How to work with a CRO

When you have chosen a contract laboratory to go on with your project, you have to take care of some important aspects that go from the first beginning to the end of the study.

- **CDA / NDA**: First of all things, you have to sign a confidentiality agreement, non-disclosure agreement, confidential disclosure agreement, proprietary information agreement, secrecy agreement, or whatever you call. Signing one is absolutely worth doing after the first contacts with a contract laboratory and before going to the subject-related business. Having a confidentiality agreement significantly eases lives for both sides; you can share the issues related to your compounds & projects already when asking the CRO to suggest studies and protocols suitable for you project or problems. It is worth signing even if you think you are not going to do actual business at the time, because it probably speeds things up in the future. Also, confidentiality agreement may actually be the factor that triggers the business between you and the CRO, as without that some pivotal issues or words may be left as not said and shared. If it looks like you are going to do lots of business with a certain CRO, it may be worth writing and signing a longer version that includes also some main principles about the other general issues in mutual business, such as invoicing & payment terms or turn-around times, and in this case the paper is usually called master agreement.

- **Trust and interact**: Ask your CRO to plan the most suitable total package for your needs. Moreover, let them know what you already know and what your aims are. After you have the CDA/NDA in place, there is no reason to hide study-related information or not to tell what they ask. Even if the questions may not sound relevant to you, those may have a high importance to your partner and large impact on how the study goes. In the end, shared information is one of the best quality guarantees that your CRO may get – from you. After hearing your thoughts, they may come up with something very different than what you initially had in mind as a right experiment to conduct. They are the experts in their field and know what kind of study is the most time and cost effective to answer questions relevant for you project/compound. They may also help you to save time and money by suggesting additional studies to support or complement the information from the initial planned experiment – by doing this in a cost effective manner in a one bunch. Building up a package with several studies usually creates several synergies, decreasing the total cost in comparison to certain independent studies.

- **Contact person**: Many people say they want one and the same contact person to take care of all their communication at the CRO. In many cases your contact will then be the customer service manager or sales representative, who may often be experienced or competent for discussing with you all subject related aspects. But you have to take care, that you can deal the scientific and study related issues directly with the scientists planning the studies and being responsible for their execution.

- **Study protocol:** After discussing studies and experiments suitable for your needs, take care that the study protocol is clear and describes all relevant issues before signing it to confirm an order. Not to mean it has to include every single detail of the study, that is what the study report will have to do later, but it is advisable that the study protocol contains a description of the main variables in study set up, such as study compounds, aim of the study, species, enzymes or enzyme sources, concentrations, time points, number of samples, etc, brief description of analytical procedures, deliverables, level of reporting turnaround time and data/sample storage.

- **Authorities' recommendations**: Not so relevant in the discovery phase, where the main thing in the study is get data enabling you go / no-go decisions, but when going forward with a decreased number of molecules, it is time to start noticing what the authorities think about the way how studies are conducted and what information is obtained. Discuss with your contract laboratory, they should have knowledge about the FDA/EMA/ICH guidelines and recommendations.

- **Level of experimental optimization**: Comparison of the fixed study packages from several contract laboratories is often difficult due to different level of optimization in experimental procedures. It is worth asking if the experimental conditions are optimized specifically for your compound, or do they work just with the generic protocol in every single case. In some cases there may not be a big difference in the outcome, but there are some studies where high level of optimization may be useful, e.g. if conditions with respect to incubation kinetics are important (e.g. drug-drug interaction studies), or if the physicochemical properties of the study compound prevents the use of standard protocols. The most important field with respect to use of method optimization is often analytical method development; no matter how well the other experiments (incubations, animal work, permeation experiments) have been conducted, the poorly adjusted or use of non-suitable analytical technique may ruin the results. Most of the analytical work in ADME research is nowadays conducted using liquid chromatography interfaced with mass spectrometry (LC/MS), and because optimum analytical conditions for different compounds may vary very much from both chromatographic and/or mass spectrometric

(ionization) point of view, the use of optimized analytical methods, instead of use of one and the same generic LC/MS conditions for each analyte, may sometimes have remarkable effect to the quality and usability of the results.

- **Reporting and interpretation of the results**: After your partner has completed the experimental work in a way combined with superlatives, the next step is to present the results so that only thing left for you is easy reading and enjoying the presentation. Agree the level of reporting and what is to be presented in the report, so that you know what to expect. After first report with a new partner, spend some time for couple of re-iterating comment rounds with the draft report before the final report, so that in the next study you can expect all the commented issues to be as you wish – as the CRO now has an approved report template for your studies. Alternatively, write the report template yourself and send it to CRO already before the first study, and ask them to use that in the first place.
  Regarding the level of reporting, it is also worth considering what are you actually satisfied with, as overkill in a form of too detailed or too discussed report may also slow down finding the right meaningful results from the report, or increase the turn-around time and increase the costs. Therefore, in many simpler studies a "light" report containing just numbers in an agreed format (e.g. MS-excel table with some calculations & representative graphs) might be much more useful than written report with tens of pages, especially if the field of study is something you are scientifically comfortable with. But if you think you need something help in interpretation of the results and what they mean, go for the written report with a higher level of data interpretation, including discussion of the results in the light of practice and recommendations in the field. Also, if you have some old data or knowledge related to the issue, you may share that with a CRO and ask if that data helps them in providing you more exact conclusions when combined with the new data. Finally, you may ask them also include recommendations with respect to the next follow-up studies.

- **Storage of study data and samples after the study**: Essential if there emerges a need for checking the raw data or for further follow up studies with the same samples. If an error is suspected, or a need for mining up new information from the same data emerges, both the original instrumental data and data processed to numbers or figures may be needed. Need for old samples might come up from need of re-analyses (with similar or completely different methodology). So it is recommendable that all raw data and the study samples are stored for a considerably long time, e.g. 1 – 5 years, depending on study type or sample type, after which it is a usual procedure to contact you agreeing about the actions, i.e. discarding or perhaps sending to your own facility.