

**Study Number:** S0939  
**Test Type:** Human Liver Microsome

**PA49: Summary of Cytochrome Activity**  
**Test Compound:** Z-guggulsterone  
**CAS Number:** 39025-23-5

**Date Report Requested:** 11/26/2019  
**Time Report Requested:** 09:53:42  
**Lab:** Research Triangle Institute

**C Number:** S0939  
**Study Gender:** NA  
**PWG Approval Date** See web page for date of PWG Approval

Study Number: S0939  
Test Type: Human Liver Microsome

PA49: Summary of Cytochrome Activity  
Test Compound: Z-guggulsterone  
CAS Number: 39025-23-5

Date Report Requested: 11/26/2019  
Time Report Requested: 09:53:42  
Lab: Research Triangle Institute

|  | Treatment Groups (uM) |                     |                      |                       |                       |
|--|-----------------------|---------------------|----------------------|-----------------------|-----------------------|
|  | 0                     | 0.3                 | 1                    | 10                    | 20 uM Ver             |
| Cytochrome P450 1A2<br>(acetaminophen)<br>(nmol/min/mg protein)      | 0.524 ± 0.041 (3)     | 0.505 ± 0.027 (3)   | 0.521 ± 0.012 (3)    | 0.496 ± 0.020 (3)     | NR                    |
| Cytochrome P450 2A6 (7-<br>OH Coumarin)<br>(nmol/min/mg protein)     | 0.589 ± 0.058 (3) **  | 0.475 ± 0.012 (3) * | 0.454 ± 0.007 (3) *  | 0.439 ± 0.019 (3) *   | NR                    |
| Cytochrome P450 2C8<br>(6a-OH-paclitaxel)<br>(nmol/min/mg protein)   | 0.101 ± 0.009 (2)     | 0.086 ± 0.028 (3)   | 0.091 ± 0.026 (3)    | 0.118 ± 0.051 (2)     | NR                    |
| Cytochrome P450 2C9 (4-<br>OH tolbutamide)<br>(nmol/min/mg protein)  | 0.085 ± 0.001 (3) **  | 0.073 ± 0.001 (3) * | 0.056 ± 0.000 (3) ** | 0.057 ± 0.002 (2) *   | NR                    |
| Cytochrome P450 2C19<br>(HO-methenytol)<br>(pmol/min/mg protein)     | 5.889 ± 0.382 (3) *   | 6.184 ± 0.203 (2)   | 5.052 ± 0.374 (2)    | 4.351 ± 0.104 (3)     | NR                    |
| Cytochrome P450 2D6<br>(Dextrorphan)<br>(nmol/min/mg protein)        | 0.079 ± 0.004 (3)     | 0.088 ± 0.004 (3)   | 0.075 ± 0.015 (3)    | 0.082 ± 0.006 (3)     | NR                    |
| Cytochrome P450 2E1 (4-<br>nitrocatechol)<br>(nmol/min/mg protein)   | 1.059 ± 0.031 (3)     | NR                  | NR                   | 1.097 ± 0.139 (3)     | NR                    |
| Cytochrome P450 3A4 (1-<br>OH Midazolam)<br>(nmol/min/mg protein)    | 0.134 ± 0.017 (3)     | 0.145 ± 0.021 (3)   | 0.095 ± 0.048 (3)    | 0.141 ± 0.028 (3)     | NR                    |
| Cytochrome P450 3A4<br>(6b-OH Testosterone)<br>(nmol/min/mg protein) | 2.427 ± 0.205 (3)     | 2.822 ± 0.212 (3)   | 2.628 ± 0.113 (3)    | 2.337 ± 0.146 (3)     | NR                    |
| Cytochrome P450 4a (12-<br>OH Luic Acid)<br>(nmol/min/mg protein)    | 0.029 ± 0.002 (3)     | 0.029 ± 0.007 (3)   | 0.023 ± 0.005 (3)    | 0.021 ± 0.002 (3)     | NR                    |
| P-glycoprotein ATPase<br>Activity (nmol/min/mg<br>protein)           | 0.807 ± 0.426 (6) **  | 5.630 (1)           | 16.350 ± 1.520 (2) * | 45.020 ± 27.330 (2) * | 44.053 ± 1.109 (6) ** |

**Study Number:** S0939  
**Test Type:** Human Liver Microsome

**PA49: Summary of Cytochrome Activity**  
**Test Compound:** Z-guggulsterone  
**CAS Number:** 39025-23-5

**Date Report Requested:** 11/26/2019  
**Time Report Requested:** 09:53:42  
**Lab:** Research Triangle Institute

#### LEGEND

---

Data are displayed as mean  $\pm$  SEM (N) unless otherwise noted.

Statistical analysis performed by Jonckheere (trend) and Shirley or Dunn (pairwise) tests.

Statistical significance for a treatment group indicates a significant pairwise test compared to the vehicle control group

Statistical significance for the control group indicates a significant trend test

Statistical analysis for the positive control group compared to the vehicle control group was performed using the Wilcoxon test.

\* Statistically significant at  $P \leq 0.05$

\*\* Statistically significant at  $P \leq 0.01$

Cytochrome P450 2E1 was not measured for the 0.3 and 1  $\mu\text{M}$  dose groups. Positive controls were only run for the ATPase activity assay.

The 0.3  $\mu\text{M}$  results for P-glycoprotein ATPase Activity was not include in the statistical analysis since there was only one value in that group.

Ver = Verpamil

NR not recorded

**\*\* END OF REPORT \*\***