National Institute of Neurological Disorders and Stroke

Epilepsy Therapy Screening Program (ETSP)

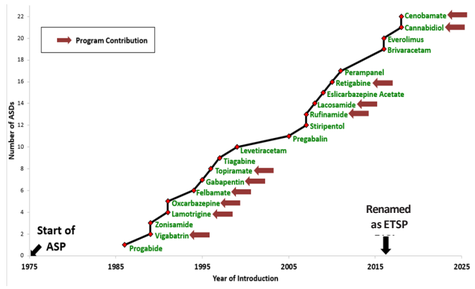
ETSP Mission

To facilitate the discovery of new therapeutic agents addressing the unmet medical needs in epilepsy

ETSP Goals

- The ETSP builds upon the legacy of the Anticonvulsant Screening Program (ASP). The name was changed in 2016 to reflect a refinement of the program's goal to support world-wide researchers in the identification of therapeutic approaches that can:
  - provide seizure control in individuals with drug resistant epilepsy (30% of patients not adequately treated; need for drugs that are clearly differentiated from those currently marketed)
  - prevent epilepsy and modify disease severity (there are no existing approved treatments)
- Continue to offer services free of charge to qualified applicants world-wide

A Strong Foundation: Anticonvulsant Screening Program (ASP)



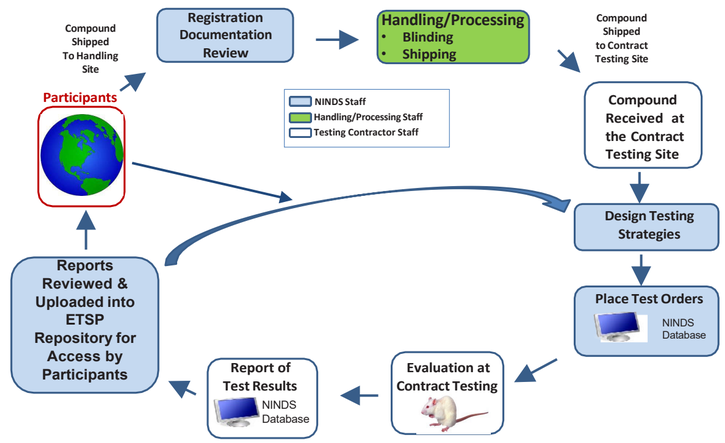
- ASP was established in 1975 to facilitate the discovery of new drugs for epilepsy to augment the limited options available at the time
- For > 40 years, ASP has provided free testing in rodent antiseizure screens run by the testing site contractor (University of Utah)
- >600 total participants representing industry and academic institutions from 38 countries
- >32,000 compounds tested against different targets so far contributed to the identification of 11 FDA-approved antiseizure medications

Modalities Accepted for Testing

ETSP tests all types of treatment modalities including:

- Small Molecules
- Next generation peptides
- Oligonucleotides and RNAi
- Gene Therapy
- Antibodies
- Cell Based Therapy
- Devices

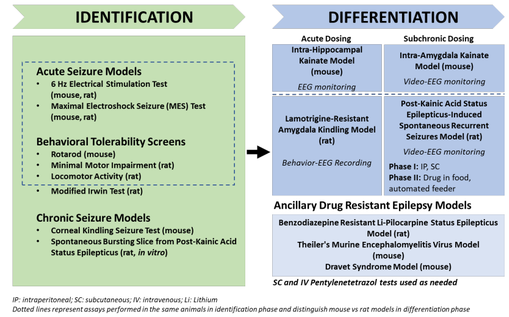
Operational Overview of ETSP



Key Principles of ETSP Testing

- Ensure that compound submissions are of high quality
  - Strict criteria for identity and purity (>95% for small mol & peptide)
  - Chemical/biological rationale, pharmacokinetics, and other supporting data used to evaluate suitability for participant project entry into the program
- Screening aligned with specific program goals for different types of treatments
  - Drug resistant epilepsy, disease prevention, and disease modification
  - Build comparative pharmacology data on models, monitor the effectiveness of screening flows and decision trees
- Perform testing with high scientific rigor
- To inquire about becoming a participant please contact ETSP Program Director, Brian Klein PhD, brian.klein@nih.gov

Drug Resistant Epilepsy Workflow



IP: intraperitoneal; SC: subcutaneous; IV: intravenous; Li: Lithium
Dotted lines represent assays performed in the same animals in identification phase and distinguish mouse vs rat models in differentiation phase

Models of Disease Prevention and Modification

- Rat model of systemic kainate injection induced chronic epilepsy
- Mouse model of focal kainate injection into amygdala induced chronic epilepsy
- TBI-induced chronic epilepsy model – under evaluation

Submitting Compounds to the ETSP

- Initial contact with NINDS ETSP staff and including an introductory discussion to learn about program and general project goals
- Signing of a participant agreement which outlines conditions for confidentiality, intellectual property protection, etc
- Further in-depth confidential discussions on suitability of the proposed project
- If mutually agreed upon, participant registers compound(s) online
- If approved by ETSP, participant ships compound to handling site, which blinds and submits compound to testing site for evaluation
- NINDS ETSP staff work with participant to plan testing, review test results, and discuss future steps
- Interim and final quality-controlled reports are provided to the participant

Learn More About ETSP Testing

PANAChE (Public Access to Neuroactive & Anticonvulsant Chemical Evaluations)
https://panache.ninds.nih.gov/

- Publicly accessible database for non-confidential data and information from the ETSP