Pediatric Advisory Committee
September 11, 2017

Presented by:

Leonard Lawrence

Regulatory Affairs

Sovereign Pharmaceuticals, LLC

SOVEREIGN PHARMACEUTICALS, LLC

- Phase IV, open-label, single arm, single-dose pharmacokinetic study for hydrocodone and guaifenesin.
- 25-35 Symptomatic Children between the ages of 6 and 17 divided relatively evenly between ages 6 to under 12 years of age and 12 to under 18 years of age.

SOVEREIGN PHARMACEUTICALS, LLC

Phase IV, open-label, multi-center, multiple dose, single arm study to determine the safety of the proposed combination hydrocodone and guaifenesin product in symptomatic pediatric patients ages 6-17.

FDA is restricting the use of codeine and tramadol medicines in children. These medicines carry serious risks, including slowed or difficult breathing and death, which appear to be a greater risk in children younger than 12 years, and should not be used in these children. These medicines should also be limited in some older children. Single-ingredient codeine and all tramadol-containing products are FDA-approved only for use in adults. FDA is also recommending against the use of codeine and tramadol medicines in breastfeeding mothers due to possible harm to their infants.

- FDA's strongest warning, called a Contraindication, to the drug labels of codeine and tramadol alerting that codeine should not be used to treat pain or cough and tramadol should not be used to treat pain in children younger than 12 years.

- A new Warning to the drug labels of codeine and tramadol to recommend against their use in adolescents between 12 and 18 years who are obese or have conditions such as obstructive sleep apnea or severe lung disease, which may increase the risk of serious breathing problems.

SOVEREIGN PHARMACEUTICALS, LLC

Codeine + CYP2D6

Morphine

Hydrocodone

Hydromorphone

SOVEREIGN PHARMACEUTICALS, LLC

- **§50.53 Clinical investigations involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder or condition.**
- Any clinical investigation within the scope described in §§50.1 and 56.101 of this chapter in which more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is not likely to contribute to the well-being of the subject, may involve children as subjects only if the IRB finds that:
- (a) The risk represents a minor increase over minimal risk;
- (b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- (c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (d) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians as set forth in §50.55.