MEDSAFE

NEW ZEALAND MEDICINES
AND MEDICAL DEVICES
SAFETY AUTHORITY

A BUSINESS UNIT OF
THE MINISTRY OF HEALTH

Guideline on the Regulation of Therapeutic Products in New Zealand

Part 4:

Manufacture of medicines

MINISTRY OF HEALTH
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Section 1: Good Manufacturing Practice Documentation

Section summary

- *This section explains when evidence of compliance with GMP is required and what evidence is acceptable.*

1.1. When is GMP Documentation Required?

Medsafe requires evidence of **Good Manufacturing Practice** (GMP) compliance for each finished product manufacturing site and packaging site specified in a New Medicine Application or Changed Medicine Notification and manufacturers of active pharmaceutical ingredients that are prescription medicines.

Evidence of GMP compliance is required for products regarded as medicines in New Zealand, whether or not they are considered medicines in the country of origin.

In the case of related products, evidence of compliance with GMP is required for NRPAs and CRPNs for products taken internally (e.g., throat lozenges, and vitamin and mineral tablets).

Evidence of GMP is not required for related products used externally. However, evidence is still required to show that the manufacturer complies with an internationally recognised quality system (e.g., ISO accreditation).

For bulk active pharmaceutical ingredients evidence that the material is manufactured consistently and produced with acceptable quality is required.

GMP certification, or equivalent documentary evidence, stating the products or product classes for which it has been granted is required for all:

- Manufacturers of active pharmaceutical ingredients that are prescription medicines
- manufacturers of the finished product (including manufacturers of intermediate products)
- sterilisers of the finished product
- packers of the finished product
- sites where products are overlabelled

A manufacturing site for a finished product is any site which contributes to a manufacturing operation which converts bulk raw materials to a finished dose form. This includes sterilising sites. A packing site means any site which contributes to a packing operation which places the final dose form into its labelled primary or secondary container.

Manufacturers and/or packers with premises in New Zealand must hold an appropriate current licence to manufacture and/or pack medicines. The licence must have been issued for the site for the manufacture and/or packaging of the type of product or packaging operation before manufacture or packaging of the product for distribution can commence. Provided they hold such current licences, certification need not be provided with each application or notification.

For overseas manufacturers and packers, Medsafe requires that certification be included with each NMA or CMN which relates to a change of site, even if the site already supplies product to New Zealand and certification has been supplied previously with an earlier application or notification. This reduces delays associated with locating other files, and because it is desirable for the certification to be product- specific and up-to-date.

Acceptable evidence of GMP compliance normally consists of copies of appropriate certificates, manufacturing licences or reports issued by a regulatory authority whose competence is recognised by Medsafe. Details of the documentation that is acceptable and a list of authorities whose competence to certify GMP compliance is recognised by Medsafe, is given below in Section 1.5.

The certificate, licence or report should be no more than 3 years old when the NMA or CMN is submitted and must be current at the time of approval of the new or changed product for distribution in New Zealand.

If the original documentation was in a language other than English, then copies of both the original documents and a certified English translation must be submitted.

If acceptable evidence of GMP compliance is not available, an audit of the site by Medsafe auditors can be arranged at the applicant's request and expense.

Medsafe also require Sponsors to continue supplying evidence of current GMP compliance on an ongoing basis, to ensure registered products continue to meet consented requirements. Updated evidence should be submitted as soon as it becomes available for each site involved in the manufacturing activities listed above.

1.2. Recognised Documentation

GMP certification recognised by Medsafe can be any document issued by a recognised authority which attests to GMP compliance. Legible photocopies of the documents are acceptable.

Documents should contain the following information:

- the street address of the site concerned
- reference to the product or product class
- reference to GMP acceptability and/or to a GMP audit

- name and address of the issuing authority
- date and signature.
- date of expiry of the certification or licence

The following are examples of acceptable evidence of GMP certification:

- licence to manufacture issued by a recognised authority where such a licence is issued only where the site is inspected and regularly re-inspected for GMP compliance
- current registration and entry (for the product, product class or process concerned) of the site in the Australian Register of Licensed Manufacturers
- United Kingdom Product Licence or Product Licence Variation where name and address of site is shown
- certification of pharmaceutical product issued under the WHO scheme by a recognised authority which certifies the quality of pharmaceuticals moving in international commerce
- Canadian Drug Plant Inspection Rating Report
- a letter or file note from a recognised authority which attests to GMP compliance.The most usual example seen is an extract from FDA files obtained by the manufacturer under the US Freedom of Information Act. It usually states that an audit occurred on the given date and gives the outcome of the audit
- a certificate issued by the Australian TGA confirming that it has confirmed (eg, with the US FDA) that GMP compliance at the particular site is satisfactory. Note that Medsafe also has access to the FDA's electronic GMP database and can check the GMP status of manufacturing sites inspected by the FDA.

The following are NOT acceptable as evidence of GMP compliance:

- a licence to manufacture which is not issued by a recognised authority
- certification issued by a pharmaceutical company - even if the company
- certifying is not the same as the manufacturer or packer
- Annual Registration of Drug Establishment (USA). This document is not indicative of GMP compliance.

1.3. Classes of Medicine

Certification should preferably be product-specific. Certification in the WHO format or a manufacturing or product licence listing the product are the most easily obtained examples of this type.

If product-specific certification cannot be obtained, the certification must relate to a medicine or medicines of the same class(es) (see below) as the one which is the

subject of the application or notification. A medicine may belong to more than one class. In such cases, the certification should be for a product belonging to the same classes.

I	Medicines containing penicillin
II	Medicines containing cephalosporin
III	Vaccines or sera
IV	Sterile medicines
V	Hormones and steroids
VI	Microdose preparations (other than vitamins), ie, containing 5 mg or less per unit dose
VII	Antineoplastic agents and immunosuppressant agents (other than steroids)
VIII	Solid dose forms
IX	Recombinant DNA medicines
X	Metered dose aerosol preparations
XI	Liquids, creams, ointments
XII	Non-metered dose aerosols
XIII	Powders
XIV	Wound dressings
XV	Transdermal patches

1.4. Sites which Manufacture Bulk Active Pharmaceutical Ingredients

Evidence of GMP is required for *all sites* which manufacture bulk active pharmaceutical ingredients for prescription medicines. Such evidence should be included with each application or notification which relates to a change of site.

Applications and notifications must include the name and address of the *actual site of manufacture* and applicants should ensure that there is no confusion between sites of manufacture and addresses of company head offices or brokers. Any documentary evidence of GMP must refer to the actual site of manufacture.

Any of the following is acceptable as evidence for manufacturers of bulk active pharmaceutical ingredients used in OTC medicines and related products.

- A GMP certificate or inspection report issued by a recognised authority. Note that not all authorities issue certification for sites manufacturing bulk active substances.
- A Drug Master File or equivalent data submitted as part of the dossier for a new chemical entity or new biological entity medicine.
- A European Pharmacopoeial "Certificate of Suitability" for a substance controlled according to the European Pharmacopoeia.
- Batch analytical data demonstrating consistent quality of the substance produced (accepted as adequate evidence only for lower risk medicines and related products).

Note: A GMP certificate alone is not acceptable as a substitute for a DMF, Certificate of Suitability or batch analytical data where these are normally required.

1.5. Recognised Authorities

GMP certification issued by the authorities listed below is recognised by Medsafe. The authorities listed includes most of the competent authorities in the European Community, certain member authorities of the PIC and/or PIC/S organisations, and other authorities where Medsafe has information that GMP assessment systems that are compatible with New Zealand expectations exist. The inclusion of most of the European Community competent authorities is a consequence of the Mutual Recognition Agreement in Relation to Conformity Assessment that became effective between New Zealand and the European Community on 1 January 1999. Omission of an authority from the list generally indicates that Medsafe has not assessed that authority's systems, and should not be construed in any way as an adverse reflection on the competence of the authority itself. The inspectorates recognised by Medsafe are listed below.

Logo (for information only)	Recognised Authority (alphabetical by country)
Australian Government Department of Health Therapeutic Goods Administration	**AUSTRALIA** Therapeutic Goods Administration (**TGA**) Website: http://www.tga.gov.au/
AGES	**AUSTRIA** **Austrian Agency for Health and Food Safety** *Österreichische **A**gentur für **G**esundheit und **E**rnährungs-**s**icherheit* (**AGES**) Website: https://www.ages.at/en/healthy-life-for-humans-animals-and-plants/
famhp federal agency for medicines and health products	**BELGIUM** Federal Agency for Medicines and Health Products ***A**gence **F**édérale des **M**édicaments et des **P**roduits de **S**anté* (**AFMPS**) ***F**ederaal **A**gentschap voor **G**eneesmiddelen en **G**ezondheidsproducten* (**FAGG**) Website: https://www.fagg-afmps.be/en
Health Canada Santé Canada	**CANADA** **Health Canada** *Regulatory **O**perations and **R**egions **B**ranch (**RORB**)* *Direction **g**énérale des **o**pérations **r**églementaires et des **r**égions (**DGORR**)* Website: https://www.canada.ca/en/health-canada.html
SÚKL State Institute for Drug	**CZECH REPUBLIC** State Institute for Drug Control ***S**tátní **Ú**stav pro **K**ontrolu **L**éčiv* (**SÚKL**) Website: http://www.sukl.eu/index.php?lang=2

Logo (for information only)	Recognised Authority (alphabetical by country)
LÆGEMIDDELSTYRELSEN DANISH MEDICINES AGENCY	**DENMARK** **Danish Medicines Agency (DKMA)** Website: http://laegemiddelstyrelsen.dk/en/
fimea Finnish Medicines Agency	**FINLAND** **Finnish Medicines Agency (FIMEA)** Website: http://www.fimea.fi/web/en
ansm Agence nationale de sécurité du médicament et des produits de santé	**FRANCE** **French National Agency for Medicines and Health Products Safety** ***Agence nationale de sécurité du médicament et des produits de santé* (ANSM)** Website: http://ansm.sante.fr/
Federal Ministry of Health ZLG	**GERMANY*** **Federal Ministry of Health** Website: http://www.bundesgesundheitsministerium.de/ **AND** Central Authority of the Lander for Health Protection with regard to Medicinal Products and Medical Devices *Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten* (ZLG) Website: https://www.zlg.de/en/ * The PIC/S website contains the statement *"The German Ministry of Health (BMG) and the German Authority of the Lander (ZLG) count as one PIC/S participating Authority."* Therefore both authorities are recognised by Medsafe.
Paul-Ehrlich-Institut	**GERMANY (IMMUNOLOGICALS):** Website: http://www.pei.de/EN/home/node.html **Paul-Ehrlich-Institut - Federal Institute for Vaccines and Biomedicines**
	GERMANY REGIONALSTATE AUTHORITIES LISTED BELOW ARE ALSO ACCEPTABLE GERMAN AUTHORITIES* * The PIC/S website states *"All German Medicinal Authorities, which are listed on the ZLG website, are considered as PIC/S Participating Authorities and are represented in PIC/S by ZLG."* The list of authorities below has been provided to Medsafe by ZLG. Current authorities can be verified at https://www.zlg.de/arzneimittel/deutschland/laenderbehoerden.html (website is in German only)

Logo (for information only)	Recognised Authority (alphabetical by country)
	BADEN-WÜERTTEMBERG Regierungspräsidium Tübingen (Referat 25) Leitstelle Arzneimittelueberwachung Baden-Wuerttemberg; Sachgebiet Pharmazeutische Angelegenheiten Sachgebiet 3 Arzneimittel-, Apotheken- und Medizinproduktewesen Pharmazeutische Angelegenheiten Regierungspräsidium Freiburg (Referat 25) Regierungspräsidium Karlsruhe (Referat 25) Regierungspräsidium Stuttgart (Referat 25) **BAYERN** Regierung von Oberbayern Sachgebiet 53.2 - Pharmazie Regierung von Oberfranken **BERLIN** Landesamt für Gesundheit und Soziales Berlin (LAGeSo), Referat I F 3 Arzneimittelwesen (Pharmazeutisches Inspektorat) **BRANDENBURG** Landesamt für Umwelt, Gesundheit und Verbraucherschutz Referat G4 Apotheken, Arzneimittel Medizinprodukte **BREMEN** Senator für Gesundheit Referat 44 Pharmazie, Toxikologie, Gentetechnik **HAMBURG** Behörde für Gesundheit und Verbraucherschutz **HESSEN** Regierungspräsidium Darmstadt Dezernat II 23.1 und 23.2 **MECKLENBURG-VORPOMMERN** Arzneimittelüberwachungs- und –prüfstelle Mecklenburg-Vorpommern LALLF Rostock **NIEDERSACHSEN** Staatliches Gewerbeaufsichtsamt Braunschweig Staatliches Gewerbeaufsichtsamt Hannover Staatliches Gewerbeaufsichtsamt Lüneburg Staatliches Gewerbeaufsichtsamt Oldenburg Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit

Logo (for information only)	Recognised Authority (alphabetical by country)
	NORDRHEIN-WESTFALEN Bezirksregierung Arnsberg Bezirksregierung Detmold Bezirksregierung Düsseldorf Bezirksregierung Köln Bezirksregierung Münster Gesundsheitamt der Stadt Landesamt für Natur, Umwelt und Verbraucherschutz **RHEINLAND-PFALZ** Landesamt für Soziales, Jugend und Versorgung Kreisverwaltung Mainz-Bingen **SAARLAND** Ministerium für Soziales, Gesundheit, Frauen und Familie Referat E3 / Referat E4 **SACHSEN** Landesdirektion Sachsen Referat 24L Pharmazie, GMP-Inspektorat **SACHSEN-ANHALT** Landesverwaltungsamt Sachsen-Anhalt Referat 604 Gesundheitswesen, Pharmazie **SCHLESWIG-HOLSTEIN** Landesamt für soziale Dienste des Landes Schleswig-Holstein **THÜRINGEN** Thüringer Landesamt für Verbraucherschutz
	GREECE National Organisation for Medicines ***Εθνικός Οργανισμός Φαρμάκων*** (**EOF**) Website: http://www.eof.gr/web/guest
	HUNGARY **National Institute of Pharmacy and Nutrition (NIPN)** Website: https://ogyei.gov.hu/
	ICELAND Icelandic **M**edicines **A**gency (**IMA**) Website: https://www.ima.is/

Logo (for information only)	Recognised Authority (alphabetical by country)
	IRELAND Health Products Regulatory Authority (**HPRA**) Website: https://www.hpra.ie/
	ITALY Italian Medicines Agency ***A**genzia **I**taliana del **Fa**rmaco* (**AIFA**) Website: https://www.aifa.gov.it/en/l-agenzia
	JAPAN **Ministry of Health, Labour and Welfare (MHLW)** Website: http://www.mhlw.go.jp/english/ **Pharmaceuticals and Medical Devices Agency (PMDA)** Website: http://www.pmda.go.jp/english/
	LIECHTENSTEIN Office of Healthcare ***A**mt für **G**esundheit* (**AG**) Website: http://www.llv.li/#/1908/amt-fur-gesundheit
	LUXEMBOURG* Ministry of Health *Direction de la Santé Villa Louvigny Division de la Pharmacie et des Medicaments* Website: https://sante.public.lu/fr/index.php *Note: Luxembourg Ministry of Health is not a PIC/S member, however is recognised under the New Zealand – European Community Mutual Recognition Agreement of Conformity Assessment, Certificates and Markings (L 229/62, 17.8.98).
	MALTA Malta Medicines Authority (**MAM**) Website: http://www.medicinesauthority.gov.mt/home?l=1
	NETHERLANDS Health Care Inspectorate *Inspectie voor de Gezondheidszorg* (IGZ) Website: https://www.igz.nl/english/

Logo (for information only)	Recognised Authority (alphabetical by country)
Statens legemiddelverk Norwegian Medicines Agency	**NORWAY** Norwegian Medicines Agency (**NOMA**) Website: https://legemiddelverket.no/english
Chief Pharmaceutical Inspectorate	**POLAND** **Chief Pharmaceutical Inspectorate** Website: https://www.gif.gov.pl/en
Infarmed Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.	**PORTUGAL** National Authority of Medicines and Health Products, IP *Autoridade Nacional do Medicamento e Produtos de Saúde IP* (**INFARMED**) Website: http://www.infarmed.pt/web/infarmed-en/
National Agency for Medicines and Medical Devices of Romania	**ROMANIA** National Agency for Medicines and Medical Devices (**NAMMD**) Website: https://www.anm.ro/en/
HSA Health Sciences Authority	**SINGAPORE** Health Sciences Authority (**HSA**) Website: https://www.hsa.gov.sg/
SÚKL STÁTNY ÚSTAV PRE KONTROLU LIEČIV	**SLOVAK REPUBLIC** State Institute for Drug Control (**SIDC**) Website: http://www.sukl.sk/
	SPAIN* Spanish Agency of Medicinal Products and Medical Devices *Agencia Española del Medicamento y Productos Sanitarios* (AEMPS) Subdirección General de Inspección y Controlo de Medicamentos Division de Inspección y Control Farmaceútico Website: https://www.aemps.gob.es/informa-en/

Logo (for information only)	Recognised Authority (alphabetical by country)
	SPANISH REGIONAL STATE AUTHORITIES LISTED BELOW ARE ALSO ACCEPTABLE SPANISH AUTHORITIES *
	* The PIC/S website states *"The competence for GMP/GDP inspections in Spain is shared between the central authority, Spanish Agency for Medicines and Medicinal Devices (AEMPS) and the Spanish regional authorities, which count as one PIC/S Participating Authority. All Spanish Medicinal Authorities which are listed on the AEMPS website are considered as PIC/S Participating Authorities and are represented in PIC/S by the AEMPS."*
	ARAGON Departamento de Sanidad, Dirección General de Planificación y Aseguramiento
	ISLAS BALEARES Dirección General de Planificación, Evaluación y Farmacia. Conselleria de Salud
	CANARIAS Servicio Canario de la Salud. Servicio de ordenación farmacéutica
	CASTILLA Y LEON Consejería de Sanidad. Junta de Castilla y León, Dirección General de Salud Pública. Servicio de Control y Evaluación de Centros y Actividades Sanitarias
	CATALUNA Generalitat de Catalunya. Departament de Salut. Dirección General de Ordenación y Regulación Sanitarios. Subdirección General de Farmacia y Productos Sanitarias. Servicio de Control Farmacéutico y Productos Sanitarios
	GALICIA Consellería de Sanidade. Xunta de Galicia. Servizo Galego de Saúde. Servizo de Inspección Farmacéutica Subdirección xeral de Inspección, Auditoría e Acreditación de Servizos Sanitarios. Secretaría Xeral Técnica
	REGION DE MURCIA Consejería de Sanidad, Dirección General de Planificación, Ordenación Sanitaria y Farmacéutica e Investigación. Servicio de Ordenación y Atención Farmacéutica

Logo (for information only)	Recognised Authority (alphabetical by country)
	COMUNIDAD FORAL DE NAVARRA Departamento de Salud. Gobierno de Navarra. Sección de Inspección Farmacéutica
	COMUNIDAD VALENCIANA Conselleria de Sanidad Universal y Salud Pública. Dirección General de Farmacia y Productos Sanitarios. Servicio de Ordenación, Control y Vigilancia de Productos Farmacéuticos
LÄKEMEDELSVERKET MEDICAL PRODUCTS AGENCY	**SWEDEN** **M**edical **P**roducts **A**gency (**MPA**) Website: https://lakemedelsverket.se/english/
swissmedic Swiss Agency for Therapeutic Products	**SWITZERLAND** Swiss Agency for Therapeutic Products (**Swissmedic**) Website: https://www.swissmedic.ch/?lang=en
Medicines & Healthcare products Regulatory Agency	**UNITED KINGDOM** **M**edicines and **H**ealthcare Products **R**egulatory **A**gency (**MHRA**) ebsite: https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency
FDA U.S. FOOD & DRUG ADMINISTRATION	**UNITED STATES OF AMERICA** **F**ood and **D**rug **A**dministration (US FDA) Website: https://www.fda.gov/

Version History

Revision Date	Revision Number	Summary of changes
October 2014	Draft	Published version
7 September 2018	1.0	Information in Part 4, section 1.5 of the Guideline, updates to include Malta, Poland and Catalonia. Regulators' logo included and to include websites for each regulator.
02 February 2022	2.0	Added requirement for GMP for API that are prescription medicines. Added requirement for ongoing evidence of current GMP compliance to be provided. Updated logos for Romania, and Switzerland Updated websites for Canada, Hungary, Italy, Luxembourg, Romania, Singapore and Spain. Removed reference to Part 5 of NZRGM.