Investigator Initiated Research (IIRs) within the NIHR CRN Cancer portfolio

Considerations to guide reasonable access to and sharing of trial data with pharmaceutical company partners

Background & Introduction

Collaboration between the academic clinical research community and pharmaceutical company partners is a key aspect of UK clinical cancer research. Many successful UK cancer trials have been developed as Investigator Initiated Research (IIRs) trials utilising a model of sponsorship by a non-commercial organisation (usually university or NHS Trust), management of the trial within a UKCRC registered CTU (often also a designated NCRI Cancer CTU), with provision of drug and a component of research funding obtained from a partner pharmaceutical company, all working with a designated clinical Chief Investigator to develop and deliver ambitious, high quality trials. Many of these trials are peer reviewed by independent scientific committees usually convened by the funding body; for example the Cancer Research UK Clinical Expert Review Panel and Clinical Research Committee (previously Clinical Trials Awards and Advisory Committee), providing supplementary funding or endorsement in the case where no additional funding was required. Such trials can be adopted onto the NIHR Portfolio as non-commercial trials with many run under the model approved for AMRC charity funded trials.

The scientific questions being addressed in these trials are by necessity complementary to the trials undertaken by the pharmaceutical company manufacturers to directly secure the marketing authorisation of novel therapeutics. Many such trials have been conducted under the auspices of the original NCRN Alliance programme and derivatives thereof. In this instance access was offered to researchers to test pipeline drugs in disease areas outside of the company's main clinical development pathway, however changes in clinical development priorities during a trial's life cycle may mean that a trial's results are of more commercial interest to the partner pharmaceutical company than was originally envisaged at the outset of the trial.

The contemporary transparency and data sharing agenda will encourage sharing of anonymised trial data once a trial has been completed enabling a greater degree of evidence synthesis and also of exploratory hypothesis generating subgroup analyses. Within a framework of data sharing for research purposes issues may also arise as to how and when data is shared where the request is for commercial use of the data given the non-commercial conduct of the trial.

In the UK non-commercial trials have two distinct differences from trials conducted from the outset for commercial purposes: i) they are conducted within the AcoRD framework without full cost recovery for the NHS, utilise the research funding infrastructure within the sponsor institution (and CTU) and in many cases receive direct project grant funding from an NIHR partner or AMRC charity; ii) trials are usually conducted to (and inspected against) the principles of GCP as set out in UK legislation, not to the specifics of ICH GCP as required by trials intended to be conducted for marketing, commercial or registration purposes. As non-commercial trials, the Intellectual Property (IP) associated with the trial (but not the drug) and custodianship of the data will lie with the sponsor entity and not the pharmaceutical manufacturer.

The increased interest in the data from such trials has led to the desire of the NCRI CTU Group in partnership with the NCRI CSG Chairs to compile guidance on data access requests from commercial partners, to outline what may be considered reasonable for such trials with the aim of bringing a degree of consistency and avoiding the need to re-discuss each of these issues on a trial by trial basis. Such guidance will still need to be implemented within the context of the legally defined contractual agreements associated with specific trials between the sponsor and the pharmaceutical company. For trials where the pharmaceutical company partner has invested a substantially higher financial contribution than may usually be expected for an IIR it is likely that the issue of access to trial data will have been an explicit consideration in contract negotiation. In essence however the same principles apply as for other IIRs given the non-commercial sponsorship of the trial.

The text below provides guide answers to several questions which are being raised:

What requests for access to data are and are not reasonable (timing, use of)?

In an era of transparency and data sharing it is reasonable to consider sharing of anonymised data with trial collaborators and subsequently with external researchers providing any requested access to data:

a. does not undermine the scientific integrity of the trial (i.e. not prior to the reporting of the relevant trial endpoints usually via the completion of the Clinical Study Report)

b. is for academic research purposes

c. has been subject to review and sign off by an independent group (usually the TSC and potentially a data access committee) and

d. is covered by the consent given by trial patients.

It is therefore not usual to share knowledge of or access to outcome data prior to the report of the primary analysis nor to share pseudo-anonymised or identifiable data.

Sharing of drug specific safety data for pharmacovigilance requirements may require separate considerations but will still require consent.

It is reasonable to start with a premise that pharmaceutical company collaborators (on IIR trials) should have similar access (no more, no less) to academic collaborators, subject to the same review of the scientific use, review and sign off by an independent TSC, a signed agreement as to how the data will be used, how the trialists will be acknowledged in any use, and sharing of any relevant IP between those receiving the data and the sponsor or other public entity.

The original funding/supply agreement with the pharmaceutical company collaborator usually specifies the how/when the company can acquire access to the trial data, the exact terms and conditions of such access detailed in the separate sharing agreement will depend on the intended purpose of access (i.e. for internal research and development purposes, update of the IB, support of a wider patent, explanation as to why drug 'failed', or for licensing purposes). (N.B. There may be the option for the CTU to undertake additional statistical analysis (funded) for the company therefore not needing the release of data to the company statisticians). The unique requirements of any further agreement are governed by the type of analysis of the data required

(hence the SAP would need to be agreed), the depth of source verification required (hence the possible need for independent monitoring), future use of the data and costs, both internal and external, incurred in gathering the data (see appendix for further details).

What are the considerations in relation to "ownership" or "custodianship" of the data?

The sponsor would be expected to be the data custodian and as such has responsibilities in relation to the data during the trial and subsequently in perpetuity. Even after a trial is published and a copy of the dataset has been conveyed to a collaborator (pharmaceutical company partner or academic researcher) usage of those data for any new purpose or analysis should only be granted after a request has been made to the sponsor/CTU and use should be restricted to the approved purpose.

Whilst generic requests may be made, lack of specificity in the intended use of data may be challenging to the data custodian due to their need to fulfil Data Protection Act (DPA) requirements of fair processing. It is unlikely that data could be shared for future unspecified purposes. It would be usual for the data to be shared in an anonymised format (not pseudo anonymised) such that the data could not be linked back to patient records at participating sites. Any exception to anonymisation would need to be clearly, carefully justified and covered within the patient information forms and consent. Special consideration, including the terms of the original consent, is likely to be required in the case of potential commercial benefit of the organisation requesting access. In all cases it will be necessary to execute a specific data sharing agreement including not just the intended use but the definition of the specific data required.

In what situations should financial recompense be sought and to whom (inc. NIHR CRN)?

It is reasonable that costs to defray CTU time/effort should be requested in nearly all circumstances (involving pharmaceutical companies and research collaborators). If the data are to be used for direct commercial purposes, in support of licensing or similar, this cost recovery should be at rates that are similar to commercial rates. This funding would be required by the CTU to expand its overall capacity if it is required to provide support for commercial use of academic data. Additionally in the case of commercial use it is reasonable to request that a portion of funding might also flow to charity funders of the research, or to the NHS. The key principle is that the sponsor/CTU should seek for there to be a reimbursement of the 'academic research enterprise' rather than there being a strict accounting as to whether it is the university, the NHS, a specific Trust, a charity or NIHR that benefits.

Does a data access request from a pharmaceutical company partner differ from a general request for third party data sharing (inc. not putting restrictions on the latter)?

The principles of data sharing should be the same with academic and industry based collaborators and follow procedures for scientific review of proposed use of data as outlined above. Access requests by those collaborators involved in a trial (e.g. academic translational researchers) generally occur from an earlier time point in the trials evolution (i.e. often once primary analysis conducted) than wider external data access requests. Consideration should also be given to how to process requests from other non-affiliated commercial organisations and whether such requests are deemed appropriate if there is the potential for commercial sensitivity

with the pharmaceutical company who partnered in the trial. These issues would be expected to be considered during the scientific review of any data access request.

In the case however that the pharmaceutical company partner wishes access to the data for commercial use (in particular for use of data for registration purposes) the additional costs of providing that data (costs on top of the academic costs) should be at roughly 'commercial rates' (for discussion).

Additionally in the case that data be proposed to be used to support a marketing authorisation application due consideration should also be given to recompense academic funders / sponsors and the NHS for costs incurred in conducting the trial. Trials whose primary intent is to be used for registration are conducted within the NHS according to the commercial costing template offering advantages in terms of NIHR portfolio access (no peer review) and for which the NHS employs a full cost recovery model (including all research, service support and service costs).

The justification for doing collaborative trials at less than full cost is that they address questions in a way that differs from, or adds to, what a pharmaceutical company can achieve under a commercial model (e.g. with a CRO). The corollary follows however that, having done a study using the non-commercial model for less money because the company was not yet committed to using the data for registration, if the company subsequently decides they do want the data for direct commercial use, any negotiation recognises that the company would now be liable for the full cost of putting the data in the shape needed for regulatory submission.

Appendix

Summary of terms of access to be included in data sharing agreements

i. Scope of use of the data

ii. Form of the Data Set to be provided

iii. Statistical Analysis Plan agreed

iv. Timings

v. Internal costs to be incurred in collating the data

vi. Consideration of the appointment of an independent audit and costs to be agreed and paid for by the commercial company

vii. Consideration of other jurisdictions

viii. Licence fee for access to the data (dependent upon any original contribution by the pharmaceutical company collaborator to the trial).