager, Health & Care Research Wales
Alastair Nicholson	Policy Development Lead – HRA Assessment and Approval, HRA

AGENDA

Time	Item	Topic details	Owner
10:30	Welcome	Agenda overview Introductions	Jose V-G/All
10:40	Health & Care Research Wales	• Update from Health & Care Research Wales	Lydia Vitolo Matthew Harris
11:10	HRA Updates	• Update from HRA	Alastair Nicholson
12.45	**Lunch break**		
13:30	NIHR	• NIHR News	Lorraine Fincham
14:20	Other member groups update	• R&D forum • Road Map • CREN • Costing Group	Member group representatives
14:45	Points for Discussion/Hot Topics	Proposed discussion topics: • Radiation Assurance to become a part of HRA and HCRW Approval – current status and how this will work going forward? Expected to take 40 calendar days. – Darron Green- • Management requests for a patient stipend and if there is a feel for what is a reasonable amount to pay (enough without being an inducement) - Liz Sheasby- • R&Ds and unexpected requests – Claire Jones- • transition to the NIHR Costings Tool, particularly how NHS sites are preparing for this – Pauline Pert- • eRT failing to sign the latest MIA – Jose VG- • Proportionate review of monitoring visit reports, risk-based approach to visit report review. Has anyone implemented this approach with positive results – Jose VG-	All
16:00	AOB	**AOB**	All

		• Confirm chairs (ICON/) • Confirm minute takers (Pfizer)	
16:15	**Meeting close**		

Meeting Minutes

Introductions:

Action: Update members list for Janssen and Servier.

HRA Updates (Alastair Nicholson)

1. UK organisation information document implemented today, 5June2019:

- Applicable for England, Wales, Scotland and N. Ireland
- Replaces SSI form and statement of activities (non-commercial studies)
- Sponsors asked to use standard template e-mail with the organisation information document, otherwise local information pack won't be considered valid,
    - Lists documents, providing clarity on what needs to be sent to R&D's
    - Defines to whom to send the UK local information pack
- IRAS updated to remove SSI & addition of guidance to changes
    - Sponsor shares local UK info pack with Scotland/N. Ireland sites once REC application validated
    - Sponsor shares local UK info pack with England/Welsh sites on receipt of Initial Assessment Letter
    - England/Wales/N. Ireland will be confirming ccc – signing contract to confirm study can commence
    - Scotland will continue to issue a separate letter/ confirmation stating study can start
- Support for new process can be found:
    - Contacting Alastair directly
    - IRAS Help
- Feedback on new process can be via IRAS, link on guidance document or via organisation information document itself
- Organisation information form is partially completed and submitted to REC. The partially complete form is used to localised the document for each participating organisation
- Unable to build organisation information form into IRAS so currently is a paper document, however allows the flexibility to modify as needed
- Intended to standardise behaviour across sites, ensuring R&D facilitates conversations between sponsor/site support departments/clinical team to set up study

Q: Are RECs aware of new process?

A: Not a REC process, but a process describing how sponsors provide documents to sites.

Q: Is the organisation information document applicable for private institutions providing specific services to the site?

A: No, if it is acting as a service provider where a service level agreement would be in place. Always check on the set up of the study at the individual organisation.

Q: Please confirm that if new sites are added to an existing study, an outline version of the organisation information document is required?

A: Yes, to be submitted as part of the substantial amendment to REC to add a new site.

Q: Is the HRA monitoring implementation of the new process and what metrics are being used?

A: HRA will monitor how the approach works across devolved nations. HRA requested Sponsors feedback if any issues/delays/not working.

Q: What is the value of the IAR?

A: No data yet, intended to identify errors with the application early and correct, but also to act as a trigger for sites to start looking at budgets/contracts. HRA looking at this at the moment as this is a major sticking point across devolved nations. Assessment of current process with a view to improve and incorporate into new IRAS model.

2. Non-NHS SSI form:

- Non-NHS SSI form replaced with NHS/HSC assessment form + CV + site insurance certificate for CTIMP/medical device studies (except Phase I trials where sites have MHRA accreditation)

- Handled by RECs to confirm Investigator suitability

3. CWOW

- Continuing pilot. ~50 studies progressed through pilot
- Timelines: mean 51 days (pilot) vs mean 81 days current process
- Phase I timelines: mean 32 days (pilot) vs mean 37 days current process
- Continuing to increase number of studies through pilot although not default process yet. Need to approach HRA if want to include a study through the pilot.
- Helping to align MHRA & REC responses

Q: Comment from BMS - REC did not receive IRAS application.

A: RECs do not receive IRAS form anymore and should not be asking for it.

4. Amendments

- On 1Apr19, Service Improvement Program ended. Subsequently HRA implemented a new staffing structure in HRA operations division. There is an integrated workforce between REC & assessment staff at HRA. However, experiencing teething problems, as new staff unfamiliar with process and this is impacting amendments approvals.
- Resolution: Senior HRA staff will support approvals of the backlog of amendments.

Q: Is this affecting initial submissions as several sponsors have noticed delays in receiving IAL?

A: HRA will review metrics as not aware initial submissions are being impacted and will need to action. Requested to escalate to HRA for new studies.

Q: Sponsors unaware of these issues, how are these types of issues usually communicated?

A: Via cCOG/CREN, HRA newsletter

5. mCTA

- Noted that many sponsors are making change to mCTA to try and comply with GDPR. Formal advices is not to do this, but if your DPO is demanding this then keep Alastair involved so it can be determined whether the new draft mCTA language can be used rather than bespoke language.

Q: When will the updated mCTA (with GDPR language) become available?

A: Hoping to finalise draft this week. Challenges with data transfer language. If unable to resolve, will release the update mCTA with a blank appendix regarding data transfer for Sponsors to complete.

Q: Sponsors concern is there is still no GDPR language in our contracts?

A: HRA confirmed no further recommendations. Advice will be issued regarding bringing old contracts up to date. ICO are aware and aware of HRA guidance to sponsors and remain content with it. GDPR implementation is work in progress and healthcare sector are well managed in this area already. Also sites have been obligated to sign the current mCTA only.

6. MIA

- No further update. Still waiting to hear back from DHSC to see if the impasse can be resolved and something can be put in place.
- HRA aware of implications of the current situation and asking Sponsors to escalate issues/particular sites to HRA for support.

7. Informed Consent Forms (ICF)

Q: Do sponsors seek approval from patient groups (Patient & Public Involvement - PPI) to review ICFs?

A: Some sponsors use PPI, some use lay people to review study specific ICFs or ICF templates. Becoming more and more of a requirement by the RECs to see this review in our applications. HRA have a PPI program and NIHR working with PPI support groups (upcoming conference on 13June2019). Many PPI groups want input into the protocol rather than the ICF and some global teams are reaching out to these groups during the protocol design stage.

<u>HCRW Updates (Lydia Vitolo)</u>

1. Expression of Interest

- Quality and appropriateness are now the focus. Now linking with speciality teams (30 across therapeutic areas). Firstly, sent to Key Opinion Leader of speciality team, then forwarded to appropriate clinical network for distribution. Initial review takes 48 hours, then consultants have 10 days to complete. Currently working well, but very quiet on feasibility stakes.

2. One cost/One Contract

- One review of the cost/contract by lead site/centre of excellence on behalf of all Welsh sites. Sense check will be performed by all sites to ensure pass though costs are appropriate. Has resulted in faster set up times, especially where rescue sites in Wales are added at a later date.
- Currently reviewing every study in Wales to complete a sense check to determine if additional sites in Wales can be added to the study.

3. One Line Costing Template

- Aligning with England on one line interactive costing tool (iCT).
- Expect to have in place by the end of 2019.

4. General Comments

- Commercial studies automatically eligible to receive funding in Wales
- Not seeing efforts translating into studies coming to Wales. Need to understand why, hence need sponsor feedback. Concerns over investigator fatigue at completing expressions of interest and not being awarded studies. Milestone schedule has been updated to allow feedback for both Welsh and English sites.

Costing Group Feedback

- Disbanded, to be reformed as an NHS England let group with some new and some existing members. Need to establish role / governance of group.
- NHS sites given insight into tool at R&D Forum – all Trust aware, but formal training will be via online training.
- Phil Good and Industry Operations Managers at LCRN's can be used to support you with costs and sites.

Q: Is the iCT mandatory?

A: Not mandatory yet. Sponsors can use iCT or current excel spreadsheet, both are acceptable. Sponsors are encouraged to become familiar with the iCT as it is likely to become mandatory by end of this year. There is no separate primary care costing template.

Q: Should all sites be using the iCT as Sponsors aware there are some Trusts that will not use the iCT.

A: Yes – no exceptions. Any issues should be escalated to Phil Good.

Q: Can Sponsors have guidance on what sites can push back on with a rationale?

A: Sites may have differences with centralised assessments and need to provide a reason. Beauty of the iCT is that a reason can be included in the tool so it is visible and transparent. Phil Good has spent time discussing tool with Trusts to get buy in and feedback to try and achieve uniformity.

Q: Can sites see each other's costs when iCT is localised?

A: To be clarified.

NIHR News (Lorraine Fincham)

See slides. Key messages:

- Joining up across nations for feasibility & performance monitoring using speciality groups including KOLs for all 30 therapeutic areas.
- New interactive route map to understand support NIHR CRN offer
- Advised to take advantage of Early Contact & Engagement service (currently under utilised) to provide early input into protocol/validation
- New! – start up call offered between local Industry Operations manager and sponsor. Help to identify any issues nationally with studies
- Updated study milestone spreadsheet – ability to leave feedback on why sites not selected
- Performance monitoring calls available with designated perform lead for study. New studies will be allocated a Performance lead once study added to the portfolio to provide support as required by the sponsor.
- Pilot underway to establish timeline differences between LCRN vs R&D validating costing template. Sponsors may be asked to agree to participate.
- Collection of research activity data, e.g recruitment is changing to link Local Portfolio Management System (LPMS) with CPMS. System up and running and sponsors/investigators/CROs will be asked to validate date in Jun/Jul 19 and on a monthly basis. All sponsor study contacts should have received an e-mail notification of the change of process.
- UK Clinical Trials Gateway revamped – data pulled from clinicaltrials.gov. Patients can become more aware of clinical trials
- Patient Engagement service to support industry to include PPI in their research.
- Metrics/stats discussed and the need to understand the data behind the metrics, especially start up timelines. Sponsor expressed concern on challenges with setting up NHS organisations,

which do not seem to be improving. Questions raised on how we can continue to attract clinical research to the UK with our poor start up timelines and sub-optimum recruitment. Requested NIHR to escalate to NHS England with a view understanding challenges associated with NHS sites and look to support clinical research infrastructure at sites.

Radiation (and Pharmacy) Assurance (Sarah Grimshaw)

Key points Radiation Assurance:

- Radiation Assurance available for ~1 year for certain therapeutic areas. Approximately 60 studies have been through the review.
- Currently not mandatory
- Timelines 40 calendar days for review; averaging 27 days.
- No expedited review available.
- "Tips for successful application" on HRA website provides guidance for applications and necessary sections from IRAS form that need completing prior to the review. Will help to speed up the review if application correct.
- Designed to standardise review making it more consistent across CREs/MPEs, RECs, ARSAC
- HRA website lists CRSs/MPEs registered for Radiation Assurance
- Legislation requires each site to review, check and sign off exposure
- £500/reviewer (initial submission); £250/reviewer (substantial amendment)

Key points Pharmacy Assurance:

- Pharmacy assurance in place since Nov 2018 and running well. Designed to decrease site start up times by having a central pharmacy review the study documentation. Sites should be accepting of the pharmacy assurance and not raise further questions.
- Differences across devolved nations, depending on lead nation however output is the same.
- Timelines 30 calendar days for review; averaging 16 days.
- Should start as early as possible at the time of Sponsors receive global documents. Should submit before or at the time of the REC submission. Pharmacy assurance should be in place before IAL sent out so can be included in the UK local information pack.
- Information on what needs to be submitted and how is available on IRAS help
- Cost £500/reviewer.

Q: Will template consents be adequate for Radiology Assurance review?

A: Yes, provided it contains language associated with radiation risk.

Q: is the total exposure for all possible scans required even though it is unlikely that any patient would receive that amount of radiation?

A: New definition provided for radiation exposure (see guidance on IRAS). IRAS wants maximum exposure, REC want's maximum risk, but needs to be explained in the comments section of the application.

Q: What are the confidentiality disclosure arrangements (CDA) with the reviewers?

A: No signed document, however HRA have a statement from each CRE/MPE covering CDA. Is that sufficient for sponsors?

Q: How are payments made to the reviewers?

A: Sponsors have to make their own arrangement with the CRE/MPE's Trusts. Challenging as Sponsors need contract + due diligence checks performed in advance of the work being completed. Unable to pay HRA instead. Would like payments to form part of mCTA, but CRE/MPE not always from a research site involved with the study and invoices raised prior to executing contract. Same challenges associated with pharmacy assurance. HRA will looking into possibility of a Service Level Agreement (SLA) to cover both HRA technical assurances.

Q: Do sponsors still pay the full pharmacy set up fee for each site if the study undergoes pharmacy assurance?

A: No, because sites have to do additional work locally to set up the study for their organisation. HRA will review this.

Q: Can sponsors specify which site/pharmacist completes pharmacy assurance?

A: Yes, the list of registered reviewers is available on the HRA website.

Q: When will it be mandatory?

A: Not known at present and unlikely to happen in 2019, but the intention is to make it mandatory.

Points for Discussion/Hot Topics

1. Investigators bombarded to requests to sign off on different platforms, e.g. Transcelerate Confirmed this is ongoing with most sponsors (especially SIP). Would help to have a joined up effort across sponsors.
2. Discussed use of therapeutic are networks approaching investigators and bypassing NIHR for feasibility. Challenges with getting good feasibility from this approach.
3. Patient stipend, how do sponsors determine a stipend and manage it?
   Usually termed "inconvenience" payment/fee and is calculated based on the procedures in the study that sponsor is expecting patients to complete. May also include child-care costs if appropriate. The general consensus was if sponsors can justify the cost in the REC application and it is REC approved, then this is acceptable. Some sponsors calculate based on average wage or minimum wage. It cannot be seen as an inducement to take part in the study. EMC annual meeting received feedback from patients who felt an inconvenience payment should be included.
4. R&D issues discussed including: R&D approving studies then sponsor receives an unexpected request and the study can no longer proceed, R&D reducing recruitment commitment, R&Ds/clinical team not receiving funding from clinical trial budget to support staff/resource. NIHR suggests contacting Industry Operations Manager and/or business team for support. NIHR limited and suggested Sponsors do not keep returning to the same sites which do not deliver. Challenges as there is a limited number of sites with the specific patient populations. To follow up with R&D Forum and NIHR will follow up with Department of Health.
5. Risk based monitoring raised, but limited experience in the room.
6. Sites with ongoing studies working to old contracts have started to request a review of the staff costs as payment is not covering the annual increase in pay. Not many sponsors re-visit this on a 2-yearly basis.
7. Discussed if any sponsors completing an assessment of archiving facilities. No, however as per HRA guidance we are owners of the data, so we should be checking.

Location next Meeting:

AZ offices, Luton.

Actions:

- Sponsors to internally share information/guidance on the organisation information documents
- HRA to provide feedback on implementation of UK local information pack at next cCOG meeting
- Sponsors to feedback on CWOW experience
- Sponsors to let HRA know if there are any urgent amendments pending approval which can be prioritised from the backlog
- Sponsors to escalate to HRA regarding particular MIA issues/challenges with specific sites.
- HRA to check REC stance on provision of translated documents/certificates for information and approval of end of study information sheet.
- Sponsors to provide feedback for English/Welsh HCP who complete expression of interest as to why their site was not selected – can use updated study milestone schedule
- NIHR to clarify if sites can see other site's localised iCT.
- NIHR to confirm how the UK Clinical Trials Gateway is maintained and frequency of updates
- NIHR to escalate to NHS England challenges Sponsors facing in working with NHS organisations to set up clinical trials.
- Sponsors to confirm whether the confidentiality statement collected by HRA from CRE/MPEs is adequate for Sponsors.
- HRA to discuss possibility of SLA for HRA technical assurance.
- HRA to review pharmacy set up costs in light of payment for pharmacy assurance.
- R&D Forum representations to raise R&D issues at the next R&D forum.