

Cerebricon Preclinical CRO FAQ

1) What is the definition of a Contract Research Organization (CRO)?

A CRO can be defined as an organization which specializes in research which it offers to undertake for a client in return for payment. This can be an academic or purely commercial organization.

2) What is a preclinical CRO?

Preclinical research takes place before a compound is deemed safe or effective enough to be tested on humans. The preclinical research can take the form of efficacy studies in *in vivo* and *in vitro* disease models, basic pharmacology, toxicology or safety studies.

3) Where does a preclinical CRO fit into the drug development “value chain”?

Once a compound has been identified as a potential drug from a chemical series, its actions against receptors, cells, tissues, organs and whole animal systems has to be determined. If the organization or the originators of the drug under development do not have the internal resource to explore these actions ‘in house’ a reliable CRO can be employed to undertake the preclinical development that is essential prior to entering the compound into clinical development. In addition a reliable CRO like Cerebricon can be used as an independent validation body to confirm in-house results.

4) How regulated are preclinical CROs?

No regulatory body exists for preclinical CROs. It is therefore important that a CRO is self regulating and that if they undertake *in vivo* studies that these are done under the auspices of an ethical review board. Reliable CROs should be able to provide client references that speak to the high standards of their work as well as all regional and national standards related to the nature of the research performed in their laboratories.

Final reports always comply with ICH, FDA, OECD and EMEA regulations for non-clinical studies.

5) How are the ethical issues handled?

Ethical issues concerning animal welfare should be dealt with by the local governmental ethical review board. Governmental ethical review boards differ greatly from region to region and a potential client should always ensure that the strictest ethical guidelines are observed at all times. Cerebricon also has an internal ethical committee that works to ensure that all studies are carried out in accordance with the highest possible ethical standards.

6) How are issues of Intellectual Property Handled?

ALL IPR is owned by the study originator not Cerebricon. Cerebricon works to ensure that there is no discrepancy about this issue. Cerebricon Ltd. works exclusively for, and on behalf of, the client. The research services contract that Cerebricon signs will be explicit with regards to client ownership of results, IPR and publication rights. Since Cerebricon is not an academic organization there are none of the ownership issues that traditionally surround academic research.

7) How are issues of confidentiality handled?

A non disclosure agreement (NDA) is always signed before discussion of project details takes place. This NDA will ensure that all matters discussed remain in strictest confidence.

8) Can results be published on without authorship of Cerebricon

The results belong to the client and can therefore be published in any form and with any authorship the client sees fit. However, Cerebricon's service extends much farther than simply generating results and we are enthusiastic to be involved in all aspects of data reporting and communication. We feel this reflects the strong relationships we build with our clients which allows them to avail themselves of the wealth of experience within the company. However, as with items 6 and 7 above the final decision on these issues always resides with the client.

9) What about the independent validation of in-house generated results?

Before moving a compound into clinical development many investigators will demand the reproduction of 'in house' data in another laboratory. A preclinical CRO is ideally placed to provide an unbiased study based on the original

which can validate existing efficacy data and so allow the compound to be developed with the confidence that the efficacy data is robust and reproducible.

- What about cost?

Prices charged for preclinical contract work can vary dramatically. A client should be aware of the cost of the resources involved in undertaking the experiment and also the value placed on the difficulty of the model and experience needed to successfully execute the study design.

- Penalties for late reports?

Unless clear reasons are stated in good time, reports should always be delivered in full and on time. Failing to do so may result in a CRO being liable to penalties. These penalties must be clearly stated in the initial agreement. Cerebricon regularly negotiates penalty fees in the event that study schedules have not been kept. In actuality it is only on the rarest of occasions that Cerebricon has not met both quality standards and timelines for its studies.

- Other kinds of penalties?

The initial agreement should also state when penalties should be applied if clearly defined goals are not met within an experimental paradigm. These may apply to reference compounds used within the study as well as the induction of diseases within the particular model being employed.

- What about blindedness?

All studies performed at Cerebricon are performed in a double blinded fashion. This is without fail and is explicit within the study design.

10) What can I tell about the overall efficacy of the compound after a Cerebricon study?

Cerebricon studies will always apply the most pertinent statistical analysis to data sets so a client can be confident that when a statistical difference is observed it is reflected in the results reported. Cerebricon scientists are continually striving to generate the maximum value from any given assay and the creativity and innovation we apply to our model platforms is geared toward reflecting compound efficacy in each assay.

11) What about translational factors or “bridging to the clinic”?

The generation of data in animal models that can be directly comparable to the data generated in patients is becoming an essential part of a preclinical data package. Cerebricon are acutely aware of this concept and as such work very hard to include parameters seen in the clinic, such as behavioral testing, imaging and biomarkers analysis in preclinical studies so that we deliver maximum value to the client. This translational strategy aims to maximize the potential of success of a client’s compound in the clinic.

12) How quickly can studies be started?

The time to commence a study depends on the nature of the CRO and the study. Cerebricon works within its own proprietary laboratories with its own dedicated staff so studies can be scheduled within weeks of an agreement being reached with the client. As the nature of studies varies so does the time to commence studies, for example, if the study involves transgenic subjects then one must take into account the time needed to breed the requisite number of subjects for the study unless, as is often the case, there are cohorts of these animals readily available.

13) Can models be customized?

Virtually every study which Cerebricon undertakes has been tailored to the requirements of the client. Studies differ with regards to route of administration (I.V, I.M, I.P, ICV, Intrathecal administration etc.) Every client has different needs and an effective CRO should always look to tailor a study to suit the needs of a client, and more importantly, to the premise behind the clients compound

14) The issue of the positive control?

There are some models for which there are very effective positive controls or reference compounds. These can be used to great effect to validate the assay and compare efficacy with a compound under development. Not all assays, however, have a compound that can be relied upon to produce consistent results. This is due either to the complexity and severity of the assay or the quality of available pharmacological tools.