KNOWLEDGE IS POWER...

CLINICAL TRIALS

A clinical trial is a study to research the effect of a new drug or any other therapy or surgical procedure to cure, treat or to improve symptom management of a disease. If the study is to test a new drug, it goes through many stages before it eventually gets to us humans.

These trials or studies, are critical to furthering access to new and improved therapies for medical conditions, but most of us have little or no knowledge of how they work:

• Why do they take so long to get started and so long to complete?
• Why do they restrict access and deny some people the right to take part/enroll in a trial?
• What is the difference between approval by the FDA and approval by Health Canada, and why don't these two organizations work hand in hand?
• Why do new drugs cost so much when they are approved for use and become available at a drug store in my community?

Sometimes the identification of a substance of interest to researchers is carefully planned - a compound or chemical is created or developed because it has specific characteristics that make it attractive for testing. But sometimes it is an AHA! moment. Sometimes a scientist is testing a compound or chemical for a specific purpose and during testing realizes that it may be useful for another purpose. Regardless of how the compound or chemical comes to attention, it must still undergo many phases of study (research) before it finally makes it to a drug store near you.

Clinical research is medical research involving people, but research for new drugs or other therapies begins long before human subjects are ever involved. First these chemicals or biological substances are tested in tissue cultures (in vitro) or in small animals (in vivo). Some of these animals have been specially bred to mimic diseases that only occur in humans. The purpose of this testing is to make sure that the substance is not toxic (can cause serious harm) and that it appears to have some efÞcacy (works the way it is expected to work).

After the chemical or substance has been thoroughly tested in vitro and in vivo, it is time for clinical research to begin. Clinical testing (or trials) has many different phases:

Phase 1: Healthy volunteers are given the new drug in various doses, to see how much the human body can tolerate and if there are immediately identifiable side effects. In most cases between 20 to 80 volunteers are included in this group, which may include persons with the disease that the new drug is intended to treat. Phase 1 trials may offer information about how best to administer the drug to maximize beneÞt and minimize risk. At the end of this phase, about 70% of new drugs successfully proceed to Phase 2.

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Phase 2: People with the disease that the new compound, or drug, is intended to treat are enrolled at this stage. Usually only a few hundred people are treated in this phase of the trial, and this is not a sufficient group size to prove that the drug works well, or at all. What Phase 2 trials are designed to do are to gather additional safety data, and to develop the questions and protocols needed to set up the Phase 3 trial – the phase that is meant to really prove that the drug works and is safe to use! Only about 33% of drugs that complete Phase 2 trials successfully make it to Phase 3 trials.

Phase 3: This stage of a clinical trial is designed to prove if a new drug actually works in the population for which it is intended. Phase 3 trials enroll between 300 and 3000 people with the medical condition, and the trial goes on for much longer than the previous phases. Entry criteria (the specific details of the group to be accepted in the trial) are strictly controlled so that the best possible information can be obtained. Entry criteria are used to ensure that the new drug is given the very best opportunity for success. For ALS drugs, most trials are open only to those in the early stages of the disease, to control against failure to perform in those who are already well advanced in their course. If entry criteria was not controlled, and anyone who wanted to take part in the trial was accepted, the data gathered could be so contaminated that a drug with a very good response rate for persons in early stages of disease could be abandoned for poor results and thus denied to those for whom it might offer benefit.

Sometimes different doses of the drug are tested, and routinely one 'arm' of the trial does not receive active drug at all. This type of clinical trial is what is called 'double blind, placebo controlled' – that means that neither the patient nor the researcher/doctor knows if the patient is receiving the active drug (or a specific dose) or is receiving the placebo. A placebo is an inactive substance or other intervention that looks the same as, and is given the same way as, an active drug or treatment being tested (sometimes called a 'sugar pill', although there may in fact be no sugar included in the pill). Many phase 3 trials progress to what is known as 'open label', if early results show that the drug is working and is safe. In 'open label' trials, there is no placebo arm; every person enrolled receives the drug being tested.

Because Phase 3 trials last longer, and involve more people, it is more likely that rare and/or long term side effects will be uncovered before the drug goes forward for government approval. Only 25-30% of drugs move on to the next phase.

Taking a newly identified compound/substance/drug through all of the phases described so far can take many years (some estimate anywhere from 9-14 years in total).