CHANGED MEDICINE NOTIFICATION
FORM B

This form is to be used when notifying a material change (including self-assessable changes) to an approved **Type III (biological or biotechnological)** product (i.e., a vaccine, recombinant product, monoclonal antibody or variant thereof, or a medicinal product derived from blood or plasma).
Use CMN Form A for any other (Type I/II) medicine, including antibiotics and like substances derived from micro-organisms.
Do not use this form for notifying a changed related product. Use the CRPN form instead.

Section 1: Product details

Copy details from the database report for the currently approved product. A separate form must be used for each different product (name + dose form + active ingredient(s) + strength + classification, as applicable).

Product name:

Medsafe File No: TT50-

Dose form:

Strength/Potency:

Classification:

Product currently available[1]: **Yes** ☐ **No** ☐

If no, please state the date the product was last supplied in New Zealand:

Section 2: Applicant and Sponsor details and declaration

Name, designation and address of person submitting the notification:
[All correspondence (including the invoice) will be sent to this person.]

Email address:

New Zealand sponsor name and street address:

Postal address (if different from street address):

[1] For further information on the meaning of not available please refer to http://www.medsafe.govt.nz/Medicines/registration-situation.asp

In accordance with section 24 of the Medicines Act 1981, I hereby notify the Director-General of Health of material changes proposed for this product. I certify that the information supplied is correct to the best of my knowledge and that no relevant information has been omitted.

Signature: _____ Date: _____

Section 3: Proposed changes

Instructions

1. Tick the box(es) in the left hand column beside the description(s) that most accurately reflects the changes for which approval is sought. The main change and the consequential changes listed under the "Description of change" are all covered by the fee shown in the "Product type & fee" column. Where no product type is specified in the "Product type and fee" column, the same fee applies to all product types.
2. Enter the number of changes in the "Tick box" where the product type and fee is based on a fee for *each* change. For example, if there are two product name changes, enter "2" in the "Tick box".
3. It is not necessary to submit pages listing change descriptions that are not relevant to the notification.
4. When a self-assessable change is notified at the same time as other changes for which a fee is paid, the $360 administrative fee for the self-assessable change will not apply (except in the case of a data sheet update, where the update is independent and not a consequence of any of the proposed changes).
5. All fees listed are GST inclusive.

Product name

Note: If a product is to be marketed under a new name in addition to the existing name, it is a new product and a New Medicine Application must be completed.

Tick box	*Description of change*	*Product type & fee*
	Product name • **new product name to replace existing name** • **no change in formulation** Consequential changes included (if applicable) are: • revised data sheet and labelling	$720 for *each* new name

Formulation/Excipients

Note: If a formulation change is associated with a change in the actual bulk active manufacturing process, this must be separately notified as a "Bulk Active manufacturing process" change in the "Bulk Active" section of this form

Tick box	*Description of change*	*Product type & fee*
	Formulation - Grade 1 • **change of excipients including the addition or removal of excipients** Consequential changes included (if applicable) are: • new or revised specifications for excipient • revised data sheet and labelling • amended batch manufacturing documentation, provided there is no significant change in manufacturing process	$2,880 for any number of excipient changes
	Formulation – Grade 2 • **strain update of active ingredient for influenza vaccines**	$720 for any number of strains

Bulk Active

Tick box	*Description of change*	*Product type & fee*
	Bulk Active manufacturing site • **Change in site of manufacture of any stage in the process up to, and including, the manufacture of the final bulk.**	$2,880
	Active ingredient method of manufacture – Grade 1 • **Change in any step of the method of manufacture. This would include, but is not restricted to:** – **batch scaling** – **type of equipment** – **new master cell bank** – **new working cell bank (unless use of advisory notes is acceptable as described in Guidelines on the Regulation of Therapeutic Products in New Zealand, Part 2)** – **revised specifications for cell banks** – **new suppliers of plasma for blood products** – **changes to the manufacturing processes used to isolate and purify drug substance from plasma**	$2,880 for *each* step change to a maximum of $43,875
	Active ingredient method of manufacture – Grade 2 • **No change to the actual manufacturing process or type of equipment used** • **Active ingredient specifications/test methods unchanged** • **Updates to raw materials tests and specifications** • **Change in starting material supplier and/or starting material manufacturing process** • **Changes to in-process control limits (other than tightening limits)** • **New in-process test site (test methods unchanged)** • **Additional/alternative storage facilities for the cell bank** • **Change in room for cell substrate preparation activities**	$720 for *each* change
	Active ingredient method of manufacture – Grade 3 • **Editorial changes to the manufacturing process records only.** • **Tightening in-process control limits**	$360 (self-assessable)

Finished product manufacture and packing

Tick box	*Description of change*	*Product type & fee*
	Finished product manufacturing site • **new site for manufacturing product, lyophilising product, or dispensing final bulk finished product into primary containers**	$2,880 for *each* new site
	Finished product secondary packing site • **new secondary packing site that is not a site of manufacture** • **packing finished product into cartons** • **includes overlabelling**	$720 for any number of sites
	Finished product testing site • **new site for testing finished product** • **implementation of additional (previously approved) test methods at a current finished product testing site**	$1440 for *each* site
	Finished product manufacturing process - Grade 1 • **type of manufacturing process unchanged, but changes to mixing time, batch scaling, type of equipment etc.** Consequential changes included (if applicable) are: • new site of manufacture and packing	$2,880
	Finished product manufacturing process – Grade 2 • **new type of manufacturing process** Consequential changes included (if applicable) are: • revision or reconfirmation of shelf life • new site of manufacture and packing	$2,880

	Finished product manufacturing process – Grade 3 • **Changes to in-process control test methods or limits other than tightening limits** • **Changes to manufacturing room classification(s)** • **Change from a single product to a multi-product manufacturing facility**	$720
	Finished product manufacturing process – Grade 4 • **No change to the actual manufacturing process or type of equipment used** • **Specifications/test methods unchanged** • **Editorial changes to the manufacturing process records only** • **Tightening in-process control limits** • **Update(s) to Section 3.2.A.1 'Facilities and Equipment' information due to 'like for like' equipment changes or building/floor plan changes.**	$360 (self-assessable)

Test methods and specifications

Tick box	*Description of change*	*Product type & fee*
	Test methods and specifications - Grade 1 • **change to any method used to assay/potency of each active moiety**	$2,880
	Test methods and specifications - Grade 2 • **change to specifications used to describe assay/potency**	$2,880 for *each* active moiety potency specification
	Test methods and specifications - Grade 3 • **change to primary standard used in assessment of potency/assay** • **change to secondary standard used in assessment of potency/assay, if no protocol for use of a self assessable change for introduction of a new secondary standard has been previously approved.**	$2,880
	Test methods and specifications - Grade 4 • **change to any method used to assess other physical or chemical properties of the active ingredient , finished product, or reference standard (used in the assessment of potency/assay).**	$1,440 for each change
	Test methods and specifications - Grade 5 • **addition / removal / change to any specification used to describe other physical or chemical properties of the active ingredient, finished product, or reference standard (used in the assessment of potency/assay).** • extension of retest period or expiry period for a reference standard if the protocol used for this extension has not been previously approved.	$1,440 for each change
	Test methods and specifications - Grade 6 • **tightening of specification limits for active ingredient or finished product** • **change to secondary standard used in assessment of potency if the protocol used for introducing a new secondary standard has been previously approved for use in a SACN.** • **Extension of reference standard expiry or retest period, if the protocol used for extension of the expiry or retest period has been previously approved for use in a SACN**	$360 (self assessable) for any number of active ingredients

Tick box	*Description of change*	*Product type & fee*
	Excipient specifications/test methods - Grade 1 • **revised specifications/test methods for a substance controlled according to a pharmacopoeial monograph (resulting from change to a different pharmacopoeia, not simply updating to the latest edition)**	$360 (self-assessable) for any number of excipients
	Excipient specifications/test methods - Grade 2 • **revised specifications/test methods for a substance not controlled according to a pharmacopoeial monograph**	$720 for *each* excipient
	Excipient specifications/test methods - Grade 3 • **adoption of additional or different specifications/test methods not specified in the pharmacopoeial monograph for an excipient otherwise controlled according to a pharmacopoeial monograph**	$720 for *each* excipient

Stability and packaging

Tick box	*Description of change*	*Product type & fee*
	Shelf life/storage conditions - Bulk Actives and Intermediate Bulks • **revised shelf-life and/or storage conditions with no other changes**	$1,440 for *each* bulk active or each process intermediate
	Shelf life/storage conditions - Finished Product • **revised shelf life and/or storage conditions with no other changes** Consequential changes included (if applicable) are: • revised labelling and data sheet	$1,440
	Shelf life/storage conditions - Reference standard used for potency/assay • **revised shelf life and/or storage conditions with no other changes**	$720
	Container/closure/packaging - Grade 1 • **new container or closure and/or new pack size and/or new packaging material type** • **revised shelf-life and/or storage conditions** • **supporting stability data provided** • **no effect on dose measurement or dose delivery** Consequential changes included (if applicable) are: • revised packaging specifications • revised labelling and data sheet	$1,440
	Container/closure/packaging - Grade 2 • **new container or closure and/or new pack size and/or new packaging material type** • **revised shelf-life and/or storage conditions** • **supporting stability data provided** • **changes affect dose measurement or dose delivery** Consequential changes included (if applicable) are: • revised packaging specifications • revised labelling and data sheet	$2,880 for *each* container/closure packaging combination

	Container/closure/packaging – Grade 3 - **no change to container, closure, or pack size** - **revised specifications for container or closure**	$780
	Container/closure/packaging - Grade 4 • **new pack size** • **evidence provided that no stability data required** • **no effect on dose measurement or dose delivery** Consequential changes included (if applicable) are: • revised labelling and data sheet • revised packaging specifications	$360 (self assessable)

Changes affecting the Diluent component of Type III (biological or biotechnological) products.

- **If the diluent contains biological/blood product ingredient, use CMN Form B and select appropriate category of change.**
- **If the diluent DOES NOT contain biological/blood product ingredient, use CMN Form A and select appropriate category of change.**

Indications and dosage

Tick box	*Description of change*	*Product type & fee*
	Indications/dosage - Grade 1 • **new indication** • **supporting clinical data required** Consequential changes included (if applicable) are: • new dosage instructions • revised data sheet and labelling **Note:** CMN will generally be referred under section 24(5)	$2,880 for *each* new indication
	Indications/dosage - Grade 2 • **modified indication** • **supporting clinical data required** Consequential changes included (if applicable) are: • new dosage instructions • revised data sheet and labelling **Note:** CMN will generally be referred under section 24(5)	$2,880 for *each* modified indication
	Indications/dosage - Grade 3 • **new dosage regimen** • **no change to indications** • **supporting clinical data required** Consequential changes included (if applicable) are: • new dosage instructions • revised data sheet and labelling	$2,880 for *each* new dosage regimen

Indications and dosage (cont'd)

Tick box	*Description of change*	*Product type & fee*
	Indications/dosage - Grade 4 • **revised wording of indications/dosage with no actual change to indications or dosage** Consequential changes included (if applicable) are: • revised data sheet and labelling	$720
	Indications/dosage - Grade 5 • **new or revised indications/dosage for a multi-source medicine to match indications approved for innovator product** Consequential changes included (if applicable) are: • revised data sheet and labelling	$720
	Contraindications, Warnings and Precautions • **relaxation of contraindications, and/or** • **relaxation of warnings and precautions regarding use in pregnancy, lactation or particular population/patient subgroups** • **supporting clinical data required** Consequential changes included (if applicable) are: • revised data sheet and labelling	$2,880

Labelling

Tick box	*Description of change*	*Product type & fee*
	Labelling - Grade 1 **Labelling for this category must be based on, and submitted with, currently approved labelling.** • **re-design of label, and/or** • **change in name and address of distributor** • **no change to product name, strength, dose form, dosage instructions or indications, or** • **change in dosage to "as directed by a physician"**	$360 (self-assessable)

Labelling (cont'd)

Tick box	*Description of change*	*Product type & fee*
	Labelling - Grade 2 • **design or re-design of a New Zealand compliant label** • **no change in actual strength, but a change in the way the strength is expressed (if applicable)** • **any labelling change not covered by Labelling – Grade 1 or Labelling – Grade 3**	$720
	Labelling - Grade 3 • **request for a labelling exemption, or** • **request for renewal of a labelling exemption**	$720 (plus $360 for *each* additional name/ dose form/strength/ flavour)

Data Sheet

Tick box	*Description of change*	*Product type & fee*
	Data sheet - miscellaneous changes • **update or addition to safety information with no change to approved product details, and/or** • **expansion of pharmacokinetic and/or pharmacodynamic data, and/or** • **change in name or address of distributor with no change to approved product details**	$360 for *each* data sheet. Please state the number of datasheets. (self-assessable)

Other

Tick box	*Description of change*	*Product type & fee*
	Sponsor • **change of product sponsor from one company to another (not simply a change in the name or address of an existing sponsor)** Consequential changes included (if applicable) are: • change of name and address of distributor on label and in data sheet. **Note:** A CMN for change in packing site(s) may also be required.	$360 (self-assessable)

Section 4: Summary of proposed changes

Use a separate summary sheet for each change.

Description of change (copy heading from "Description of change" box in Section 3):

Summary of current and proposed details:

Current product details	Proposed details
Reason for change:	
Consequential changes:	
Acceptance overseas (provide approval letters and evaluation reports if available):	

Section 5: Declarations and Commitments

New Zealand Medicines Terminology:

A New Zealand Medicines Terminology Listing Certificate should be provided as part of the Medsafe application process for changes to **product name, pack size and container**.

The New Zealand Medicines Terminology Listing Certification has been attached ☐

(Refer to http://nzulm.org.nz or email listings@nzulm.org.nz for further details on NZMT listings)

1. Compulsory declaration for all CMNs

I confirm that other than the changes proposed in this CMN, all other aspects of API and finished product quality, equipment, process, and packaging etc, are the same as those previously approved.

Signature: _____ Date: _____

2. Removal of sites from TPDR

Not applicable ☐

I confirm that there is no further stock, currently marketed or stockpiled for future sale or use in New Zealand, either manufactured at or using any ingredients sourced from the site(s) required to be removed.

Note: Site(s) cannot be removed until all stock has been depleted from the New Zealand market.

Signature: _____ Date: _____

3. Labelling

Not applicable ☐

One representative label has been submitted for all pack sizes of the same strength and presentation. I certify that all other pack sizes are identical, except for the statement of pack size.

Labels are provided at % of full scale.

Signature: _____ Date: _____

I certify that all of the label(s) for all of the proposed products have been assessed and are in compliance with the requirements of the legislation. All information on the label(s) is consistent with the details of the medicine currently approved in New Zealand or described in the current Changed Medicine or Related Product Notification.

Signature: _____ Date: _____

or

A labelling exemption is requested as follows (repeat as necessary):

Label for which the exemption is requested:

Part of label that is non-compliant:

Justification for exemption (see Guideline on the Regulation of Therapeutic Products in New Zealand Part 5):

4. Declaration to accompany a DATA SHEET submitted for APPROVAL

Not applicable ☐

☐ Requires evaluation (CMN).

I declare that this data sheet has been prepared in compliance with the current edition of the *Guideline on the Regulation of Therapeutic Products in New Zealand* and that it accurately reflects the changes proposed in the CMN.

Signature: _____ Date: _____

☐ Is self-assessable (SACN).

I declare that this data sheet has been prepared in compliance with the current edition of the *Guideline on the Regulation of Therapeutic Products in New Zealand* and that it accurately reflects the existing New Zealand terms of approval for the medicine.

Signature: _____ Date: _____

5. CMI:

Not applicable ☐

Following consent to distribute, an electronic copy of the CMI will be submitted to Medsafe and will comply with the requirements published on the Medsafe website. The CMI will not be used or included as a package insert unless these requirements have been met.

Signature: _____ Date: _____

6. Post approval stability

Not applicable ☐

At least one commercial scale batch of each strength, pack size and pack type of the changed product will be placed on stability trial (with bracketing as appropriate) under real time conditions for the duration of the proposed shelf life per year of production. The batches will be identical in every respect to those destined for the New Zealand market and Medsafe will be informed of any out of specification results or data indicating that batches may be out of specification before the shelf life is reached.

For stability studies that are on-going, Medsafe will be informed of any out of specification results or data indicating that batches may be out of specification before the shelf life is reached.

Signature: _____ Date: _____

Section 6: Other products affected

Complete this section once for each notification package submitted. If you are simultaneously notifying an identical change or set of changes to a number of products, list all the products covered by the notification in the following table. Each dose form and each strength and flavour of each dose form of a product must be separately listed.
Note: A separate copy of Sections 1 and 2 of this notification form must be completed for each of the products listed. Only one copy of Sections 3 and 4 is required. All the forms must be submitted in the same notification package.

File No.	Product name	Dose form	Strength

Check and indicate that the notification package sent to Medsafe contains the following (as applicable):

(Y or N/A)

A completed copy of Sections 1 and 2 of the CMN/CRPN form for each product covered by the notification	
One completed copy of Sections 3, 4 and 5 of the CMN/CRPN form	
One copy of the supporting data	
A copy of the current product database report(s)	
A copy of the label and a completed checklist and declaration if the notification includes a self-assessed labelling or data sheet change	
A copy of an assessment report from an appropriate overseas regulatory authority	

Notes on Fee Calculation and Payment of Fees

Note 1: If you are notifying identical changes to a number of products, the evaluation fee shown will be the largest fee that would apply to any single product. For example, if the notification covers Type I and Type II products, the evaluation fee applicable for a Type II product will apply.

Note 2: In no case will the CMN/CRPN fee for a single product exceed the fee for a new medicine application for a product of the same type.

Note 3: When the same change or set of changes is made to other names, dose forms, strengths and flavours of a product, a $360 (administrative) fee is charged for each of the other affected products.

Note 4: The fee for a changed data sheet is $360 **per data sheet.**

Note 5: Upon receipt of an application/notification Medsafe will issue a tax invoice which will be sent to the applicant with the acknowledgement letter. Payment will be requested within 7 days and will be required to validate the application/notification. Payments are to be made on an invoice basis only - do not send payment with the application/notification.

Note 6: A customer reference (maximum 20 characters) can be quoted on the invoice. Quote reference here: _____

For Medsafe Office Use Only

Application Fee – single product	***$_____.00***
Administrative fee for _____additional products @ $360 each	***$_____.00***
	_____
Invoice amount	***$_____.00***

Invoice number:_____ ***Date:_____***

(End of form)