Australian Government
Department of Health
Therapeutic Goods Administration

TGA use only

This form, when completed, will be classified as '**For official use only**'.
For guidance on how your information will be treated by the TGA see: Treatment of information provided to the TGA at <https://www.tga.gov.au/treatment-information-provided-tga>.

Additional strengths biowaiver template

- Refer to guidance document 'Completing the biowaiver templates' when completing this template.
- **Do not** include any text in fields or text boxes indicated for "**TGA use only"**.

For more information, refer to TGA website regarding bioequivalence data summary templates

1. Administrative information

Active Pharmaceutical Ingredient (API) in Australian Approved Name format	
Dosage form	
Proposed strength(s)	

2. Summary of requirements and outcomes

Select the finding in the outcome column that applies to your proposed products (test products)

Requirements	Outcome
Therapeutic range and dose	☐ Narrow ☐ Non-narrow
Solubility	☐ High ☐ Low

Requirements	Outcome
Pharmacokinetic Characteristics	☐ Linear ☐ Non-linear (less than proportional) ☐ Non-linear (greater than proportional)
Qualitative composition of the excipients of the different strengths	☐ Sufficiently similar ☐ Unacceptable differences
Quantitative composition of the excipients of the different strengths	☐ Proportional ☐ Identical amount of excipients ☐ Identical amount of excipients except filler (diluent) ☐ Others:
Dissolution profiles	☐ Similar and rapidly dissolving ☐ Similar and very rapidly dissolving ☐ Similar and non-rapidly dissolving ☐ Non-similar
Certificates of Analysis (CoAs)	Difference between biobatch test product and reference product assays within 5% ☐ Yes ☐ No

TGA use only - Comments for Section 2	
Conclusion	☐ Acceptable ☐ Not acceptable

3. Additional strength biowaiver

3.1 Application objective

Reason for the application of a biowaiver for not providing bioequivalence study data for all proposed dose strengths

TGA use only - Comments from review of Section 3.1

3.2 Nature of the dosage form

What was the dosage form of the additional strength test product(s)?

Do all additional strengths have the same dosage form and mechanism of release as the biobatch test product(s)?

Yes ☐ Go to question 3.3

No ☐ Justify differences in the nature of the dosage form below.

TGA use only - Comments from review of Section 3.2

3.3 Solubility

What is the solubility of the drug substance?

TGA use only - Comments from review of Section 3.3

3.4 Pharmacokinetic characteristics

Were linear pharmacokinetics observed over the dose range?

Yes ☐ Provide source of the evidence:

No ☐ State at which concentrations non-linearity occur and provide any known explanations:

Is the API a narrow therapeutic index (NTI) drug substance? Yes ☐ No ☐

Provide evidence on whether the API is NTI below.

TGA use only - Comments from review of Section 3.4

3.5 Test product formulation(s)

3.5.1 Product details

	Test product (Biobatch)	Additional strength 1	Additional strength 2	Additional strength 3
Drug Product Batch number				
Batch size and number of dose units				
Date of manufacture				
Expiry date				
Assay /Potency				
API lot number				

3.5.2 Product formulation(s)

Ingredients	Test product (Biobatch)	Additional strength 1	Additional strength 2	Additional strength 3
	Quantity in formulation (e.g. mg and %)			

3.5.3 Assurances

a. Were the different strengths manufactured by the same manufacturing process?
☐ Yes ☐ No

TGA use only - Comments from review of Section 3.5.1a

b. Was the qualitative composition of the different strengths the same?
☐ Yes ☐ No

TGA use only - Comments from review of Section 3.5.1b

c. Were the compositions of the strengths quantitatively proportional?

i.e. Was the ratio between the amount of drug substances(s) the same for all strengths (not applicable to immediate release products, the coating components, capsule shell, colour agents, and flavours)?
☐ Yes ☐ No

d. Was the composition of the strengths quantitatively identical in excipients?

§ If so:

- Were the quantities of all excipients identical and the amount of drug substance change was less than 5% of the weight (excluding coating components and capsule shell)?

or

- Was the difference in the quantity of drug substance between strengths compensated with a difference in the quantity of the filler to maintain the same core weight for all strengths and the amount of drug substance change was less than 5% of the core weight?
☐ Yes ☐ No

TGA use only - Comments from review of Section 3.5.1c and 3.5.1d

3.6 *In vitro* dissolution comparison between the different strengths of the test product

Location of the information

Dissolution study report	
Dissolution study protocol	

Validation of experimental analytical methods	
Individual and mean results and respective summary statistics	
Certificate of analysis of the reference product	
Certificate of analysis of the test products	

3.6.1 Summary of dissolution test method parameters

Apparatus	Are sinkers used? ☐ Yes ☐ No
Rate of operation	☐ 50 rpm for paddle ☐ 100 rpm for basket ☐ other system: If other system was selected, provide explanation:
Dissolution media	
Volume	
Temperature	
Sampling times	
Sample handling and storage	
Number of Dosage Units	
Sampling time (release)	
Filtration methods (in-line filtration or immediately after sampling)	
De-aeration method	

Reference pharmacopoeia (e.g. EP, BP, USP)	

3.6.2 Dissolution results of the biobatch test product

Strength:	
Batch number:	n = dosage units/ pH medium

n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					
Mean					
Range					
%RSD					
pH:					
Mean					
Range					
%RSD					
pH:					
Mean					
Range					
%RSD					
Release medium (if different to above):					
Mean					
Range					
%RSD					

3.6.3 Dissolution results of the additional strengths of the test products

Additional strength: Batch number: n = dosage units/ pH medium

n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					
Mean					
Range					
%RSD					
pH:					
Mean					
Range					
%RSD					
pH:					
Mean					
Range					
%RSD					
Release medium (if different to above):					
Mean					
Range					
%RSD					

3.6.4 Dissolution profile comparison

Additional test product strength:	Biobatch test product strength:
Batch number:	Batch number:

pH	Similarity factor (f2)	Time points used for f2 calculation

TGA use only - Comments from review of Section 3.6

4. List of questions to the applicant

TGA use only – List of questions

5. Applicant’s response to the list of questions

6. TGA’s assessment and conclusion

TGA’s assessment of applicant’s responses

TGA use only – Assessment of applicant’s answers to the list of questions

TGA’s overall conclusion and recommendations

TGA use only – Conclusion and recommendations