MEDSAFE
New Zealand Medicines and Medical Devices Safety Authority

Proposed updates to the Guideline on the Regulation of Therapeutic Products in New Zealand: Bioequivalence of medicines

18 November 2025

Consultation outcome

Contents

Executive Summary

Background

Medsafe is the New Zealand Medicines and Medical Devices Safety Authority and is responsible for the regulation of therapeutic products in New Zealand by administering the Medicines Act 1981 and Regulations 1984. Therefore, Medsafe has specific New Zealand legislation to administer, and the requirements under the legislation are further outlined throughout the Guideline on the Regulation of Therapeutic Products in New Zealand (GRTPNZ).

The GRTPNZ: Bioequivalence of Medicines (the Guideline) provides information for sponsors on the data requirements regarding demonstration of bioequivalence for new and changed medicines.

The Guideline aligns its principles as much as possible with internationally recognised bioequivalence guidelines. The Guideline provides options for those submitting bioequivalence studies in support of regulatory applications for entry into the New Zealand market.

Medsafe reviewed the current GRTPNZ: Bioequivalence of Medicines (Edition 2.0, February 2018) and proposed updates throughout the Guideline. From 9 June 2025 to 4 July 2025, Medsafe consulted on the proposed updates. The consultation was aimed at pharmaceutical companies seeking to demonstrate bioequivalence of medicines to support applications to Medsafe for regulatory approval of new and changed products. Prescribers and healthcare professionals with an interest in medicine regulation, in particular generic medicine approval, were also encouraged to participate. This report is a summary of the submissions received.

Consultation results

We received 8 responses to the consultation. Respondents were pharmaceutical companies, organisations, or prescribers with an interest in the bioequivalence of medicines in New Zealand.

Respondents generally agreed with the proposed updates. The updates to Section 3 (Bioequivalence study reference product) of the Guideline received the most discussion. Respondents suggested changes in wording to several sections to improve clarity. Respondents also suggested additions or alterations to the proposed updates to improve the practicality of some implementations.

Some respondents suggested changes that were out of the scope of the intention of the Guideline. Where considered relevant, clarifications are made to the intended scope of the updated Guideline.

Revised Guideline and implementation

We have published the revised Guideline:

• Guideline on the Regulation of Therapeutic Products in New Zealand: Bioequivalence of Medicines (Edition 3.0)

The revised Guideline comes into effect from the date of publication. However, applicants may refer to either the previous or updated versions of the Guideline for applications already under

evaluation or those received by Medsafe during the implementation period, which will end on 31 March 2026. From 1 April 2026, all new applications received by Medsafe must comply with the new Guideline.

Medsafe would like to thank everyone for their contribution to this consultation.

1. Summary of responses – Section 1: Introduction

Question 1: Do you agree with proposed changes to Section 1? Associated comments.

Y/N/Somewhat

- Yes, n = 6
- No, n = 1
- Somewhat, n = 1

There were three respondents who provided comments or suggestions for this question. One respondent made a general comment on the guideline. The remaining two comments are addressed in the themes below.

Scope of the Guideline

One respondent queried whether Medsafe would waive Phase 3 clinical trials in biosimilar product development.

Medsafe response

Biosimilar development, and guidance on biosimilar products in general are out of the intended scope of this guideline and thus this question will not be addressed in this forum. However, a new guideline covering biosimilar medicines is planned for development. A sentence has been added to Section 1 to state that biosimilars are out of the scope of the Guideline.

Case-by-case approach

One respondent commented that although the updates to the Guideline may facilitate market entry and applications for generic medicine sponsors, Medsafe should adopt a case-by-case basis when making decisions regarding local reference product waivers, considering the physicochemical, pharmacokinetic, and pharmacodynamic characteristics of the medicines.

Medsafe response

Although Section 3 of the Guideline lists general options for the selection of bioequivalence study reference products, a case-by-case approach is always applied, and sponsors are encouraged to contact Medsafe prior to submitting an application if a selected reference product does not clearly meet one of the Options in Section 3 of the Guideline.

2. Summary of responses – Section 2: International bioequivalence guidelines

Question 2: Do you agree with proposed changes to Section 2? Associated comments.

Y/N/Somewhat

- Yes, n = 6
- No, n = 0
- Somewhat, n = 2

There were three respondents who provided general comments or queries for this question.

Adoption of future international guidelines

One respondent queried whether Medsafe plans to adopt the ICH M13B guidance once the ICH guideline is finalised.

Medsafe response

Medsafe will consider adoption of additional international guidelines as they are implemented.

3. Summary of responses – Section 3: Bioequivalence study reference product

Question 3: Do you agree with proposed changes to Section 3? Associated comments.

Y/N/Somewhat

- Yes, n = 3
- No, n = 0
- Somewhat, n = 5

There were 7 respondents who made suggestions, comments, and queries on the updates to this section. Where considered relevant, queries, suggestions, and comments are grouped into the themes below.

Bioequivalence study reference product sourced from New Zealand

Two respondents identified that the introductory paragraph to this section and Option 1 did not indicate that the choice of the New Zealand reference product as the bioequivalence study reference product is the preferred option.

Medsafe response

Medsafe acknowledges this point omitted in the draft guideline for consultation. A sentence is added to Option 1 to restore this acknowledgement for clarity. The introductory paragraph of Section 3 is also updated to clarify that the bioequivalence study reference product can be sourced from the New Zealand market or overseas.

Practicality of Option 2 (paper comparison with overseas reference product)

Five respondents raised concerns about their ability to meet the requirements of Option 2, especially regarding the ability to confirm that the same manufacturing process and sites are used in the production of the bioequivalence study overseas reference product and the New Zealand reference product.

Medsafe response

The intention of Option 2 is to allow for the waiving of *in vitro* characterisation studies where the sponsor has extensive knowledge of the reference products. Since *in vitro* studies are not required to meet Option 2, a higher level of evidence in the form of paper documentation is expected. Medsafe understands that this information is likely to be unobtainable in most cases. The proposed Option 2 is retained in its entirety but for an added sentence pertaining to an acknowledgement of this point.

Data requirements for Option 3

Several respondents raised concerns about the inclusion of quantitative analysis as a data requirement to fulfil Option 3 requirements.

Two respondents queried whether abridged certificates of analysis for *in vitro* comparison of two reference products would be acceptable (eg, such as omission of microbial testing).

One respondent raised the possibility of performing Fourier transform infra-red (FTIR) spectra and powder X-ray diffraction (XRD) spectra of each product overlaid for comparison instead of generating certificates of analysis for reasons of cost.

One respondent queried whether 20 or 10 units are required for dimensions and uniformity of weight tests, as British (BP), European (Ph.Eur.) and United States (USP) pharmacopoeias are referenced.

One respondent asked Medsafe to clarify what information is expected to be compared between the data sheets/consumer medicine information between two reference products.

Medsafe response

A full *in vitro* quantitative analysis of reference products is not a requirement to fulfil Option 3. In the draft document for consultation, this point is followed by the words 'where practicable'. The intention of the inclusion of quantitative analysis is to encourage companies to provide these data if readily available. The Guideline is revised with a footnote clarify this point.

Abridged certificates of analysis (with omission of justified parameters) are considered acceptable. Option 3 of the Guideline is updated to include this point.

Although comparative FTIR and XRD spectra analysis are not considered direct substitutes for comparative certificates of analysis, the option to perform these tests instead of generating certificates of analysis is added to the updated Guideline to reflect the status quo requirements. This should provide sponsors with greater flexibility when seeking to demonstrate essential similarity.

For demonstration of similarity of dimensions/uniformity of weight between reference products, any of the referenced pharmacopoeial tests are acceptable. Therefore, the usage of 10 units is acceptable when aligned with pharmacopoeia recommendations.

The requirement to compare data sheets/consumer medicine information leaflets of different reference products as evidence of essential similarity in line with Option 3 has been removed in the updated Guideline.

For the pharmaceutical dosage forms listed in section 4 (product types that require bioequivalence), other than oral dosage forms, the requirement for comparative dissolution data has been added to the revised Guideline (for dosage forms for which a dissolution test is included in the proposed product's specifications).

Product types (Option 3)

One respondent requested Medsafe to clarify what product types are applicable for Option 3 essential similarity testing (solid and non-solid oral dosage forms).

Medsafe response

The tests listed under 'Solid oral dosage forms' apply to both immediate and modified release products. The guideline is updated to include a statement to this effect.

The tests listed under 'Non-solid oral dosage forms' apply, but are not limited to oral solutions, suspensions, and syrups.

***In vitro* comparison with Australian innovator product (Option 5)**

One respondent sought clarification of Option 5 and the data requirements to support essential similarity of an overseas reference product with an Australian reference product in an abbreviated application based upon TGA approval.

Medsafe response

An error in the text of Option 5 of the draft guideline for consultation (Option 5 was referenced instead of Option 4) is acknowledged and corrected, which should clarify this point.

Reference product not available (Section 3.2)

One respondent raised concerns that for a proposed generic version of an overseas innovator was never approved in New Zealand, the Guideline on one hand requires safety and efficacy data for the proposed product, while on the other hand states bioequivalence data against the overseas innovator and safety/efficacy data for the overseas innovator are required.

One respondent requested clarification to understand under which situations literature data and bioequivalence studies can support an application.

One respondent noted that Medsafe does not currently have specific guidelines for the use and content of literature-based or hybrid submissions.

One respondent queried whether the following approaches would be acceptable:

- essential similarity testing as per Option 3 between the bioequivalence study reference product (overseas innovator) and New Zealand market leader.
- essential similarity testing as per Option 3 between the bioequivalence study reference product (generic market leader in the overseas market) and New Zealand market leader.

Medsafe response

Where an overseas innovator was never approved in New Zealand that generic versions may be supported by either data from clinical studies using the proposed product OR a combination of bioequivalence data and evidence to support the safety and efficacy of the overseas innovator.

In the absence of specific Medsafe guidelines regarding the use and content of literature-based or hybrid submissions, relevant guidance adopted by other regulatory authorities (eg, TGA Literature-Based Submission guidance) may be used, as proposed in the draft Guideline.

Essential similarity testing between a bioequivalence study reference product (overseas innovator) against the New Zealand generic market leader is not acceptable.

Essential similarity testing between a bioequivalence study reference product (overseas generic market leader) against the New Zealand generic market leader may be acceptable if it is expected

that they are the same product. This is likely a rare scenario, and companies may request pre-submission advice from Medsafe if needed.

4. Summary of responses – Section 4: Product types that require bioequivalence

Question 4: Do you agree with proposed changes to Section 4? Associated comments.

Y/N/Somewhat

- Yes, n = 4
- No, n = 0
- Somewhat, n = 4

There were four respondents who provided general comments or specific queries regarding new fixed-dose combination products.

New fixed-dose combination products

Two respondents noted that bioequivalence studies for new fixed-dose combination products against innovator fixed-dose combination products should be allowable, whereas the draft updated guideline states that bioequivalence should be demonstrated against products with the active ingredients in separate registered formulations.

Medsafe response

Medsafe acknowledges that bioequivalence studies can be conducted against innovator fixed-dose combination products. This point had not been updated in the draft Guideline for consultation. The intention of this point was to confirm that bioequivalence studies should be conducted against separate registered formulations if there is no reference product with the proposed combination of active ingredients. This point has been updated for clarity in the Guideline.

5. Summary of responses – Section 5: Generic medicines for which a bioequivalence study is not appropriate

Question 5: Do you agree with proposed changes to Section 5? Associated comments.

Y/N/Somewhat

- Yes, n = 6
- No, n = 1
- Somewhat, n = 1

Two respondents left comments regarding the requirements for therapeutic equivalence studies for inhalational products.

Therapeutic equivalence of Inhalational products

Two respondents raised concerns that current international guidance regarding inhalational products does not require in all instances therapeutic equivalence studies involving pharmacodynamic endpoints.

Medsafe response

Medsafe acknowledges that there are instances where studies with pharmacodynamic endpoints are not required to demonstrate therapeutic equivalence of inhalational products. The Guideline is updated to clarify this point.

6. Summary of responses – Section 6: Product types not requiring bioequivalence

Question 6: Do you agree with proposed changes to Section 6? Associated comments.

Y/N/Somewhat

- Yes, n = 6
- No, n = 0
- Somewhat, n = 0

Two respondents made comments or queries which are grouped into the themes below.

Soft gelatin capsules

One respondent queried what specific physicochemical parameters would be required to justify a waiver of a bioequivalence study for a soft gelatin capsule product.

Medsafe response

It is acknowledged that the draft guideline for consultation does not specify the parameters to be investigated. Any critical quality attributes determined during pharmaceutical development and/or considered to impact the *in vivo* performance of the proposed soft gelatin capsule should be compared between formulations. Additionally, any tests defined in BP/Ph.Eur/USP general (eg, disintegration) or specific monographs should be comparatively tested. As the appropriate tests will generally be product-specific, the Guideline is not updated. It is considered that the phrase 'justified parameters' offers sufficient guidance.

Biosimilars

One respondent was concerned to note that biosimilars were included in Section 6 as a product type for which bioequivalence studies are not required for registration. Additionally, they note the draft guidance for consultation includes a note that references separate guidelines regarding biosimilars, but no specific guideline is referenced.

Medsafe response

Bioequivalence studies as they relate to non-biological medicines, are not relevant for demonstrating the safety and efficacy of biosimilar medicines, and therefore biosimilars are not within scope of this Guideline. A specific guideline regarding biosimilar medicines is planned for development. The Guideline is updated to include this point.

There are certain scenarios where synthetically manufactured peptide-based medicines are developed as essentially similar versions of innovative biological medicines produced by recombinant processes. In these cases, where certain requirements are met, such medicines may be considered generic products (as opposed to biosimilars), in which case the normal

bioequivalence requirements described in the Guideline would apply. The Guideline is updated to include information regarding this scenario.

7. Summary of responses – Section 7: Biowaivers

Question 7: Do you agree with proposed changes to Section 7? Associated comments.

Y/N/Somewhat

- Yes, n = 7
- No, n = 0
- Somewhat, n = 1

There were no relevant comments for this question, despite one ‘Somewhat’ response.

8. Summary of responses – Section 8: Narrow therapeutic index products

Question 8: Do you agree with proposed changes to Section 8? Associated comments.

Y/N/Somewhat

- Yes, n = 7
- No, n = 0
- Somewhat, n = 1

There were two respondents, one of which made a comment relevant for this document.

Interchangeability

One respondent requested that Medsafe retain the term and/or section for 'Interchangeability of generic medicines' along with 'Narrow therapeutic index products' to give sponsors a clear direction as to where to find the information regarding switching brands.

Medsafe response

The referenced sections in the current version of the Guideline have been combined under the heading "Narrow therapeutic index products". The information has been updated in accordance with current language, practice and understanding regarding the substitution and switchability of generic medicines, and to ensure it is better aligned with the intent of the Guideline. However, the heading of this section has been updated in the Guideline for clarity.

9. Summary of responses – General comments and feedback

Question 9: Do you have any other general comments or feedback you wish to share regarding the proposed draft guideline?

There were three respondents who provided general comments in response to this question, however none were considered within scope of the consultation on the proposed updates to the Guideline.