Operational Procedures (OP)

Access Consortium

Operational procedures for the Generic Medicines Work-Sharing Initiative (GMWSI)

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Introduction

This document outlines operational procedures and recommendations for planning and implementing the Generic Medicines Work-sharing Initiative (GMWSI) for the regulatory agencies within the Access Consortium. The agencies are:

- Therapeutic Goods Administration (TGA), Australia
- Health Canada (HC), Canada
- Health Sciences Authority (HSA), Singapore
- Swissmedic (SMC), Switzerland
- Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom

The initiative is based on Europe's decentralized procedure, where 1 agency acts as a reference regulatory agency (RRA) and will evaluate Modules 2 to 5. Each participating agency acts as a concerned regulatory agency (CRA) and, with the RRA, evaluates their respective module 1. The CRAs peer review the assessment reports (ARs) and the proposed List of Questions (LoQ) provided by the RRA on Modules 2 to 5, consult the modules where necessary and provide supplementary comments as needed.

Each agency makes its own decision based on the recommendations made in the ARs. If, during the process, the participating agencies are unable to reconcile issues with the data, the agencies may seek additional information and undertake further independent review.

Scope

To be considered for this initiative, the proposed product should be regarded as a generic product by all the participating agencies. All pharmaceutical (dosage) forms are eligible.

Application considerations

An applicant wishing to participate in this innovative work-sharing initiative must submit an Expression of Interest (EoI) form to each agency proposed for this initiative. The applicant should submit this form at least 3 months before the planned submission date.

Applications for this initiative should be submitted at the same time to at least 2 of the Access Consortium members.

The applicant should submit the same Modules 2 to 5 to all of the agencies involved in the initiative. However, there may be **minor** differences in the applications submitted to the various agencies participating in the initiative. For example, there may be differences in packaging formats such as bottles versus unit dose blisters. **Major** differences between applications may make the work-sharing process more complicated, which may delay the assessment process. For example, submitting multiple studies using different comparator products would be considered a major difference.

If there are minor differences between datasets, the applicant should provide a 'Summary of Differences' table. This table is part of the EoI form. The table should outline the differences in the quality and bioequivalence study information provided to each participating agency. The Access agencies will discuss these differences and determine if the application is suitable for GMWSI.

Please note that all Access agencies accept the use of foreign comparator products in bioequivalence studies. Therefore, for submissions requiring clinical equivalence (whether pharmacokinetic bioequivalence or therapeutic equivalence), it may be possible to use a single comparator product, along with country-specific justifications for using the foreign comparator product. For further

information on the acceptability of a foreign comparator product in each Access jurisdiction please see Appendix 1: Access countries that will accept a previously conducted bioequivalence (BE) study using a Foreign Comparator Product (FCP), and Appendix 2: Current regulatory requirements regarding the acceptance of Foreign Comparator Products. Additional information and references are also included in the section Related Links below.

Also note that Module 1 is specific to each Access agency. Thus, it will continue to be different for the applications filed in the different Access jurisdictions (as per national requirements).

Although an applicant may propose a preferred RRA, the Access agencies will ultimately determine the RRA and CRAs for any submission. The agencies base their decision on factors such as the Access Consortium's operational needs.

In general, 1 agency (the RRA) will perform the evaluation and the other participating agencies will act as CRAs. However, in some cases, the application may be split up, with multiple agencies doing the initial assessment. The roles of each participating agency will be determined in line with operational requirements.

In the EoI, the applicant should indicate their preferred timeframe for submitting their responses to the LoQs provided by the agencies. The timeframe should be either 30 or 60 calendar days.

Applications should fully address the requirements of all jurisdictions to be included in the procedure. Applicants should also acknowledge that they will need to work collaboratively with the agencies. While a single application that covers broader issues for more than 1 agency may seem more onerous, it will ultimately reduce the overall regulatory burden.

Operational approach

The process needs to work concurrently within the regulatory systems of the participating agencies. This section outlines the steps and issues that need to be considered when implementing the procedure.

All timelines/days are based on calendar days. If a milestone falls on a weekend or a national holiday, the milestone is the preceding business day. Please note that the following timeframes are target timeframes and may be adjusted depending on the complexity of the application.

Pre-submission meeting/teleconference (minimum 2 months in advance)

Once the participating agencies receive an EoI form, they will work together to discuss the application, its suitability for inclusion in the work-sharing initiative, the RRA and CRAs, and next steps.

A pre-submission meeting/teleconference between the applicant and their local Access agency, or all participating agencies if possible (may not be granted due to operational and resource challenges), is recommended. This meeting is used to discuss the technical aspects of the submission, and to confirm the logistics and expectations related to requirements, timelines for assessment and the process. The meeting also gives agencies a chance to respond to any additional questions the applicant may have.

The teleconference should take place at least 2 months before the agreed submission date of the application. The applicant must follow the usual procedures of their local agency when requesting a pre-submission meeting.

The applicant will be asked to provide their questions at least 2 weeks before the pre-submission teleconference. Within 2 weeks of this teleconference, the applicant must provide a record of the meeting, summarizing the points that have been agreed to.

Submitting application (less than 15 days)

Applications should be submitted to each participating agency at the same time or as agreed with the participating agencies. The process begins as soon as all agencies have received the applications. This is “Day -15” of the process.

If applicable, the Active Substance Master File/Drug Master File must be submitted to each participating agency before the application is filed, with the appropriate local forms.

Accepting application (15 days)

Once the participating agencies receive the application, the RRA and CRAs screen and validate the technical and administrative information. They check that their national legislation and data requirements (for example, application forms, user fees) have been met and that the application can be accepted for assessment.

The RRA and CRAs then inform the applicant if their application has been accepted for assessment. If accepted, the applicant is also given a summary of the target timeframes for each step in the process. The day of acceptance of the application for assessment by the RRA is “Day 0” of the process. The CRAs will make efforts to accept the application on the same day as the RRA.

Round 1 assessment

Initial assessment by the RRA (60 days)

The RRA evaluates Modules 2 to 5 and prepares an AR and an LoQ. At the same time, the RRA and CRAs evaluate their national Module 1 and prepare an LoQ for this module. The RRA then shares the AR and LOQ on Modules 2 to 5 with the CRAs.

While a consolidated LoQ is the preferred option, the RRA may instead send rolling questions to the local applicant to seek clarification during the assessment process. If applicable, the responses to these clarification questions have a short timeframe (for example, 5 days). The RRA then shares these responses with the CRAs.

Peer review by CRAs (25 days)

As part of the peer review process, the CRAs:

- conduct a peer review of the AR and LoQ
- consult the modules (as needed)
- share comments and additional questions on Modules 2 to 5 with the RRA

Finalising ARs and LoQs (5 days)

The RRA and CRAs discuss the LoQ and any additional questions. The RRA prepares the consolidated LoQ on Modules 2 to 5. The RRA and each CRA forward the consolidated LoQ, as well as their questions on Module 1 (includes questions on product information and labelling), to their local applicant.

Submitting responses to the LoQ by applicant (30 or 60 days)

The applicant prepares and sends the same responses to the LoQ on Modules 2 to 5 to the RRA **and** CRAs by way of the respective local applicants. At the same time, the local applicant sends responses to the Module 1 questions to their respective agencies.

As stated, the applicant should indicate in the EoI their preferred timeframe for submitting responses to the LoQ (either 30 or 60 days). However, the applicant will be able to respond any time after 30 days and before 60 days.

Round 2 assessment

Assessing responses to LoQ (30 days)

The RRA prepares an AR of the responses on the consolidated LoQ for Modules 2 to 5 and shares it with the CRAs. At the same time, the RRA and CRAs prepare an AR of the responses to their respective country-specific questions on Module 1.

Peer review by CRAs (15 days)

The CRAs conduct a peer review of the AR of the responses to Modules 2 to 5 and provide feedback. If necessary, the RRA prepares an additional LoQ, which each agency sends to the local applicant. The 15-day timeframe includes the time for peer review and for any coordination between the RRA and the CRAs.

Finalising ARs and additional LoQ (5 days)

If an additional LoQ (in general, this corresponds to the preliminary decision in Switzerland) is not necessary, each agency makes a final decision. The agencies also undertake the necessary administrative steps to finalise the process for their country.

Submitting responses to the additional LoQ (if applicable) (15 days)

The applicant prepares and sends responses to the additional LoQ (if applicable) to the RRA **and** CRAs.

Round 3 assessment (if applicable)

Assessing responses to the additional LoQ (15 days)

The RRA prepares an AR of the responses to the additional LoQ following the process described for round 2.

Peer review of responses by the CRAs, finalising the ARs and additional LoQ (if applicable) (5 days)

The CRAs conduct a peer review of the responses and provide feedback in order for the RRA to finalise the AR.

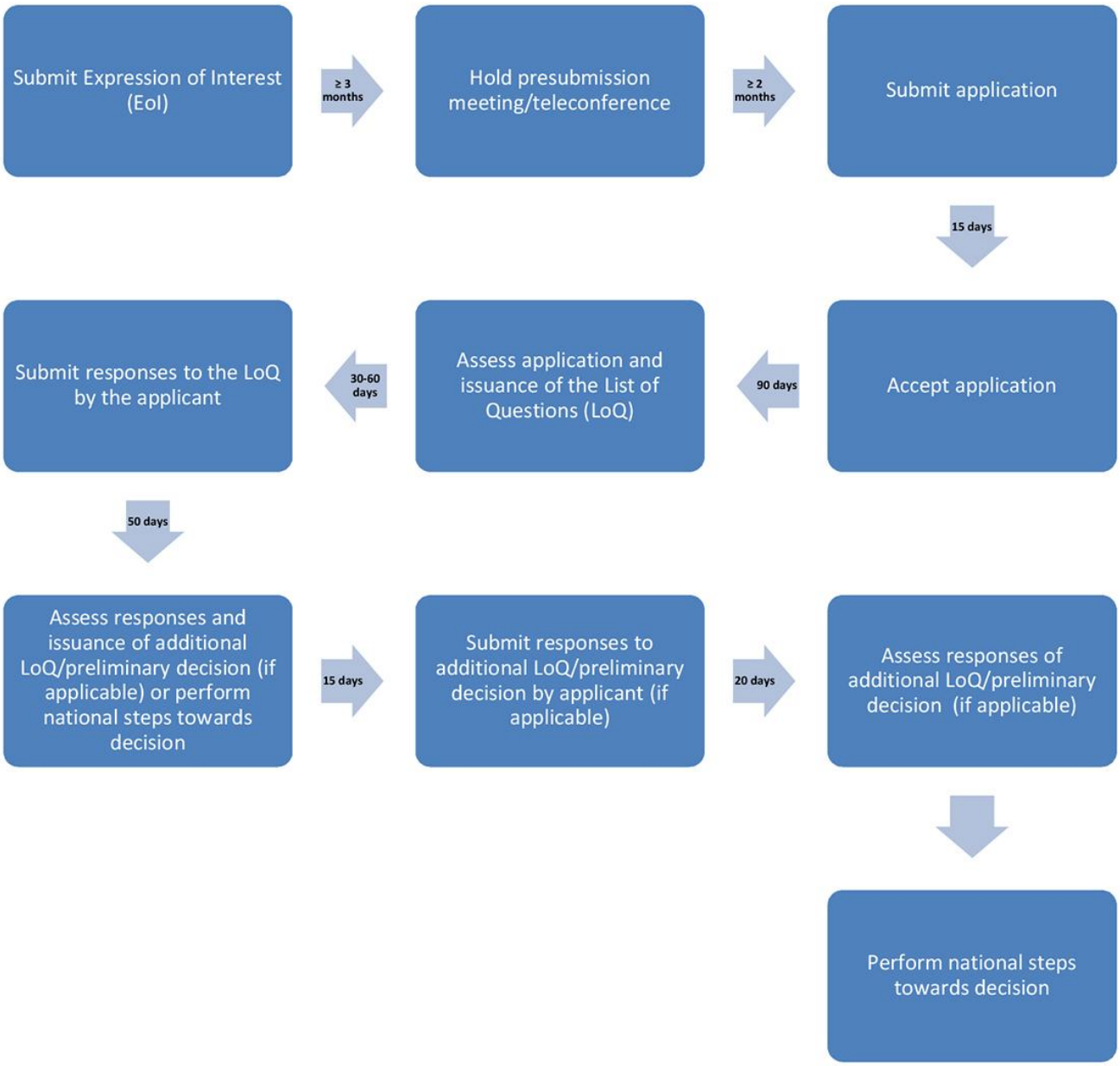
National steps

Each agency makes a final decision (or seeks further clarification on issues separately before making a final decision) and undertakes the necessary administrative steps to finalise the process nationally. Depending on each agency's assessment outcome, an authorisation letter or additional questions is issued.

These communications may not necessarily happen at the same time. Total maximum elapsed timeframe from when the application is accepted (day 0) to the start of the national steps:

- 170 to 200 calendar days (including the applicant's response time and if only 1 list of questions is required) **or**
- 205 to 235 calendar days (if an additional list of questions is required)

Figure 1: Schematic representation of the expected milestones and timelines for the various steps in the process



Any further questions about this initiative can be directed to the local regulatory authority:

- Australia: PMABinternationalevaluations@health.gov.au
- Canada: collaboration@hc-sc.gc.ca
- Singapore: HSA_TP_Enquiry@hsa.gov.sg
- Switzerland: Access@swissmedic.ch
- United Kingdom: Access-MHRA@mhra.gov.uk

Communications by e-mail should include “Access Consortium - GMWSI” in the subject line.

Related links

- A survey of the regulatory requirements for the acceptance of foreign comparator products by participating regulators and organizations of the International Generic Drug Regulators Programme
- Biopharmaceutic studies (TGA guidance)
- Comparator products in bioequivalence/therapeutic equivalence studies (MHRA guidance)
- Guidance document: Use of a foreign-sourced reference product as a Canadian reference product (HC guidance)
- Guidance on therapeutic product registration in Singapore: Product interchangeability and biowaiver request for chemical generic drugs application (HSA guidance)
- Guidance document: Authorisation of human medicinal product with known active pharmaceutical substances HMV4 (SMC guidance)

Appendix 1: Access countries that will accept a previously conducted bioequivalence (BE) study using a Foreign Comparator Product (FCP)

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
Europe (EMA Country)	Australia	Y	FCP and local CP are identical in appearance[3], are from the same global company and have similar dissolution.	Only applies to oral dosage forms. Contact the TGA for other dosage forms.
	Canada	Y	The formulation of the FCP and the local CP are qualitatively and quantitatively the same[1] and are from the same innovator company or corporate entity. The medicinal ingredient is considered to have high solubility. Depending on the drug product, comparative dissolution data, comparative physicochemical property data, *in-vitro* performance data or device attribute data may also be required.	Modified release products (exceptions may apply). Immediate release drug products that contain Critical Dose Drugs or a drug substance that is not considered to have high solubility.
	Singapore	Y	FCP is from the same global company as Singapore reference product (SRP) or marketed in its country of origin	FCP which are narrow therapeutic index drugs and not manufactured at the same drug product manufacturing site as the SRP will not be accepted.

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			through a licensing arrangement with the Singapore Product Registrant. Comparative dissolution data are only required if the FCP is not manufactured at the same drug product manufacturing site as the SRP.	
	Switzerland	Y	Pharmaceutical bridging between FCP and local RP is eligible as long as the criteria listed in the respective guidance document[1] are fulfilled. These criteria cover, among others, composition, aspects concerning the pharmaceutical form including dimension/weight as well as release mechanism, and dissolution profiles.	No exceptions.
	UK[4]	Y	The FCP would normally be expected to be: • part of the same GMA as the UK RMP, or • marketed in the country of origin through a licensing arrangement with the innovator company or	Applies to BE, PK and TE studies provided in support of generic/hybrid applications. In case of complex products, it is recommended that MHRA are consulted for specific advice. In some cases, it may be accepted to perform studies using another CP, product X, that was itself submitted as an application referring to the RMP

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			corporate entity that currently markets the medicine in the UK. The FCP used is required to be representative of the UK RMP, but it is not required to be identical to it. This means that certain minor differences between both products may be accepted if justified, provided this is supported by bridging data (see published guidance on data requirements[1]).	(e.g. new indications, strength, route of administration, pharmaceutical form), but is not part of the same GMA as the RMP. Additional non-clinical and/or clinical studies would have been submitted in support of product X. Applicants are advised to discuss the dossier requirements in such situations with the MHRA.
United States of America	Australia	Y	FCP and local CP are identical in appearance[3], are from the same global company and have similar dissolution.	Only applies to oral dosage forms. Contact the TGA for other dosage forms.
	Canada	Y	The formulation of the FCP and the local CP are qualitatively and quantitatively the same[1] and are from the same innovator company or corporate entity. The medicinal ingredient is considered to have high solubility. Depending on the drug product, comparative dissolution data, comparative physicochemical property data, *in-vitro* performance data or	Modified release products (exceptions may apply). Immediate release drug products that contain Critical Dose Drugs or a drug substance that is not considered to have high solubility.

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			device attribute data may also be required.	
	Singapore	Y	FCP is from the same global company as Singapore reference product (SRP) or marketed in its country of origin through a licensing arrangement with the Singapore Product Registrant. Comparative dissolution data are only required if the FCP is not manufactured at the same drug product manufacturing site as the SRP.	FCP which are narrow therapeutic index drugs and not manufactured at the same drug product manufacturing site as the SRP will not be accepted.
	Switzerland	Y	Pharmaceutical bridging between FCP and local RP is eligible as long as the criteria listed in the respective guidance document[1] are fulfilled. These criteria cover, among others, composition, aspects concerning the pharmaceutical form including dimension/weight as well as release mechanism, and dissolution profiles.	No exceptions.
	UK[4]	Y	The FCP would normally be expected to be:	Applies to BE, PK and TE studies provided in support of generic/hybrid applications. In case of complex

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			• part of the same GMA as the UK RMP, or • marketed in the country of origin through a licensing arrangement with the innovator company or corporate entity that currently markets the medicine in the UK. The FCP used is required to be representative of the UK RMP, but it is not required to be identical to it. This means that certain minor differences between both products may be accepted if justified, provided this is supported by bridging data (see published guidance on data requirements[1]).	products, it is recommended that MHRA are consulted for specific advice. In some cases, it may be accepted to perform studies using another CP, product X, that was itself submitted as an application referring to the RMP (e.g. new indications, strength, route of administration, pharmaceutical form), but is not part of the same GMA as the RMP. Additional non-clinical and/or clinical studies would have been submitted in support of product X. Applicants are advised to discuss the dossier requirements in such situations with the MHRA.
Canada	Australia	Y	FCP and local CP are identical in appearance[3], are from the same global company and have similar dissolution.	Only applies to oral dosage forms. Contact the TGA for other dosage forms.
	Canada	Y	Canadian Comparator Product always accepted	-----
	Singapore	Y	FCP is from the same global company as Singapore reference product (SRP) or	FCP which are narrow therapeutic index drugs and not manufactured at

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			marketed in its country of origin through a licensing arrangement with the Singapore Product Registrant. Comparative dissolution data are only required if the FCP is not manufactured at the same drug product manufacturing site as the SRP.	the same drug product manufacturing site as the SRP will not be accepted.
	Switzerland	Y	Pharmaceutical bridging between FCP and local RP is eligible as long as the criteria listed in the respective guidance document[1] are fulfilled. These criteria cover, among others, composition, aspects concerning the pharmaceutical form including dimension/weight as well as release mechanism, and dissolution profiles.	No exceptions.
	UK[4]	Y	The FCP would normally be expected to be: • part of the same GMA as the UK RMP, or • marketed in the country of origin through a licensing arrangement	Applies to BE, PK and TE studies provided in support of generic/hybrid applications. In case of complex products, it is recommended that MHRA are consulted for specific advice.

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			with the innovator company or corporate entity that currently markets the medicine in the UK. The F CP used is required to be representative of the UK RMP, but it is not required to be identical to it. This means that certain minor differences between both products may be accepted if justified, provided this is supported by bridging data (see published guidance on data requirements[1]).	In some cases, it may be accepted to perform studies using another CP, product X, that was itself submitted as an application referring to the RMP (e.g. new indications, strength, route of administration, pharmaceutical form), but is not part of the same GMA as the RMP. Additional non-clinical and/or clinical studies would have been submitted in support of product X. Applicants are advised to discuss the dossier requirements in such situations with the MHRA.
Australia	Australia	Y	Australian Comparator Product always accepted	------
	Canada	Y	The formulation of the FCP and the local CP are qualitatively and quantitatively the same[1] and are from the same innovator company or corporate entity. The medicinal ingredient is considered to have high solubility. Depending on the drug product, comparative dissolution data, comparative physicochemical property data, *in-vitro* performance data or	Modified release products (exceptions may apply). Immediate release drug products that contain Critical Dose Drugs or a drug substance that is not considered to have high solubility.

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			device attribute data may also be required.	
	Singapore	Y	FCP is from the same global company as Singapore reference product (SRP) or marketed in its country of origin through a licensing arrangement with the Singapore Product Registrant. Comparative dissolution data are only required if the FCP is not manufactured at the same drug product manufacturing site as the SRP.	FCP which are narrow therapeutic index drugs and not manufactured at the same drug product manufacturing site as the SRP will not be accepted.
	Switzerland	Y	Pharmaceutical bridging between FCP and local RP is eligible as long as the criteria listed in the respective guidance document[1] are fulfilled. These criteria cover, among others, composition, aspects concerning the pharmaceutical form including dimension/weight as well as release mechanism, and dissolution profiles.	No exceptions.

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
	UK[4]	Y	The F CP would normally be expected to be: • part of the same GMA as the UK RMP, or • marketed in the country of origin through a licensing arrangement with the innovator company or corporate entity that currently markets the medicine in the UK. The F CP used is required to be representative of the UK RMP, but it is not required to be identical to it. This means that certain minor differences between both products may be accepted if justified, provided this is supported by bridging data (see published guidance on data requirements[1]).	Applies to BE, PK and TE studies provided in support of generic/hybrid applications. In case of complex products, it is recommended that MHRA are consulted for specific advice. In some cases, it may be accepted to perform studies using another CP, product X, that was itself submitted as an application referring to the RMP (e.g. new indications, strength, route of administration, pharmaceutical form), but is not part of the same GMA as the RMP. Additional non-clinical and/or clinical studies would have been submitted in support of product X. Applicants are advised to discuss the dossier requirements in such situations with the MHRA.
Singapore	Australia	Y	FCP and local CP are identical in appearance[3], are from the same global company and have similar dissolution.	Only applies to oral dosage forms. Contact the TGA for other dosage forms.
	Canada	Y	The formulation of the FCP and the local CP are qualitatively and	Modified release products (exceptions may apply). Immediate release drug

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			quantitatively the same[1] and are from the same innovator company or corporate entity. The medicinal ingredient is considered to have high solubility. Depending on the drug product, comparative dissolution data, comparative physicochemical property data, *in-vitro* performance data or device attribute data may also be required.	products that contain Critical Dose Drugs or a drug substance that is not considered to have high solubility.
	Singapore	Y	Singaporean Comparator Product always accepted	-----
	Switzerland	Y	Pharmaceutical bridging between FCP and local RP is eligible as long as the criteria listed in the respective guidance document[1] are fulfilled. These criteria cover, among others, composition, aspects concerning the pharmaceutical form including dimension/weight as well as release mechanism, and dissolution profiles.	No exceptions.

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
	UK[4]	Y	The F CP would normally be expected to be: • part of the same GMA as the UK RMP, or • marketed in the country of origin through a licensing arrangement with the innovator company or corporate entity that currently markets the medicine in the UK. The F CP used is required to be representative of the UK RMP, but it is not required to be identical to it. This means that certain minor differences between both products may be accepted if justified, provided this is supported by bridging data (see published guidance on data requirements[1]).	Applies to BE, PK and TE studies provided in support of generic/hybrid applications. In case of complex products, it is recommended that MHRA are consulted for specific advice. In some cases, it may be accepted to perform studies using another CP, product X, that was itself submitted as an application referring to the RMP (e.g. new indications, strength, route of administration, pharmaceutical form), but is not part of the same GMA as the RMP. Additional non-clinical and/or clinical studies would have been submitted in support of product X. Applicants are advised to discuss the dossier requirements in such situations with the MHRA.
Switzerland	Australia	Y	FCP and local CP are identical in appearance[3], are from the same global company and have similar dissolution.	Only applies to oral dosage forms. Contact the TGA for other dosage forms.
	Canada	Y	The formulation of the FCP and the local CP are qualitatively and	Modified release products (exceptions may apply). Immediate release drug

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
			quantitatively the same[1] and are from the same innovator company or corporate entity. The medicinal ingredient is considered to have high solubility. Depending on the drug product, comparative dissolution data, comparative physicochemical property data, *in-vitro* performance data or device attribute data may also be required.	products that contain Critical Dose Drugs or a drug substance that is not considered to have high solubility.
	Singapore	Y	FCP is from same global company as Singapore reference product (SRP) or marketed in its country of origin through a licensing arrangement with the Singapore Product Registrant. Comparative dissolution data are only required if the FCP is not manufactured at the same drug product manufacturing site as the SRP.	FCP which are narrow therapeutic index drugs and not manufactured at the same drug product manufacturing site as the SRP will not be accepted.
	Switzerland	Y	Swiss Comparator Product always accepted	-----

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
	UK[4]	Y	The FCP would normally be expected to be: • part of the same GMA as the UK RMP, or • marketed in the country of origin through a licensing arrangement with the innovator company or corporate entity that currently markets the medicine in the UK. The F CP used is required to be representative of the UK RMP, but it is not required to be identical to it. This means that certain minor differences between both products may be accepted if justified, provided this is supported by bridging data (see published guidance on data requirements[1]).	Applies to BE, PK and TE studies provided in support of generic/hybrid applications. In case of complex products, it is recommended that MHRA are consulted for specific advice. In some cases, it may be accepted to perform studies using another CP, product X, that was itself submitted as an application referring to the RMP (e.g. new indications, strength, route of administration, pharmaceutical form), but is not part of the same GMA as the RMP. Additional non-clinical and/or clinical studies would have been submitted in support of product X. Applicants are advised to discuss the dossier requirements in such situations with the MHRA.
UK	Australia	Y	FCP and local CP are identical in appearance[3], are from the same global company and have similar dissolution.	Only applies to oral dosage forms. Contact the TGA for other dosage forms.

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
	Canada	Y	The formulation of the FCP and the local CP are qualitatively and quantitatively the same[1] and are from the same innovator company or corporate entity. The medicinal ingredient is considered to have high solubility. Depending on the drug product, comparative dissolution data, comparative physicochemical property data, *in-vitro* performance data or device attribute data may also be required.	Modified release products (exceptions may apply). Immediate release drug products that contain Critical Dose Drugs or a drug substance that is not considered to have high solubility.
	Singapore	Y	FCP is from same global company as Singapore reference product (SRP) or marketed in its country of origin through a licensing arrangement with the Singapore Product Registrant. Comparative dissolution data are only required if the FCP is not manufactured at the same drug product manufacturing site as the SRP.	FCP which are narrow therapeutic index drugs and not manufactured at the same drug product manufacturing site as the SRP will not be accepted.
	Switzerland	Y		
	UK	Y	UK comparator always accepted	

BE study used a Comparator Product (CP) from?	Access Country	Potentially Acceptable	Key Criteria[1]	Key Exceptions/other comments[2]
				In some cases, it may be accepted to perform studies using another CP, product X, that was itself submitted as an application referring to the RMP (e.g. new indications, strength, route of administration, pharmaceutical form), but is not part of the same GMA as the RMP. Additional non-clinical and/or clinical studies would have been submitted in support of product X. Applicants are advised to discuss the dossier requirements in such situations with the MHRA.

1 Further information can be found in Appendix 2 below and the Access Country specific guidelines.

Australia: The Australian Regulatory Guidelines for Prescription Medicines (ARGPM) presents both a decision tree and checklist to establish the requisite evidence

Canada: *Guidance Document: Use of a Foreign-sourced Reference Product as a Canadian Reference Product (2018)*.

Singapore: Appendix 10 Product Interchangeability and Biowaiver Request for Chemical Generic Drug Applications (April 2022)

Switzerland: Guidance document: Authorisation of human medicinal product with known active pharmaceutical substance HMV4

United Kingdom: Comparator products in Bioequivalence/Therapeutic Equivalence studies - GOV.UK (www.gov.uk).

2. Additional exceptions to the criteria outlined in Appendix 1 may exist; as a result, the appropriate Access regulator should be consulted.

3 Same appearance means same size, mass, shape, colour and markings.

4 Applications to Northern Ireland (NI) only need to comply with EU requirements for comparator products as these will be submitted through EU mutual recognition or decentralised procedures.

Appendix 2: Current regulatory requirements regarding the acceptance of Foreign Comparator Products (FCPs)

The following table summarises the current criteria for accepting FCPs among the Access countries.

Core requirements for accepting foreign comparator products (✓: Permitted; X: Not permitted)

Foreign Comparator Criteria	TGA	HC	HSA	Swissmedic	MHRA*
Drug substance properties					
Narrow Therapeutic Index/Critical Dose	✓	X	✓#	✓	(✓)**
Complicated PK, variable/incomplete absorption, substantial first pass metabolism	✓	(✓)**	✓	✓	(✓)**
Low solubility	✓	X	✓	✓	✓
Drug product properties					
Immediate-release	✓	✓	✓	✓	✓
Modified-release (delayed and sustained)	✓	(X)**	✓	✓	(✓)**
Inhalation products	✓	✓	✓	✓	(✓)**
Nasal products	✓	✓	✓	✓	(✓)**
Similar drug product physical characteristics (e.g. size, weight, shape, colour, scoring, coating)	✓	✓	✓	✓	(✓)***

Foreign Comparator Criteria	TGA	HC	HSA	Swissmedic	MHRA*
Similar excipient composition	✓	✓	✓	✓	✓
Comparable physicochemical testing other than dissolution	✓	✓	✓	✓	✓

* FCPs may be used for applications made UK wide. Applications to Northern Ireland-only require compliance with EU requirements. See published guidance applicable from 1/1/25. https://www.gov.uk/guidance/comparator-products-in-bioequivalencetherapeutic-equivalence-studies

** Pre-application discussion with MHRA or Health Canada is recommended in these cases to confirm acceptability of approach.

*** Certain minor differences between both products may be accepted if justified, provided this is supported by bridging data.

FRPs can be accepted only if they were manufactured at the same drug product manufacturing site as the Singapore reference product.