1. Buproprion (Rx Wellbutrin) has the following pharmacokinetic properties:

- Absorption: Nearly complete and rapid absorption from the intestinal tract.
- Distribution: Readily crosses the blood-brain barrier and placenta as well as into other organs and tissues. Protein binding is 85%.
- Metabolism: Extensively and exclusively metabolized by the liver. Four metabolites are produced, with possible lesser therapeutic activity than the parent drug. Intrinsic clearance (enzymatic activity) = 2180 L/hr.
- Elimination: Half-life is 14 hours. Systemic clearance is 1.14 L/hr/kg of body weight.

A) What is the calculated hepatic clearance of buproprion in Jerry B., (age 50, weight 62 kg, height 5’9”, with normal hepatic blood flow of 1500 ml/min and normal hepatic function)?

B) What is Jerry B.’s oral bioavailability ($F_h$)?

2. Predict the changes in $Cl_h$ given the following scenarios:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Direction of change</th>
<th>effect on $Cl_h$ for a low E drug</th>
<th>effect on $Cl_h$ for a high E drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>fraction of unbound drug</td>
<td>decreases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>intrinsic clearance</td>
<td>increases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hepatic blood flow</td>
<td>decreases</td>
<td></td>
<td></td>
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</tbody>
</table>

3. The USPDI monograph for fluvoxamine (Rx Luvox) gives the following pharmacokinetic information:

- Absorption: The absolute bioavailability of fluvoxamine is low.
- Distribution: The apparent volume of distribution is 25 L/kg.
- Protein binding: High (~80%)
- Metabolism: Extensively metabolized in the liver. All metabolites are inactive.
- Half-life: 15.6 hours

A) What is the calculated hepatic clearance of fluvoxamine for Sally T.(age 25, weight 70 kg, liver blood flow of 1500 ml/min)?

B) Is fluvoxamine a high or low clearance drug?

C) What is the extraction ratio of fluvoxamine in Sally T.?

D) What is the oral bioavailability ($F_h$)?