What Does it Take to Run a Clinical Trial?

开展一项临床试验需要**哪些条件**？

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Ever wondered how easy or hard it might be to run a clinical trial, or what researchers have to do to be able to run a study? Here we'll outline some key differences between an academic study and an FDA-regulated study, and talk about our own ketamine clinical trial planned to start this fall. If you didn't realize there were 2 types of studies, you're not alone.

大家有没有想过进行临床试验的难易度到底如何？或者，研究人员需要做**到什么程度**才能开展临床研究？这里我们会概况性的介绍学术研究和 FDA 监管下的研究之间的一些主要区别，同时也会讨论我们计划将于今年秋季开始的 ketamine（氯胺酮，一种 NMDA 拮抗剂，临床用于麻醉和镇静）**的**临床试验。如果你没有意识到临床研究其实有两种类型，不要紧，**并**不**只**是你一个人这样。

An academic study is one where the physician or researcher at the site often takes full responsibility for the study design, conduct, and reporting, and acts alone to complete the study or may work in collaboration with a pharma company to use a treatment supplied by them. Often an academic study is done in one or a few centers. The researcher receives permission from their local regulatory body, the Institutional Review Board (or IRB), to conduct the study at their site. Every site that performs research will have an IRB to regulate and approve research. In a drug study for example, IRBs often consider how often the patients come to the clinic, what dose levels the patients receive, and ensure enough safety measures are in place to protect patients. Only studies that are IRB-approved may be conducted.

一项学术研究是指在研究机构中的医生或研究人员对研究设计、实施和报告负全部责任，并独自或者有时候与制药公司合作使用他们提供的治疗方案来完成的研究。学术研究通常在一个或数个中心进行。研究人员在获得研究机构的机构审查委员会 (Institutional Review Board，IRB) 的许可后就可以在他们机构开展研究。每个进行研究的机构都会有一个 IRB 来管理和批准临床研究。例如，在药物研究中，IRB 经常会考虑患者来医疗机构的频率、患者接受的剂量水平、以及确保**有**能足够的保护患者的安全措施。只有经 IRB 批准的研究才可以开展。

Once the academic study is approved, the study can begin to recruit patients and treat them exactly as described in the protocol. All patients must provide written informed consent to participate in the study. Deviations from the protocol are not allowed and often need to be reported to the IRB so they can assess if the patients are at an increased risk due to the deviation. At the end of the study, the researchers can analyze and write up the data collected, often from excel spreadsheets, and publish their findings in a scientific journal.

一旦学术研究获得批准，该研究就可以开始招募患者，并严格按照计划中的项目进行治疗。所有患者必须提供书面的知情同意书才能参与研究。研究中通常不允许出现方案偏离，并且若出现时通常需要向 IRB 报告，这样他们

就可以评估患者是否因方案偏离而面临着更高的风险。在研究结束时，研究人员可以分析整理收集到的数据（通常就用 Excel 电子表格记录），然后将研究结果发表在科学期刊上。

An FDA-regulated study, in addition to meeting local IRB requirements, must also adhere to federal regulations as well as international standards for data integrity and patient protection. FDA requires an auditable database for the study data, which means a database (most often an electronic database) must be designed and built with the ability to track changes to the data points, know who changed them, why, and when. All data must be submitted to the FDA as well as they will conduct their own analyses on the data, which is important especially if the study sponsor is trying to get a new drug on the market.

一项 FDA 监管下的研究，除了满足当地 IRB 的要求外，还必须遵守联邦法规以及有关数据完整性和患者保护的国际标准。FDA 要求研究数据有一个可供审计的数据库，这意味着数据库 (通常是电子数据库) 在设计和构建时必须能够追溯所有数据的更改，知道谁更改了数据、更改原因和更改时间。所有的数据都必须提交给 FDA，并且 FDA 也将对数据进行自己的分析，这一点对于那些研究赞助者致力于将一种新药上市销售的情况是非常重要的。

Another requirement is data monitoring, which means independent consultants must review the data collected, verify that the data corresponds to a real patient, and the data recorded in the study database is accurate representation of the patient's medical record. Once the database is considered clean and no more changes or updates are needed, the database is locked. A pre-planned statistical analysis will be performed on the dataset to determine safety, efficacy, and other outcomes planned for the study. The statistical analysis plan for the study is completed prior to the database lock to ensure analyses aren't biased and altered based on the results of the study.

另一项要求是数据监测，这意味着必须由独立顾问来审核收集的数据，验证数据是否与真实的患者相符，同时研究数据库中记录的数据是否真实反映了患者的医疗记录。一旦数据库被认为是干净的，不再需要修正或更新时，就会对数据库进行锁库。之后将会按照预定的统计分析计划来对数据库进行分析，以确定研究的安全性、有效性和其他计划研究指标的结果。研究的统计分析计划会在数据库锁库之前完成，以确保数据分析流程不会被研究结果影响而产生偏差和更改。

In addition to the statistical analysis plan, every other aspect of governing the study must be clearly documented so that FDA can review how the study was conducted, how it was recorded, and how compliant the research was with the study plan. Due to these requirements, most FDA-regulated studies are conducted by pharma companies and their affiliates who specialize in these types of tasks and documentation. The pharma company is then responsible for meeting all of the FDA requirements for their FDA-regulated study.

除了统计分析计划之外，管理该研究的其他所有方面的内容都必须清楚地记录下来，以便 FDA 能够审查该研究是如何进行的，如何记录的，以及该研究进行的情况与计划的符合度如何。由于这些要求，大多数 FDA 监管下

的研究是由制药公司和他们附属的专门从事这类研究和资料存档工作的机构进行的。然后由制药公司负责保证符合 FDA 对于 FDA 监管下的研究的每一个要求。

However, academic studies may also be regulated by the FDA, and often FDA-regulation is requested by researchers if a treatment is being used differently than intended as in a new route of administration (IV to oral, for example), in a patient population that is considered vulnerable (children, for example), or for a disorder where patients can't consent to the research directly (as in a neurodevelopment disorder like Rett syndrome). RSRT is funding an FDA-regulated academic study to evaluate ketamine dosed orally in Rett syndrome patients aged 6-12 years, for exactly these reasons. We are glad to know that our study will be held to the highest standards as industry-sponsored studies are, and we are hopeful that our ketamine study will provide additional experience to our Rett Investigators to facilitate the success of other FDA-regulated research in Rett syndrome. To learn more about our clinical trial, visit www.clinicaltrials.gov and search "Rett Syndrome" and "ketamine", or NCT 03633058.

不过，学术研究也可能受 FDA 监管，并且研究者在某些情况下经常要求接受 FDA 监管，比如通过药物注册证中适用范围之外的给药途径来治疗 (例如 IV 期临床采用口服方式)，或者研究对象被认为是较脆弱的患者人群 (例如儿童)，或者针对那种患者无法自己直接同意研究的疾病 (比如雷特综合征这样的神经发育疾病)。RSRT 正在资助一项由在 FDA 监管下的学术研究，评估口服氯胺酮对 6-12 岁雷特综合征患者的治疗效果。我们很高兴得知我们的研究将按照业界资助研究中的最高标准进行，我们希望我们的氯胺酮研究项目能为我们的 Rett 研究人员提供更多的经验，以促进其他 FDA 监管下的针对雷特综合征研究项目的成功。要了解更多关于我们临床试验的信息，请访问 www.clinicaltrials.gov，搜索“Rett Syndrome”和“ketamine”，或 NCT 03633058。