Protocol after the ILSI/HESI International Act. Study

（as of 2003）

CIEA
SINCE 1952

- Preliminary test

  Period: 4 weeks

  Animals: wild type（non-Tg for rasH2）

  Purpose: Dose finding for 26-week study

- Carcinogenicity test

  Period: 26 weeks

  Group composition:

  GM: nega. con. group＋3 dose groups＋posi. con. group

  wild type (non-Tg): nega. con. group + high-dose group. (crucial)

  Animal: 25/sex/group

Robinson D.E. & MacDonald J. S.,
Toxcol. Pathol. 29 (Supple.): 13-19 (2001)

Present protocol for the FDA application

（interview from people in US CROs & Pharmaceuticals ）

CIEA SINCE 1952

- Preliminary test

  Period: 4 weeks

  Animals: wild type（non-Tg for rasH2）

  10 mice /sex/group + TK

- Carcinogenicity test

  Period: 26 weeks

  Group composition:

  GM： nega. con. group＋3 dose groups＋posi. con. group

  wild type (non-Tg)： no need (stated by FDA in DIA, 2005)

  Animal: 25 mice/sex/group + TK

  15 mice/sex for positive control group (from Nov. 2009)