Supplementary information S2 (box)

**Investigational new drug application**

Several aspects of an investigational new drug (IND) application are unique for drugs to be developed for the treatment of addiction. One unique aspect is that the pharmaceutical industry is likely to have other indications for a drug that may be of significant value to addiction (see discussion of CRF1 antagonists in the main Review). Such a situation has both advantages and disadvantages. The disadvantage is obvious—addiction trials could be seen as counterproductive to the main commercial goal and thus be delayed or eliminated from development. Nevertheless, a reliable mechanism for generating INDs is to have an investigator initiate an IND application on a drug that already has another indication. Approval for studies on addiction is relatively straightforward if the drug is approved for other indications as long as the dose range required for addiction treatment is in the same dose range as the approved medication. This process will also work for drugs approved outside of the United States. A key element and critical point for medications development is submitting an IND application to the FDA, or its equivalent in other countries, so that the drug can be tested in humans. The International Commission on Harmonisation (ICH) developed strict regulations and requirements that have been mandated by the FDA for the testing of a substance (drug) for a previously unapproved therapeutic indication by an investigator. ICH guidelines have also been incorporated by regulatory agencies in most other countries, resulting in a high degree of consistency in the requirements for chemistry, manufacturing, control, safety, and toxicology prior to testing of a drug in humans. In the U.S., the application for the initial clinical testing of a compound by an individual is governed by the sponsor-investigator submission of an IND application. This process involves FDA Forms 1571 and 1572 (complete instructions can be found at [http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm](http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm); accessed October 10, 2008). The data that must be supplied, in addition to the proposed clinical trial protocol and information on the investigators, include detailed information on the chemistry (i.e., synthesis, formulation, stability), toxicology, pharmacology, and prior human studies.