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>.

Biopharmaceutics Classification System (BCS)-based 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 and strength(s)	
Daily dose	
Final (test) product manufacturer name and address	
Dissolution testing laboratory name and address	
Test product details: batch size and batch number	
Reference product name, sponsor, and country of procurement	

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
Stable drug substance throughout *in vitro* testing	☐ Yes ☐ No
Human absorption	☐ >85% ☐ <85%
Permeability	☐ High ☐ Low
BCS class	☐ I ☐ II ☐ III ☐ IV
Dosage form characteristics	☐ Oral ☐ Systemically acting ☐ Immediate release (Note, all three must apply)
Comparison of excipients in the formulations between test and reference products	☐ Quantitatively - and qualitatively identical ☐ Qualitatively identical but not quantitatively identical ☐ Neither quantitatively nor qualitatively identical (only applicable for BCS class I)
Dissolution profiles	☐ Similar and very rapidly dissolving ☐ Similar and rapidly dissolving ☐ Non-similar ☐ Non-very rapidly dissolving ☐ Non-rapidly dissolving
Certificates of Analysis (CoAs)	Difference between test and reference product assays within 5% ☐ Yes ☐ No

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

3. Introduction

Provide brief introduction of the drug substance and the proposed finished drug products (test products)

Is the Active Pharmaceutical Ingredient (API) a narrow therapeutic index (NTI) drug substance?

Yes ☐	**Stop** The drug substance should not belong to the group of narrow therapeutic index drugs. Please discuss suitability of a BCS-based biowaiver with TGA if you wish to proceed further. To contact TGA, see TGA contact details for enquiries about prescription medicines. Provide location in the dossier of TGA correspondence regarding the suitability of a BCS-based biowaiver (if any):
No ☐	Provide evidence to support the API is not a NTI below.

3.1 Application objective

Reason for application of biowaiver and BCS Classification

Were the drug substance and test product used in the studies for the BCS-based biowaiver justification:

- manufactured by the same proposed drug substance and drug product manufacturers listed in Module 3, and
- manufactured in the same manner as proposed for marketing purposes?

Yes ☐	Go to section 3.2
No ☐	State the difference in the formulation proposed for marketing and those used for comparative dissolution studies and justify below why a BCS-based biowaiver can be applied:

3.2 Comparison between the test and reference products

What were the similarities and differences between the test and reference products?

3.3 Basic pharmacokinetic information

Was the mass balance and absolute BA studies conducted on the highest strength dose?

Yes ☐ Go to section 4

No ☐ Go to next question in this section

Were linear pharmacokinetics observed over the dose range?

Yes ☐ Provide source of the evidence:

No ☐ Please discuss suitability of a BCS-based biowaiver with TGA if you wish to proceed further. To contact TGA, see TGA contact details for enquiries about prescription medicines.

Provide location in the dossier of TGA correspondence regarding the suitability of a BCS-based biowaiver (if any):

TGA use only - Comments from review of Section 3

4. BCS biowaiver assessment

4.1 Solubility

Location of the information

Study report	
Study protocol	
Description of solubility method and conditions	
Description and validation of the stability-indicating analytical method	

Dates of the study

Name and address of the study site

4.1.1 Solubility method

Apparatus	
Volume	
Time	
Dose/ amount	
Temperature	
pH values	
Buffer composition	

4.1.2 Solubility at different pH values and replicates

Theoretical pH	Repeat	Observed pH	Adjusted pH	Individual concentration at saturation (Cs) values	Cs (mean)	Quantity dissolved in 250 ml
pH 1.2	1					
	2					
	3					
Intermediate pH:	1					
	2					
	3					
pH 4.5	1					
	2					
	3					

Theoretical pH	Repeat	Observed pH	Adjusted pH	Individual concentration at saturation (Cs) values	Cs (mean)	Quantity dissolved in 250 ml
Intermediate pH:	1					
	2					
	3					
pH 6.8	1					
	2					
	3					
Other intermediate pH values**:	1					
	2					
	3					

** Other intermediate pH values e.g. pKa, pKa-1, pKa+1

Insert the solubility (concentration at saturation) vs. pH plots based on the data provided in the table above to identify the pH of minimum solubility below.

TGA use only - Comments from review of Section 4.1

4.2 Human absorption (methods and results)

4.2.1 Absolute bioavailability (BA) (in human)

Reference citation of the absolute BA data source	
Oral dose	
Intravenous dose	
Number of subjects	

Absolute BA result	

4.2.2 Mass balance (in human)

Reference citation of the mass balance data source	
Dose	
Number of subjects	
Mass balance result	

4.2.3 or permeability

Test system	
Concentration	
Result	

4.2.4 Other information

Influence of the transporters to absorption	

TGA use only - Comments from review of Section 4.2

4.3 Comparison of test and reference formulations / excipients

Ingredient	Function	Test product quantity	Reference product quantity (if known)

Ingredient	Function	Test product quantity	Reference product quantity (if known)

TGA use only - Comments from review of Section 4.3

4.4 dissolution comparison

Location of the information

Study report	
Study protocol	
Batch information on test and reference batches including certificates of analysis (CoAs)	
Validation of experimental analytical methods	
Individual and mean results and respective summary statistics	

Dates of the study

Name and address of the study site

4.4.1 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	
Number of Dosage Units	
Sample handling and storage	
Filtration methods (e.g. in-line filtration or immediately after sampling)	
De-aeration method	

Batch number: n = dosage units/ pH medium

n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					
Mean					
%RSD					

pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH of minimum solubility:					
Mean					
%RSD					

Batch number: n = dosage units/ pH medium

n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH of minimum solubility:					

Mean					
%RSD					

Provide the mean dissolution results of the above test batches below:

Mean of the dissolution results					
n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH of minimum solubility:					
Mean					
%RSD					

Batch number: n = dosage units/ pH medium

n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					

Mean					
%RSD					
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH of minimum solubility:					
Mean					
%RSD					

Batch number: n = dosage units/ pH medium

n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH:					
Mean					

%RSD					
pH of minimum solubility:					
Mean					
%RSD					

Provide the mean dissolution results of the above reference batches below:

Mean of the dissolution results					
n pH of medium	% Label Claim Released				
	(Mins)	(Mins)	(Mins)	(Mins)	(Mins)
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH:					
Mean					
%RSD					
pH of minimum solubility:					
Mean					
%RSD					

4.4.2 Dissolution profile comparison

Strength:	Test product batch number: Reference product batch number:

pH	Similarity factor (f2)	Time points used for f2 calculation	Discussion of dissolution profile similarity*

* Discussion provided **must not** be in terms of clinical/therapeutical relevance (i.e. *in vitro in vivo* correlation).

TGA use only - Comments from review of Section 4.4

4.5 Testing laboratory

4.5.1 Audit(s)

Name of testing facility	Location of internal quality assurance methods and results

4.5.2 GLP compliance/certification

Name of the testing facility	Location of the monitoring, auditing or inspection reports	Location of the compliance certifications/accreditations

TGA use only - Comments from review of Section 4.5

5. Essential similarity/appropriateness of drug product specification (if applicable)

What are your proposed drug product dissolution specifications?	

Do the proposed drug product dissolution specifications reflect the dissolution profile characteristics in this BCS-based biowaiver?

Yes ☐ Go to section 6

No ☐ Justify why wider dissolution specifications are proposed:

TGA use only - Comments from review of Section 5

6. References of relevant regulatory guidelines and scientific papers

7. List of questions to the applicant

TGA use only – List of questions

8. Applicant's response to the list of questions

9. 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