MEDSAFE
New Zealand Medicines and Medical Devices Safety Authority

Guideline on the Regulation of Therapeutic Products in New Zealand

New and Changed Related Products

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Contents

1. Definition of a Related Product

A related product, as defined in the Medicines Act 1981, is a cosmetic, dentifrice, or food for which a therapeutic purpose is claimed regarding its ingredient content and/or use. The definitions for cosmetics and dentifrices can be found in the Medicines Act 1981.

Related products are not permitted to contain ingredients that are:

- scheduled as Controlled Drugs under the Misuse of Drugs Act 1975
- scheduled as prescription medicines, restricted (pharmacist-only) medicines or pharmacy-only medicines under the Medicines Regulations 1984
- classified as general sales medicines.

Medsafe's searchable Classification Database can be used to check whether an ingredient is scheduled under the Medicines Regulations 1984 or is classified as a general sale medicine.

Section 58A of the Medicines Regulations 1984 exempts some cosmetics and dentifrices from being categorised as related products if only limited therapeutic claims are used.

- A dentifrice product is not considered a related product if its therapeutic claims are only for preventing dental decay and/or improving oral hygiene.
- An anti-dandruff hair product is not considered a related product if its only therapeutic claim is for controlling dandruff **and** it is claimed to be effective only by cleansing, moisturising, exfoliating, or drying the scalp and not through any other process.
- An anti-acne skin care product is not considered a related product if its only therapeutic claim is to prevent acne **and** it is claimed to be effective only by cleansing, moisturising, exfoliating, or drying the skiing and not through any other process.
- A barrier cream is not considered a related product if its only therapeutic claim is to prevent nappy rash **and** it is claimed to be effective only by providing a barrier to the transmission of moisture and not through any other process.
- An anti-bacterial skin product is not considered a related product if its only therapeutic claim is to prevent the spread of bacteria (and the therapeutic claim excludes any named bacterium) **and** the product is not intended to be used in connection with:
    - any procedure associated with the risk of transmission of disease from contact with blood or other bodily fluids
    - piercing the skin or mucous membrane for any purpose
    - venipuncture, or the delivery of an injection.

    If an anti-bacterial skin product is recommended for use in connection of the provision of health services (as defined in section 2 of the Health and Disability Commissioner Act 1994), then it will be considered a medicine.

2. New Related Product Applications

A New Related Product Application (NRPA) is an application under section 20 of the Medicines Act 1981 seeking the Minister's consent to distribute a new related product.

In practice, the power to approve medicines is delegated to a senior Ministry of Health officer, referred to as the Minister's delegate.

Each new related product is the subject of a separate product approval and has its own separate entry in Medsafe's Therapeutic Products Database (SMARTI). A unique product is defined by its name, dose form, active ingredient(s), strength, and flavour or sweetening (if applicable).

2.1 New Related Product Application data requirements

An application for consent to distribute a new related product must be made using the New Related Product Application Form and accompanying New Related Product Declarations and Commitments form. Download the forms from the Forms and Templates page on the Medsafe website – see the 'Related Products (New and Changed)' section.

Applications should be compiled as described for new medicines in section 8 of the 'New Medicine Applications' guideline and be accompanied by the following data.

Administrative information

- Cover letter and completed New Related Product Application Form
- Labels (labelling exemptions for related products are not permitted as per New Zealand Medicine Regulations 1984, Section 12(5))
- Manufacturing Quality Assurance
  - GMP certification is required for related products intended to be taken internally
  - For related products that are not taken internally, evidence is required that the finished product manufacturer complies with an internationally recognised quality system, eg, GMP, ISO, HACCP, local 'Food Safety' certification

Chemical, Pharmaceutical & Biological Documentation

- Composition and presentation of product
  - Any proprietary ingredients or colourants in the formulation must meet 'Ingredients in New Medicines and Related Products' guideline requirements
  - Product Development Pharmaceutics are not required
- Method of manufacture
- Specifications (test methods and limits) for the active ingredient(s) applied by the finished product manufacturer
- Specifications (test methods and limits), analytical method descriptions, and analytical validation data for the finished product
  - Analytical validation data should be provided for the assay/purity, preservative, and microbiological test methods and any other test methods that establish the therapeutic nature of the product
- Representative batch analytical data for the finished product
  - Certificates of analysis for a minimum of three batches should be provided
- Stability data

- Stability data are required only for related products taken internally but can be provided for other related products if relevant (eg, if a shelf life is proposed for the product)
- If stability data is not required for an application, the data should be held and able to be provided to Medsafe if requested

The above information represents minimum data requirements, and further data may be required depending on the risk profile of the related product.

A NRPA is processed as if it was a new lower-risk medicine application. The Medsafe assessment considers the aspects of the product relevant to the Medicines Act 1981. However, the product is expected to also comply with other relevant legislation applicable to the type of product eg, cosmetic standards, dietary supplements regulations, food legislation.

3. Changed Related Product Notifications

A Changed Related Product Notification (CRPN) is a notification to the Director-General of Health by the sponsor of a product, under section 24 of the Medicines Act 1981, of a planned change to an approved related product and the reasons for the change.

If any change to a related product results in a new active ingredient, new combination of active ingredients, new strength, new dose form, new flavour or new trade name an NRPA (not a CRPN) is required. A NRPA must be submitted separately from any CRPN. The new related product cannot legally be distributed until consent has been granted and published in the New Zealand Gazette.

Changes to related products are made using the Changed Related Product Notification form, available on the Forms and Templates page on the Medsafe website – see the 'Related Products (New and Changed)' section.

Details of the various types of assessable and self-assessable changes and the applicable fees are given in the CRPN form. The CRPN form includes categories for common changes (and changes consequent to these) and are designed to be as comprehensive as possible. The fee structure for the categories is reflective of the amount of Medsafe evaluation required. If the intended change is not covered by the categories in the CRPN form, please seek advice from Medsafe.

Data to support the proposed change must be provided as if the change was a change to an approved lower-risk medicine as described in Appendix 1 of the Changed Medicine Notifications and Non-notifiable Changes guideline. It is not necessary to notify a change to data that was not submitted in the original application.

3.1 Self-Assessable Change Notifications (SACNs)

For self-assessable changes for related products there is no requirement to obtain consent prior to making the change. However, the notification must precede the change. Self-assessable changes are to be notified using the same CRPN form as used for notifying assessable changes.

Except in the case of a changed label or updated specifications, no supporting data are required to be submitted with a SACN. It is the responsibility of the sponsor to ensure that the data to support the change are held and are made available to Medsafe on request.

A SACN is able to be implemented when payment for the application has been received. Medsafe **acknowledges** but does not formally approve or issue a 'consent notice' for SACNs.

Sponsors should note that SACNs submitted within the same application as an assessable change must not be implemented until the entire CRPN is approved.

Medsafe performs random audits of SACNs and, where any significant problems are identified, the sponsor is required to rectify them. Where a CRPN rather than a SACN should have been submitted, the sponsor will be required to submit a new notification, without refund of the cost of the SACN.

3.2 Making the same changes for multiple related products

A sponsor can submit a CRPN for an identical change(s) to multiple related products. This type of application applies **only** when the change does not require separate assessment for individual products, or when there is no change unique to one particular product within the group that requires separate assessment.

3.3 Priority assessment of notifications

The statutory timeframe for CRPNs requires that the initial Medsafe evaluation must be completed within 45 days (see Evaluation Timelines). Medsafe typically completes its initial evaluation in a shorter timeframe (see section 6 of the 'Overview of Regulatory Processes, Fees, and Timelines' guideline). CRPNs, therefore, are not eligible for priority assessment.

3.4 Referrals under section 24(5) of the Medicines Act 1981

Section 24 of the Medicines Act 1981 sets out restrictions on the distribution of changed medicines, including changed related products. Subsection 5 permits the Director-General (DG) of Health to refer a related product (that is the subject of a CRPN) to the Minister in certain circumstances. Referral occurs when a CRPN is of such a character or complexity that the related product should not be distributed without consent of the Minister, or that the DG is insufficiently informed about the change proposal.

The following are examples that may be referred under section 24(5).

- 'Grandmother's axe' products (when changes are so significant that the proposed product no longer resembles the approved product).
- Changes that are too complex and/or too numerous to be assessed by Medsafe within CMN evaluation timeframes.
- Failure to respond to requests for information.

The timeframe for a CRPN referred under section 24(5) of the Medicines Act 1981 is the same as a New Medicine Application.

CRPNs referred under section 24(5) of the Medicines Act 1981 are subject to the same eligibility criteria for priority assessments as New Medicine Applications (NMAs; refer to section 7 of the New Medicine Applications guideline).

3.5 Non-notifiable changes

The following are examples of changes to the regulatory file information that are considered a non-notifiable change (ie, a CRPN is not required). Sponsors can request the file to be updated at no charge.

- Removal of manufacturing/packing sites. A Request for Removal of Manufacturing, Testing or Packing Site from Therapeutic Product Database Report must be completed.
- Change in market availability or consent situation (see Section 5 of this guideline).
- Change in proprietary ingredient subject to the following conditions:
  - the new proprietary ingredient is the same type (ie, black ink, orange flavour), and
  - the new proprietary ingredient is already registered.
- New or changed New Zealand site for product release.
- Change in name of a manufacturing, testing or packing site subject to the following conditions:
  - there is no change of ownership
  - the change in name affects the whole site (ie, name change is not restricted to selected buildings)
  - a GMP certificate or other relevant documentation has been provided with the new site name.

3.5.1 Changes in pharmacopoeial specifications

A CRPN is **not** required to update the specifications for an active ingredient or finished product to conform to the most recent edition of the relevant pharmacopoeial monograph. Manufacturers are expected to keep their specifications aligned with any revisions to those monographs.

However, a CRPN **is** required if there is a change from the specifications of a monograph in one pharmacopoeia to that in another pharmacopoeia, or from in-house specifications to a pharmacopoeial monograph (or *vice versa*).

3.5.2 Changes in names of manufacturers or packers

When the name of a manufacturer, testing site, or packer is changed but there is no change in ownership and there are no changes to the address or the manufacturing or packing processes, a CRPN is not required. Instead, the sponsor should advise Medsafe (medsafeapplications@health.govt.nz) in writing so that Medsafe can update its records. A CRPN is required if the change in name is a result of a change in ownership.

When there is a change in name of a manufacturer, testing site, or packing site, each sponsor that uses the site is responsible for notifying the change to Medsafe.

3.5.3 Addition or change to New Zealand Site of Product Release

To add or change the New Zealand Site of Product Release a CRPN is not required. Instead, the sponsor should advise Medsafe (medsafeapplications@health.govt.nz) in writing so that Medsafe can update its records.

3.6 Introducing changed related products into the marketplace

It is expected that a change to a marketed related product will be introduced into the market in a timely manner with time allowed to sell through existing stock. An acceptable changeover in the market is product dependent, as low volume or seasonal products may take longer to sell through.

In general, Medsafe expects changed related products to be presented to the market within the following time periods:

- 3 months for new stock from wholesalers
- 6 months for new stock from retailers.

Sponsors considering longer lead times should include a justification in the CRPN.

Sponsors should not request a deletion of any approved regulatory information (manufacturing sites, container types, etc) until stock has exited the New Zealand market.

Changes to existing products that have been initiated for safety concerns may need to occur rapidly, and in conjunction with a product recall.

3.7 Preparing a CRPN (including SACNs) for submission

A CRPN must use the Common Technical Document (CTD) format as described in the ICH Guideline 'Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use'. Only the CTD sections relevant to the change need to be submitted.

Each CRPN must be accompanied by a cover letter and a completed CRPN form. The cover letter should briefly summarise the changes being notified, and the changes should also be clearly described in Section 4 of the CRPN Form.

A separate CRPN form should be completed for each related product and all sections of the CRPN form must be completed. Applicants should submit one copy of each completed CRPN form and any supporting documentation.

It is not acceptable to combine a CRPN with an NMA. CRPNs can only be submitted after a NMA has been consented. Any supporting documentation that is referred to in a CRPN must be provided with the CRPN; it is not appropriate to reference supporting information that was submitted in the product's NMA.

Medsafe will not accept further changes to a CRPN after it has been submitted (except, perhaps, to indicate or clarify changes consequential to the changes notified in the original CRPN). If further (non-consequential) regulatory file information changes are intended, a new CRPN and fee are required.

When Medsafe issues formal consent for a change to a related product, only those changes specifically identified and applied for in the CRPN form are covered by the consent. Changes included in any accompanying documentation but not specifically identified in the CRPN form, and consequently not assessed by Medsafe as changes, are not included in any consent that may be granted for the CRPN.

Consequential changes are grouped within some CRPN category changes for the purpose of fees calculations. However, these changes must be identified separately and supported by appropriate data or documentation, if relevant.

Each change included in a CRPN is assessed separately. In some cases, Medsafe may consider that only some of the proposed changes can be approved. This may be because the supporting data submitted with the CRPN do not justify the other changes proposed. In this situation, if the sponsor is unable to supply acceptable data to support the proposed change(s), a recommendation to withdraw those changes from the CRPN will be made to the sponsor. This will enable consent to be granted for the approvable changes.

Partial consent for some of the changes, with other changes assessed later, is not Medsafe's current practice. Any proposed changes withdrawn from a CRPN can be resubmitted as a new CRPN at a future date when the required supporting data are available. New fees will apply to this new notification specific to those particular changes.

If a CRPN consists of a number of grouped changes, the applicant must obtain consent for all the changes before any are implemented. This applies even if some of the changes could be self-assessed if submitted separately.

4. Change of sponsor

A change of sponsor should be notified using the relevant CRPN category and include letters or other evidence from both the proposed and current sponsors accepting and relinquishing sponsorship of the product(s). Additional changes to the product label should be included as part of the same notification whenever possible.

If the change in sponsor requires a change in contact details on the related product label, it is acceptable for the sponsor to manage a transition period to allow time to generate new labels and sell existing product in the distribution chain with the previous contact details.

Transition periods should be minimised to prevent confusion. As a general guide an acceptable transition for product in the distribution chain is three months for wholesale and six months for retail.

During the transition period the sponsors must have an agreement in place whereby any correspondence received by the relinquishing sponsor relating to the related product is promptly forwarded to the new sponsor.

New sponsors should ensure that they meet the requirements as detailed in section 2 of the Overview of Regulatory Processes for New and Changed Medicines, Fees, and Timelines guideline.

5. Changing the market availability or consent status of a related product

Sponsors of related products can choose to designate their products 'not available' if they wish to communicate the unavailability of the related product in the market to the public and healthcare professionals.

Sponsors who wish to surrender consent because they do not intend marketing the related product again in New Zealand may notify Medsafe and the status will be updated to 'approval lapsed'. Approval lapsed is also used to denote related products that have not been available for more than five years, as described in Section 1 of the New Medicine Applications guideline.

A change in the market availability to 'not available' or consent status to 'approval lapsed' can be made either by notification as part of a CRPN/SACN or notified to Medsafe at any other time. Sponsors should use the Product Status Change Request form, available on the Forms and Templates page on the Medsafe website – see the 'Administration and

Maintenance of Product Files' section. Sponsors should advise when the product was last marketed in New Zealand.

There is no cost associated with updating the market availability to 'not available' or consent status to 'approval lapsed'.

When changing the market availability information from 'not available' to 'consent', the sponsor should ensure that the regulatory file information approved by Medsafe for the product is up-to-date and consistent with the product being reintroduced into the New Zealand market. If the regulatory file information needs to be updated, a CRPN must be submitted and granted consent prior to the market availability information being updated and the product being reintroduced into the market. When requests to update the market availability are submitted as part of a CRPN, this should be clearly identified in the CRPN cover letter. The CRPN must undergo evaluation and self-assessable change notifications will not be accepted.

If a sponsor determines that a CRPN is not required to change market availability information to 'consent' because the regulatory file has been kept up to date, a justification letter along with a completed Product Status Change Request form should be provided to Medsafe. (The form is available on the Forms and Templates page on the Medsafe website – see the 'Administration and Maintenance of Product Files' section.) Medsafe will review the justification letter and form to ensure that all requests for CRPNs have been addressed prior to the market availability information being updated and the product is able to be reintroduced into the market.

CRPNs, justification letters and Product Status Change Request Forms must be submitted at least 90 days prior to the intended date that distribution will commence. Justification letters should be addressed to the Manager, Product Regulation (medsafeapplications@health.govt.nz).

If approval has lapsed, consent to the distribution of a new related product needs to be granted before the product can be reintroduced onto the New Zealand market.

6. Fees for related products

Fees for new or changed related products are charged in accordance with the policy outlined for medicines described in the Overview of Regulatory Processes for New and Changed Medicines, Fees, and Timelines guideline. The actual fee payable for a New Related Product Application, after application of any applicable standard waiver, is set out in a schedule of fees.

Fees for changed related product notifications are contained in the CRPN form and in the schedule of fees.

Document history

Revision Date	Version Number	Summary of Changes
January 2023	New	New document following major review and restructure of GRTPNZ Part 2, which has been obsoleted. of