



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

## Methylphenidate, prolonged-release tablet 18 mg, 27 mg, 36 mg and 54 mg and modified release capsule 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 50 mg and 60 mg product-specific bioequivalence guidance

Draft Agreed by Methodology Working Party (MWP)	23 April 2024
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Keywords	Bioequivalence, generics, methylphenidate
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### Disclaimer:

*This guidance should not be understood as being legally enforceable and is without prejudice to the need to ensure that the data submitted in support of a marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.*

### Requirements for bioequivalence demonstration (MWP)

<b>Bioequivalence study design</b>	<b>For Single Unit Formulations</b>  <b>Single dose fasting:</b> All strengths or bracketing approach, healthy volunteers.  <b>Single dose fed:</b> The highest/most sensitive strength in healthy subjects may be sufficient provided that, in addition to the usual waiver of strength criteria, the shape of the formulations of the strengths should be similar.
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	<p><b>Background:</b> Single dose fasting and fed studies are required for prolonged-release formulations without accumulation.</p> <p><b>For Multiple Unit Formulations</b></p> <p><b>Single dose fasting:</b> Highest strength, healthy volunteers.</p> <p><b>Single dose fed:</b> Highest strength, healthy volunteers.</p> <p><b>Background:</b> Single dose fasting and fed studies are required for prolonged-release formulations without accumulation.</p>
	<b>cross-over</b>
<b>Analyte</b>	<input checked="" type="checkbox"/> <b>parent</b> <input type="checkbox"/> <b>metabolite</b> <input type="checkbox"/> <b>both</b>
	<input checked="" type="checkbox"/> <b>plasma/serum</b> <input type="checkbox"/> <b>blood</b> <input type="checkbox"/> <b>urine</b>
	<b>Enantioselective analytical method:</b> <input type="checkbox"/> <b>yes</b> <input checked="" type="checkbox"/> <b>no</b>
<b>Bioequivalence assessment</b>	Main pharmacokinetic variables:  Single dose fasting: AUC <sub>0-t</sub> , AUC <sub>0-inf</sub> , C <sub>max</sub> , AUC <sub>0-3h</sub> , C <sub>max0-3h</sub> , AUC <sub>3-24h</sub> and C <sub>max3-24h</sub>  Single dose fed: AUC <sub>0-t</sub> , AUC <sub>0-inf</sub> , C <sub>max</sub> , AUC <sub>0-4h</sub> , C <sub>max0-4h</sub> , AUC <sub>4-24h</sub> and C <sub>max4-24h</sub>
	<b>90% confidence interval:</b> 80.00– 125.00%
	<p><b>To be noted:</b> <i>In vitro</i> studies of release in alcohol solutions should also be performed. <i>In vitro</i> compatibility with mixing with applesauce should be demonstrated where applicable.</p>