Guide to completing a New Medicine Application Lower-Risk Medicines

Introduction

This guide is a reference document to assist you with putting together a New Medicine Application (NMA) for a lower-risk medicine.

For intermediate-risk and higher-risk medicines and related products please refer to the relevant guides for these types of medicines (ie, Guide to completing a New Medicine Application – Intermediate-Risk and Higher-Risk Medicines; and the Guide to completing a New Related Product Application).

Not everything in this document applies to every new medicine application and the guide should only be used as a reference when completing the application form.

Additional resources that you should utilise when putting together your application include:

- the relevant New Zealand medicines legislation
- international guidelines
- pharmacopoeias
- the Guidelines for Regulation of Therapeutic Products in New Zealand (GRTPNZ), specifically the New Medicine Applications guideline.

Section 10 of the New Medicine Applications guideline describes the defines the different lower-risk New Medicine Application categories, and the key application criteria. Section 10 and Appendix 2 of the New Medicine Applications guideline should be your first point of reference in selecting the correct application category.

NOTE: Please do not send this document to Medsafe with your application.

Contents

1. Instructions for using the form for an NMA – Lower Risk Medicines

The NMA form for new lower risk medicines is designed for electronic completion. All fields of the form should be completed.

2. Application form for an NMA – Lower Risk Medicines

The form should be used when applying for consent to distribute a new lower-risk medicines.

The same form should be used for medicines in all of the categories ie, L1, L2, and L3.

Each application should also be accompanied by a completed Declarations / Commitments form.

3. Determining the application category

Before submitting an application, use the following application selection tools (located in the New Medicines Applications guideline) to determine the correct application category and data requirements:

New Medicines Applications Guideline:

- Appendix 1: Application categorisation tool
- Appendix 2: Lower risk medicine categorisation tool
- Appendix 3: Summary of data requirement for new medicine applications
- Appendix 4: Summary of lower-risk medicine application data requirements according to categorisation

The selection of the appropriate category of application will determine the data requirements and additional information that the sponsor must supply in support of the application. Sponsors may contact Medsafe for additional clarification.

Lower-risk category	Examples of each category
Category L1	• An application for a 'clone'. The 'clone' must be identical to an 'approved parent product[2]' in all respects other than the product name and labelling. • An application for a flavour/fragrance/colour (FFC) variant of an 'approved parent product[2]' where there is only a change in the content of the FFC agent(s) and where the product otherwise meets all the requirements applying to a 'clone'. • An application for an additional classification due to an additional pack size of an 'approved parent product[2]' and where the product otherwise meets all the requirements applying to a 'clone'. • New combination pack containing two or more currently 'approved parent products[2]'; container/closure for each unchanged. Combination products must be in a fully labelled outer carton; and

	the product must otherwise meet all the requirements applying to a 'clone'.
Category L2	• New application for a 'generic' lower-risk medicine, where the active ingredient, strength, combination, dose form, indications and directions for use are identical to a medicine previously approved in New Zealand. • New strength of an existing lower-risk product with no change in the administered dose of active ingredient.
Category L3	• An application for a new lower-risk product, where safety and efficacy cannot be derived from the formulation alone. This type of application includes: o modified release products (excluding enteric coated tablets/capsules o products that require bioequivalence data, or a justification for the absence of this data o products containing novel excipients o products containing excipients with a new route of administration o products that have labels claiming equivalence with another product o formulation dependent topical products o product that has been re-scheduled from 'Prescription Only Medicine' to a lower risk schedule, where no previous product has been approved as a lower-risk medicine • An application for a new product that is an extension to a 'Generic category' product including: o new therapeutic indications o new strengths with a different administered dose of active ingredient compared an existing product o new dosage forms o new directions o new combination products o different patient population. • An application for a product containing a new chemical entity as an active ingredient.

[1] Refer to the Decision tree for umbrella branded lower risk medicines in Appendix 4 of Part 2 of the GRTPNZ for determination of the correct application category for umbrella branded medicines

[2]Approved parent product must have been previously approved for safety, efficacy and quality and must comply with current standards, including the Medsafe Labelling Statements Database.

4. Application format

Applications must be submitted in the CTD format in accordance with the lower risk medicines dossier documents matrix in Appendix 4 of the New Medicine Application Guideline.

The only allowable exemption to the requirement for CTD format is for responses to RFIs, but only when the additional information or data is limited in volume. It is important for all RFI responses that the additional information or data be cross-referenced to the outstanding questions/issues in the RFI letter in numerical order.

The application must be submitted electronically. Refer to Section 3 of the 'Overview of Regulatory Processes for New and Changed Medicines, Fees, and Timelines' guideline.

One copy of the application form must be completed for each separate product – this means that any variation in the name, dose form, strength, classification, or identifier (eg, different flavour) will require a separate form.

5. Proposed product details, required for all applications

Type of application

Enter the type that best describes your application. The fee will be calculated from this information and one of the following should be entered:

Category L1 – clone

Category L1 – new pack size/additional classification

Category L1 – new combination pack

Category L1 – new flavour/fragrance/colour variant

Category L2

Category L3

Justification for selection

This is a brief description of how the application meets the application category criteria. For an application submitted under the L2 application category where there is no parent product, include the details of the reference product that justifies the use of this category. The reference product is an approved product with the same drug substance, strength, dose form, indications and directions for use.

Proposed trade name:

This is the proposed name under which the product will be marketed in New Zealand.

Identifier:

If the proposed product is an extension of an existing product range, or the trade name is the drug substance name, the point of difference between the proposed and existing products should be stated (eg, manufacturer, flavour, strength).

Drug substance:

This is the active ingredient in the proposed product. If the medicine contains multiple active ingredients, separate these by commas.

Dose form:

Select from the following list

Block
Capsule
Capsule, combination
Capsule, liquid filled
Capsule, modified release
Capsule, powder filled
Capsule, powder filled, nasal inhalation
Capsule, soft gelatin
Cement, bone, liquid component
Cement, bone, powder component
Cement, dental
Chewing gum
Chocolate, medicated
Combination
Cream, rectal
Cream, topical
Cream, vaginal
Crystals
Dermal patch, local effect
Diluent
Dressing, medicated
Drops, ear
Drops, ear/eye
Drops, ear/eye/nose
Drops, eye, powder and diluent
Drops, eye, solution
Drops, eye, suspension
Drops, nasal
Drops, oral
Elixir
Emulsion, oral
Emulsion, topical
Enema
Enema, powder
Eye strip, impregnated
Foam
Gas
Gargle
Gel, intestinal
Gel, ophthalmic
Gel, oral
Gel, oral topical
Gel, topical
Gel, vaginal
Granules, effervescent
Granules, modified release
Granules, oral
Implant, subcutaneous
Implant, intracranial
Implant, intraocular
Infusion, concentrate
Infusion, emulsion
Infusion, powder
Infusion, powder for concentrate
Infusion, solution
Inhalation, capsule, liquid filled
Inhalation, capsule, powder filled
Inhalation, powder
Inhalation, solution
Inhalation, solution, powder for
Inhalation, suspension
Inhalation, volatile liquid
Inhaler, aerosol, metered
Injection, concentrate
Injection, concentrate with diluent
Injection, depot
Injection, emulsion
Injection, gel
Injection, granules
Injection, powder
Injection, powder with diluent
Injection, solution
Injection, suspension
Irrigation
Irrigation, eye
Irrigation, powder for reconstitution
Lacquer, nail
Linctus
Liniment
Lotion, scalp
Lotion, skin
Lozenge
Mouthwash, solution
Mouthwash, solution, powder for
Oil
Oil, bath
Oil, topical
Ointment, ear/eye
Ointment, eye
Ointment, rectal
Ointment, topical
Ointment, vaginal
Pad, skin wash impregnated
Paste, oral
Paste, topical
Pastille
Pessary
Plant material
Powder
Powder, effervescent
Powder, nasal
Powder, topical
Shampoo
Skin wash
Soap
Solution
Solution, antiseptic
Solution, contact lens
Solution, dialysis
Solution, dialysis, powder
Solution, oral
Solution, oral, granules
Solution, oral, powder
Solution, topical
Solution, topical, powder
Solution, vaginal douche
Sponge, vaginal
Spray, contact lens solution
Spray, nasal solution
Spray, nasal suspension
Spray, oral
Spray, sublingual
Spray, topical
Spray, topical powder
Stick, topical
Suppository
Suppository, urethral
Suspension, intratracheal
Suspension, intratracheal, powder for
Suspension, oral
Suspension, oral, granules
Suspension, oral, powder
Suspension, rectal/oral
Syrup
Syrup, powder
Tablet
Tablet for contact lens solution
Tablet, chewable
Tablet, chewable/dispersible
Tablet, coated
Tablet, dispersible
Tablet, effervescent
Tablet, enteric coated
Tablet, film coated
Tablet, modified release
Tablet, orodispersible
Tablet, soluble
Tablet, sublingual
Tablet, uncoated
Tablet, vaginal
Toothpaste
Topical
Transdermal gel
Transdermal patch
Transdermal patch, systemic effect
Wafer

Strength:

The strength should be as stated on the labelling for each presentation of the product. The strength should be stated as the content of the active ingredient base form.

New Zealand classification:

New Zealand schedule of classifications can be found at the Medsafe website.

Enter the name of the drug substance and click search.

Route of administration:

Select from the following list

Conjunctival
Cutaneous
Dental
Endocervical
Endosinusial
Enteral
Epidural
Extra-amniotic
Gingival
Haemodialysis
Implant
Inhalation
Insufflation
Intra-amniotic
Intra-arterial
Intra-articular
Intrabursal
Intracardiac
Intracavernous
Intracervical
Intracoronary
Intradermal
Intradiscal
Intragastric
Intralesional
Intralymphatic
Intramuscular
Intraocular
Intraperitoneal
Intrapleural
Intrasternal
Intrauterine
Intrathecal
Intratracheal
Intravenous
Intravesical
Irrigation
Nasal
Opthalmic
Oral
Oromucosal
Otic
Periarticular
Perineural
Periodontal
Peri-osteal
Rectal
Subconjunctival
Subcutaneous
Sublingual
Submucosal
Systemic
Transdermal
Transmammary transfer
Ungual
Urethral
Vaginal

ATC classification:

The ATC classification system can be accessed at the WHO website.

Search for the drug substance in the product field and enter the found description and the code into the Application Form field.

Proposed indications and/or label claims:

Proposed indications or label claims should be listed for all products.

If the application is for a generic product, highlight any differences from the innovator.

If the product is required to have a data sheet and the indication(s) is lengthy, reference may be made to refer to the data sheet.

New Zealand Medicines Terminology:

See the New Zealand Universal List of Medicines for more information.

A New Zealand Medicines Terminology Listing Certificate should be provided as part of the NMA process.

6. Additional information, where applicable

All products:

Please list the details of the overseas approvals or submissions - country name, regulatory agency, and approval or submission date should be specified. Separate multiple entries by commas.

Application where Module 5 contains bioequivalence studies:

Information about the biostudy reference product should be provided.

Applications referring to a 'parent product':

An 'approved parent product' is a previously approved product where the safety, efficacy and quality of the medicine have been acceptably demonstrated, and that complies with current standards. The name and TT50 number of the approved parent product should be provided.

If the parent product is not approved (that is, it is part of the current application), the details should be consistent with the first (parent) application form.

The relationship between the two products should also be detailed in the cover letter. Full access rights to the parent product must be provided.

The differences between the parent product and new product must be described in the application form. Additional information may be included in the cover letter.

Category L1

All new lower risk medicine applications submitted via category L1 require identification of the 'approved parent product', detailed information as to the selection of category L1 (ie, clone, classification difference, flavour/fragrance/colour differences, new combination pack) and detailed identification of the differences between the proposed and 'approved parent product' as this assists with invoicing (see below).

Categories L2

For category L3 the quality (CTD Module 3) data will always be evaluated in full, except, in the circumstance where all quality aspects of the product are identical to a product which has been previously approved by Medsafe. In this case the sponsor may provide an abbreviated Module 3 dossier (see Section 10.5 of the New Medicine Applications guideline). For these abbreviated L2 applications the 'approved parent product' should be clearly identified, and the differences between the proposed and 'approved parent product' clearly detailed (see below).

Categories L3

For categoryL3 the CTD-formatted dossier must always be submitted in full. However, there may be some benefits to identifying any 'approved parent product' as this may facilitate the evaluation process.

Applications for additional name, strength, classification, flavour/fragrance/sweetener, dose form and combination pack:

Under the current Medsafe fee schedule sponsors may submit applications for additional name, strength, classification, flavour/fragrance/sweetener, dose form and combination pack. These applications require identification of aparent product'.

For ease of selection these lower risk NMA categories have been mapped against the application type below:

Application category	Application Type	Difference from 'parent product'
L1*	Additional name - Grade 1	• new name to be used in addition to existing name • all other details identical to parent product except for labelling • new label displays new name, but all other information on the label is essentially the same as on the parent product label (even if layout is different)
L1*	Additional name - Grade 2	• new name to be used in addition to existing name • all other details identical to parent product except for labelling • new label displays new name • layout of label may be different from that of parent product • some other information on the label is different from that on the parent product label

L1*	Additional classification	• new classification to be used in addition to existing classification (with or without a new name) • all other details identical to parent product except for labelling • new label displays new classification (and new name, pack size, indications, dosage instructions, all required warnings if applicable)
L1*	Additional flavour or fragrance or type of sweetening	• new and parent products have the same dose form • new product has a flavour or type of sweetening different from the parent product • all other details identical to parent product except for labelling (if applicable) and specifications
L1*	New combination pack	• new combination pack containing two or more currently approved drug products • container for each component unchanged, or any change does not affect stability/shelf-life • no change to indications or dosage of either component
L2+	Additional strength - Grade 1	• new and parent products have the same dose form and same administered dose of active ingredient • new product is a direct scale of parent product, or uses same excipient matrix • all other details identical to parent product except for labelling and specifications
L2+	Additional strength - Grade 2	• new and parent products have the same dose form and same administered dose of active ingredient • new product is not a direct scale of parent product • bioequivalence study not required • all other details identical to parent product except for labelling and specifications
L3	Additional strength - Grade 3	• new and parent products have the same dose form • new product is not a direct scale of parent product • bioequivalence study not required, but a justification for the absence of this study is required • other details different from parent product, such as different dosing or directions for use
L3	Additional dose form - Grade 1	• new and parent products have different dose forms and the same or different strengths • bioequivalence not relevant to new dose form
L3	Additional dose form - Grade 2	• new and parent products have different dose forms and the same or different strengths • bioequivalence study or clinical data included

* would be L2 if submitted with an L2 parent product; L3 if submitted with an L3 parent product.. Would also need to comply with all other requirements for applicable category as outlined in in Section 10 of the New Medicine Applications guideline.

+ would be L3 if submitted with a L3 parent product. Would also need to comply with all other requirements for applicable category as outlined in Section 10 of the New Medicine Applications guideline.

7. Applicant and sponsor details

New Zealand Sponsor:

Details, including the street address, of the licence holder (entity responsible for the product on the New Zealand market) should be provided.

Applicant:

Details of the company or individual responsible for submitting the application and for responding to all correspondence should be provided. A letter of authorisation should be included in the application, if not previously provided.

8. Fees and invoice details

Calculate the fee for the application, from the application type and application based on a parent product information. Medsafe will verify the calculation and fee. All fees are GST inclusive. A space is included for comments relevant to invoicing.

On acceptance of the application (following screening), a tax invoice and acknowledgement letter will be sent to the applicant. The invoice will be made out to the New Zealand Sponsor as this is the entity legally responsible for the application.

A customer reference can be quoted on the invoice, if required.

9. Product formulation

Formulation details should be entered as provided in Module 3.2.P.1 of the dossier. Appropriate quality standards and units should be specified for each ingredient.

The salt form of the drug substance should be entered into the table and the amount of free base should be included in brackets beside the salt form.

The details of the proprietary ingredients should be supplied. If the ingredient has been previously registered with Medsafe, include the name and reference number. If the ingredient has not been previously registered with Medsafe, include in the dossier or arrange for the supplier to provide Medsafe with details of the unique company identifier (name, number), quality specifications, quantitative and qualitative formulation, and quality standards of individual ingredients issued by the suppliers. The formulation table should only include the proprietary ingredient name, content, and quality standard.

10. Product packaging, patient information, and storage conditions

Primary packaging refers to the packaging directly in contact with the drug product.

Secondary packaging refers to the first component opened by the consumer, and any additional wallets, pouches, blister lidding, etc. All should be briefly described.

All pack sizes proposed with the application should be listed.

All applicable shelf life and storage conditions should be entered using only the provided dropdown lists.

Any package types that are not applicable should have ‘Not applicable’ entered.

11. Production

Manufacturers:

The address of the actual site of manufacture should be provided.

GMP certification should be issued by a recognised authority as listed in the GRTPNZ.

The site information should be completed for each individual manufacturing steps, even if a site conducts steps.

If a manufacturing step is not applicable to the application type 'Not applicable' should be entered in the name section.

DMF/Certificate of Suitability:

The DMF number refers to the number assigned to the DMF by Medsafe.

If the DMF number is not known, this field should be left blank. If supplying certificates of analysis as evidence of drug substance quality, this section should be left blank.

Site responsible for batch release:

This should be the site holding documentation for batches released onto the New Zealand market and is not necessarily the testing site.

If the medicine is manufactured and packed overseas, the company should advise the name and address of the company who is importing the medicine into New Zealand. This site is termed the New Zealand site of batch release and is responsible for undertaking the duties described in section 42 of the Medicines Act 1981.

Biostudy/clinical site:

This is the site responsible for the clinical phase of the bioequivalence study.

Bioanalytical testing site:

This is the site responsible for testing the samples generated from biostudy subjects.

12. Provided information

Please indicate the section in which the documents specified on the NMA form can be found, so administration staff and the evaluators can quickly locate pertinent information in the dossier.