# Dilemma in the Selection of an Appropriate Test Vehicle

Scientists at Jai Research Foundation (JRF) have immense expertise in conducting oral toxicity studies for several decades. We have our internal SOP based on guidelines for selection of appropriate vehicle. The conclusion of endpoints in tox studies are entirely dependent, on the choice of vehicle. While guidelines have clearly defined the evaluation of an appropriate vehicle defining a logical sequence to be followed, there are occasions when a study director faces unique problems.

We recently conducted a study on a certain test item, which neither formed a homogenous suspension in water nor in the aqueous carboxy methyl cellulose solution. The test item formed a homogenous suspension in the corn oil, which was chosen. Based on the published data (which was silent on the vehicle!), the $LD_{50}$ value of the active ingredient of the test item was >5000 mg/kg body weight. We started with 2000 mg/kg body weight. In all studies, with this test item with corn oil as a vehicle, pertaining to various sponsors, mortality was observed at 2000 and 300 mg/kg body weight, while animals exposed to 50 mg/kg body weight survived (Study Guideline: OECD 423)! Based on the result of the study, $LD_{50}$ value for the test Item was found to be between 50 and 300 mg/kg body weight against the reported $LD_{50}$ value of >5000 mg/kg body weight. The repeated study confirmed the same result. This was in complete contrast with the published data.

Team JRF brain stormed on the result of the test item under consideration. It should not have differed from the reported value for every sponsor. Result of a test item may vary in a case or two, depending on the manufacturing practices of sponsors, but should not vary for all the sponsors. We also went to the extent of checking out if the product had some highly toxic impurities! We then went to the forth sequential vehicle, PEG. Polyethylene glycol was chosen as a fourth option as the vehicle, since it has very low toxicity and absorption rate being below 0.5%. The test item formed a homogenous suspension with it.

We compared results in all vehicle's, CMC suspension, corn oil suspension and PEG suspension. The earlier results were exactly similar to the earlier ones. However, no mortality was observed at 2000 and 5000 mg/kg body weight and $LD_{50}$ when PEG was used as a vehicle. Results matched the published data.

It is a separate matter of scientific discussion, if change of vehicle which indicate low toxicity versus those indicating higher toxicity should be considered safe. Ideally, animal/human subject is more likely to be exposed to the test chemical through naturally occuring vehicals, rather than a synthetic PEG as a vehicle!

## About The Author

**Dr. Vishvesh Dalal**, with specialisation in inhalation toxicology is an assistant director, in the department of toxicology, having an experience of over 14 years in the CRO industry.
He is leading the team acute toxicology and has contributed commendably as a senior scientist in various repeated dose and acute toxicity studies, for regulatory research and developing data on product safety for regulatory submission.