Table 3. Incidence and severity of non-neoplastic lesions at the Skin Site of Application in F344/N Rats and B6C3F1/N Mice in the 90 day dermal study of cedarwood oil.

| **Dose** | Epidermal hyperplasia | Epidermal hyperkeratosis | Epidermal Ulcer | Chronic Active Inflammation | Hair follicle hyperplasia | Sebaceous gland hyperplasia | Dermal Fibrosis |
| --- | --- | --- | --- | --- | --- | --- | --- |

| **Female Rats** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 0 (UC) | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 0 (VC) | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 6.25 | 4\* | 1.0 a | 1 | 1.0 | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 12.5 | 7\*\* | 1.7 | 5\* | 1.0 | 1 | 2.0 | 7\*\* | 1.0 | 1 | 1.0 | 4\* | 1.0 | 1 | 1.0 |
| 25 | 10\*\* | 2.1 | 10\*\* | 1.2 | 1 | 3.0 | 10\*\* | 1.2 | 9\*\* | 1.7 | 9\*\* | 1.8 | 7\*\* | 1.1 |
| 50 | 10\*\* | 2.8 | 10\*\* | 2.5 | 4\* | 2.3 | 10\*\* | 2.4 | 10\*\* | 2.8 | 10\*\* | 2.9 | 8\*\* | 1.8 |
| 100 | 10†† | 3.0 | 10†† | 3.0 | 10†† | 3.1 | 10†† | 2.4 | 10†† | 3.6 | 10†† | 3.0 | 10†† | 2.1 |
| **Male Rats** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 (UC) | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 0 (VC) | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 6.25 | 2 | 1.0 | 0 |  | 0 |  | 1 | 1.0 | 0 |  | 0 |  | 0 |  |
| 12.5 | 4\* | 1.3 | 1 | 1.0 | 1 | 1.0 | 4\* | 1.0 | 0 |  | 0 |  | 0 |  |
| 25 | 10\*\* | 2.0 | 7\*\* | 1.1 | 1 | 3.0 | 9\*\* | 1.4 | 9\*\* | 1.3 | 9\*\* | 1.9 | 7\*\* | 1.1 |
| 50 | 10\*\* | 2.9 | 10\*\* | 1.6 | 7\*\* | 2.6 | 10\*\* | 2.3 | 10\*\* | 2.0 | 10\*\* | 2.8 | 10\*\* | 2.4 |
| 100 | 9†† | 2.9 | 10†† | 3.0 | 8†† | 3.0 | 10†† | 2.7 | 9†† | 1.8 | 10†† | 3.0 | 10†† | 2.4 |
| **Female Mice** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 (UC) | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 1 | 1.0 | 0 |  |
| 0 (VC) | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 6.25 | 10\*\* | 2.1 | 2 | 1.5 | 2 | 3.0 | 10\*\* | 2.2 | 3 | 2.3 | 4\* | 1.3 | 2 | 1.0 |
| 12.5 | 10\*\* | 3.0 | 10\*\* | 2.7 | 6\*\* | 3.7 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 2.0 | 10\*\* | 2.9 |
| 25 | 10\*\* | 3.0 | 10\*\* | 3.0 | 9\*\* | 4.0 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 2.2 | 10\*\* | 3.0 |
| 50 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 4.0 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 2.0 | 10\*\* | 3.0 |
| 100 | 10†† | 3.0 | 10†† | 3.0 | 10†† | 4.0 | 10†† | 3.0 | 10†† | 3.0 | 10†† | 2.2 | 10†† | 3.0 |
| **Male Mice** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 (UC) | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 0 (VC)b | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  | 0 |  |
| 6.25 | 10\*\* | 2.6 | 7\*\* | 2.1 | 2 | 4.0 | 10\*\* | 2.4 | 10\*\* | 2.6 | 10\*\* | 1.3 | 3 | 2.7 |
| 12.5 | 10\*\* | 3.0 | 10\*\* | 2.9 | 8\*\* | 4.0 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 2.3 | 10\*\* | 3.0 |
| 25 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 3.8 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 2.6 | 10\*\* | 3.0 |
| 50 | 10\*\* | 3.0 | 10\*\* | 2.9 | 9\*\* | 3.7 | 10\*\* | 3.0 | 10\*\* | 3.0 | 10\*\* | 2.3 | 10\*\* | 3.0 |
| 100 | 10†† | 3.0 | 10†† | 2.9 | 10†† | 3.9 | 10†† | 3.2 | 10†† | 3.0 | 10†† | 2.0 | 10†† | 3.0 |

\* Significantly different (P≤0.05) from the vehicle control group by Fisher’s exact test

\*\* P≤0.01

†† Significantly different (P≤0.01) from the untreated control group by Fisher’s exact test

a Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

b Number examined n=9, for all other endpoints n=10