CONCEPT CLEARANCE RECORD
FY 2016 RESEARCH INITIATIVE – NCATS

TITLE: Increasing Access to Compounds and Tox Data

OBJECTIVE(S): To increase access to compounds that did not have a safety signal in pre-clinical studies but were later shown to have toxicity in humans. The program would investigate underlying mechanisms for the human toxicity and explore potential reasons why pre-clinical tools failed. The information would be incorporated into predictive modeling to benefit drug development.

DESCRIPTION: This initiative would broker relationships between pharmaceutical companies and academic researchers who could conduct research to better understand and perhaps help to overcome toxicities detected in drugs that gave a safety signal in Phase I trials that were not predicted based on pre-clinical studies. The research would help answer the question of why pre-clinical tools sometimes fail to predict toxicity by providing researchers with access to the compounds, as well as associated pre-clinical and clinical data. Once the gaps are identified, it would be possible to start building complementary models or assays to increase safety and incorporate this information into predictive modeling to benefit drug development.

IMPORTANCE: The underlying mechanism of toxicity discovered in or after Phase I trials often is not investigated. NCATS would work with multiple pharmaceutical companies, the Food and Drug Administration and companies that develop predictive toxicology tools. Understanding mechanisms of toxicity would have implications for all drug development.

HISTORY: Through the New Therapeutic Uses program, NCATS has successfully facilitated collaborations between academic institutions and pharmaceutical companies to explore the therapeutic potential of investigational drugs owned by the companies. The current concept seeks to harness that collaborative spirit and aim it in the direction of predictive toxicology. Although it is uncommon, investigational drugs still may fail in Phase I trials. This means that the pre-clinical studies did not predict the safety signal that was seen in the subsequent human trial. Although pharmaceutical companies will investigate the toxicity to some degree, if not readily apparent, the underlying mechanism of toxicity discovered in Phase I trials likely would go without the kind of investigation that would lead to an understanding of the underlying mechanism of toxicity. Gaps in the pre-clinical toolbox are leading to avoidable inefficiencies and unnecessary risks for subjects. Giving academic investigators access to the compounds, the associated data and the resources needed to investigate the discordance between the pre-clinical and clinical outcomes likely will lead to a better understanding of the differences in the systems pharmacology between difference species. This understanding may lead to new animal models, as well as modifications to current algorithms used to predict toxicity in humans.

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