**A bacterial reverse mutation test of PROJECT Z**

**SUMMARY AND CONCLUSION**

In order to examine the mutagenic potential of PROJECT Z, a reverse mutation assay was conducted in *Salmonella typhimurium* (hereinafter referred to as *S. typhimurium*) TA100, TA1535, TA98 and TA1537, and *Escherichia coli* (hereinafter referred to as *E. coli*) WP2 *uvrA* with and without metabolic activation by the pre-incubation method. Water for injection was used as the vehicle for the test article.

The dose levels are shown as PROJECT Z below.

A dose-finding test was conducted with a total of 7 dose levels (6.86, 20.5, 61.7, 185, 556, 1670 and 5000 μg/plate) after the 50 mg/mL solution was diluted 6 times using a common ratio of 3. In the dose-finding test, growth inhibition by the test article with or without metabolic activation was not observed for all strains. Precipitation of the test article on the plate was not observed with or without metabolic activation. Coloration by the test article in the plate was not observed at any dose level with or without metabolic activation.

Therefore, for the main test with or without metabolic activation, the dose levels for all tester strains were set at a total of 5 dose levels (313, 625, 1250, 2500 and 5000 μg/plate) and the 50 mg/mL solution was diluted 6 times using a common ratio of 2.

**Precipitation and Coloration by Test Article**

Precipitation of the test article on the plate was not observed at any dose level with or without metabolic activation. Coloration by the test article in the plate was not observed at any dose level with or without metabolic activation.

**Growth Inhibition**

Growth inhibition by the test article with or without metabolic activation was not observed for all tester strains.

**Number of Revertant Colonies**

In the dose-finding test and the main test, there was neither test article-related increase in the number of revertant colonies nor dose-response in any test system with or without metabolic activation.

In conclusion, PROJECT Z had no bacterial reverse mutagenic activity (negative) under the conditions of this study.