

AUSTRALIA- EUROPEAN COMMUNITY
MUTUAL RECOGNITION AGREEMENT
OF
CONFORMITY ASSESSMENT, CERTIFICATES AND
MARKINGS

SECTORAL ANNEX

**MEDICINAL PRODUCTS GMP INSPECTION
AND BATCH CERTIFICATION**

AUSTRALIA- EUROPEAN COMMUNITY

**SECTORAL ANNEX - MEDICINAL PRODUCTS GMP INSPECTION
AND BATCH CERTIFICATION**

SCOPE AND COVERAGE

1. The provisions of this Sectoral Annex cover all medicinal products which are industrially manufactured in Australia and the European Community, and to which Good Manufacturing Practice (GMP) requirements apply.

For medicinal products covered by this Sectoral Annex, each Party shall recognise the conclusions of inspections of manufacturers carried out by the relevant inspection services of the other Party and the relevant manufacturing authorisations granted by the Competent Authorities of the other Party.

In addition, the manufacturer's certification of the conformity of each batch to its specifications shall be recognised by the other Party without re-control at import.

"Medicinal products" means all products regulated by the pharmaceutical legislation in the European Community and Australia as listed in the Appendix to this Annex. The definition of medicinal products includes all human and veterinary products, such as chemical and biological pharmaceuticals, immunologicals, radiopharmaceuticals, sterile medicinal products derived from human blood or human plasma, pre-mixes for the preparation of veterinary medicated feedingstuffs, and, where appropriate, vitamins, minerals, herbal remedies and homeopathic medicinal products.

"GMP" is that part of quality assurance which ensures that products are consistently produced and controlled during manufacture to the quality standards appropriate to their intended use and as required by the Marketing Authorisation granted by the importing Party. For the purpose of this Sectoral Annex it includes the system whereby the manufacturer receives the specification of the product and/or process from the marketing authorisation holder or applicant and ensures that the medicinal product is made in compliance with this specification (Equivalent to Qualified Person certification in the European Community).

2. With respect to medicinal products covered by the legislation of one Party but not the other, the manufacturing company can request, for the purpose of this Agreement, an inspection be made by the locally competent inspection service. This provision shall apply *inter alia* to the manufacture of active pharmaceutical ingredients and intermediate products and products intended for use in clinical trials, as well as agreed pre-marketing inspections. Operational arrangements are detailed under Section III, item 3 b.

Certification of manufacturers

3. At the request of an exporter, importer or the competent authority of the other Party, the Authorities responsible for granting manufacturing authorisations and for supervision of the manufacture of medicinal products shall certify that the manufacturer:
 - is appropriately authorised to manufacture the relevant medicinal product or to carry out the relevant specified manufacturing operation,
 - is regularly inspected by the Authorities, and
 - complies with the national GMP requirements recognised as equivalent by the two parties, and which are listed in Appendix 1 to this Sectoral Annex. In case different

GMP requirements would be used as a reference (in line with the provisions in Section 3, 3 b), this is to be mentioned in the certificate.

The certificates shall also identify the site(s) of manufacture (and contract testing laboratories, if any). The format of certificate is attached as Appendix 2; it may be modified by the Joint Committee, as established in Article 12 of the Agreement.

Certificates shall be issued expeditiously, and the time taken should not exceed 30 calendar days. In exceptional cases, such as when a new inspection has to be carried out, this period may be extended to 60 days.

Batch certification

4. Each batch exported shall be accompanied by a batch certificate prepared by the manufacturer (self certification) after a full qualitative analysis, a quantitative analysis of all the active constituents and all the other tests or checks necessary to ensure the quality of the product in accordance with the requirements of the marketing authorisation. This certificate shall attest that the batch meets its specifications and shall be kept by the importer of the batch. It will be made available upon request of the competent authority.

When issuing a certificate, the manufacturer shall take account of the provisions of the current WHO certification scheme on the quality of pharmaceutical products moving in international commerce. The certificate shall detail the agreed specifications of the product, the reference of the analytical methods and the analytical results. It shall contain a statement that the batch processing and packaging records were reviewed and found in conformity with GMP. The batch certificate shall be signed by the person responsible for releasing the batch for sale or supply, i.e. in the European Community the "qualified person" referred to in article 21 of Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products. In Australia, the responsible persons are for manufacturing quality control as specified in the Therapeutic Goods Regulation 19(b) under the Therapeutic Goods Act 1989:

SECTION I: LEGISLATIVE, REGULATORY AND ADMINISTRATIVE REQUIREMENTS

Subject to Section 3 "Operational provisions", general GMP inspections shall be carried out against the GMP requirements of the exporting Party. The legislative, regulatory and administrative requirements are listed in the Appendix.

However, the reference quality requirements of products to be exported, including their manufacturing method and product specifications, shall be those of the relevant product Marketing Authorisation granted by the importing Party.

SECTION II: OFFICIAL INSPECTION SERVICES

For Australia: Therapeutic Goods Administration (TGA)
Department of Health and Family Services
PO Box 100
Woden ACT 2606
Australia
Tel.: 61-6-232 8632
Fax : 61-6-232 8659

For the European Community:

BELGIUM Inspection générale de la Pharmacie
Cité administrative de l'Etat
Quartier Vésale
Algemene Farmaceutische Inspectie
Rijksadministratief Centrum
Vesalius Gebouw
B-1010 BRUXELLES Tel. : 32-2-210 4924
BRUSSEL Fax : 32-2-210 4880

DENMARK Sundhedsstyrelsen -Medicines Division
Frederikssundsvej 378
DK-2700 BRØNSHØJ Tel. : 45-44-889 320
Fax : 45-42-847 077

GERMANY Bundesministerium für Gesundheit
Am Propsthof 78a
D-53108 BONN Tel. : 49-228-941 2340
Fax : 49-228-941 4923

for immunologicals :
Paul-Ehrlich-Institut, Federal Agency for Sera & Vaccines
Postfach
D 63207 LANGEN Tel. : 49-6103-77 1010
Fax : 49-6103-77 1234

GREECE Εθνικός Οργανισμός Φαρμάκων
National Drug Organization (E.O.F.)
Mesogion 284
GR-ATHENS 15562 Tel. : 30-1-654 5530
Fax : 30-1-654 9591

SPAIN Ministerio de Sanidad y Consumo
Subdirección General de Control Farmaceutico
Paseo del Prado 18-20
E-28014 MADRID Tel. : 34-1-596 4068
Fax : 34-1-596 4069

FRANCE

for medicinal products for human use :

Agence du Médicament
143-145 boulevard Anatole France
F-93200 SAINT-DENIS Tél. : 33-1-4813 2000
Fax : 33-1-4813 2478

for veterinary medicinal products :

Agence Nationale du Médicament Vétérinaire
la Haute Marche - Javené
F - 35133 FOUGERES. Tel.: +33-9994 7878
Fax : +33-9994 7899

IRELAND

National Drugs Advisory Board
63-64 Adelaide Road
IRL-DUBLIN 2 Tel. : 353-1-676.4971 - 7
Fax : 353-1-676.7836

ITALY

Ministero della Sanità
Direzione Generale del Servizio Farmaceutico
Viale della Civiltà Romana 7
I-00144 ROMA Tel. : 39-6-5994 3676
Fax : 39-6-5994 3365

LUXEMBOURG

Division de la Pharmacie et des Médicaments
10 rue C.M. Spoo
L-2546 LUXEMBOURG Tel. : 352-478 5590 / 93
Fax : 352-22 44 58

NETHERLANDS

Ministerie van Volksgezondheid, Welzijn, en Sport
Inspectie voor de Gezondheidszorg
Postbus 5850
NL-2280 HW RIJSWIJK Tel. : 31-70-340 6839
Fax : 31-70-340 7159

AUSTRIA

Bundesministerium für Gesundheit und Konsumentenschutz
Radetzkystraße 2
A-1031 WIEN Tel. : 43-1-711 724 642
Fax : 43-1-714 92 22

PORTUGAL

Instituto Nacional da Farmácia e do Medicamento - INFARMED
Av. do Brasil, 53
P - 1700 LISBOA Tel. : 351-1-795 7836
Fax : 351-1-795 9116

FINLAND

National Agency for Medicines
P.O. Box 278
FIN-00531 HELSINKI Tel. : 358-0-396 72 112
Fax : 358-0-714 469

SWEDEN

Läkemedelsverket - Medical Products Agency
Husargatan 8, P.O. Box 26
S - 751 03 UPPSALA Tel. : 46-18-174 600
 Fax : 46-18-548 566

UNITED KINGDOM

for human and veterinary (non immunologicals) :
Medicines Control Agency
1 Nine Elms Lane
GB-LONDON SW8 5NQ Tel. : 44-171-273 0500
 Fax : 44-171-273 0676

for veterinary immunologicals :

Veterinary Medicines Directorate
Woodham Lane
New Haw, Addlestone
GB - SURREY KT15 3NB Tel. : 44-1932-336911
 Fax : 44-1932-336618

SECTION III : OPERATIONAL PROVISIONS

1. Transmission of inspection reports

Upon reasoned request, the relevant inspection services shall forward a copy of the last inspection report of the manufacturing or control site, in case analytical operations are contracted out. The request may concern a "full inspection report" or a "detailed report" (see item 2 below). Each Party shall deal with these inspection reports with the degree of confidentiality requested by the Party of origin.

If the manufacturing operations of the medicinal product in question have not been inspected recently, i.e. when the last inspection dates back to more than two years or a particular need to inspect has been identified, a specific and detailed inspection may be requested. Parties will ensure that inspection reports are forwarded in no more than 30 calendar days, this period being extended to 60 days should a new inspection be carried out.

2. Inspection reports

A "full inspection report" comprises a Site Master File (compiled by the manufacturer or by the inspectorate) and a narrative report by the inspectorate. A "detailed report" responds to specific queries about a firm by the other Party.

3. Reference GMP

- a) Manufacturers shall be inspected against the applicable GMP of the exporting Party (see Appendix 1);

- b) With respect to medicinal products covered by the pharmaceutical legislation of the importing Party but not the exporting one, the locally competent inspection service willing to carry out an inspection of the relevant manufacturing operations shall inspect against its own GMP or, in the absence of specific GMP requirements, against the applicable GMP of the importing Party. This will also be the case when the locally applicable GMP are not considered equivalent, in terms of quality assurance of the finished product, to the GMP of the importing Party.

Equivalence of GMP requirements for specific products or classes of products (e.g. investigational medicinal products, starting materials) will be determined according to a procedure established by the Joint Committee.

4. Nature of inspections

- a) Inspections will routinely assess the compliance of the manufacturer with GMP. These are called general GMP inspections (also regular, periodic, or routine inspections).
- b) "Product- or process-oriented" inspections (which may be "pre-marketing" inspections as relevant) focus on the manufacture of one or one series of product(s) or process(es) and include an assessment of the validation of and compliance with specific process or control aspects as described in the marketing authorisation. Where necessary, relevant product information (the quality dossier of an application/authorisation dossier) shall be provided in confidence to the inspectorate.

5. Inspection/establishment fees

The regime of inspection/establishment fees is determined by the manufacturer's location. Inspection/establishment fees will not be charged to manufacturers located on the territory of the other Party for products covered by this Agreement.

6. Safeguard clause for inspections

Each Party reserves the right to conduct its own inspection for reasons identified to the other Party. Such inspections are to be notified in advance to the other Party, which has the option of joining the inspection. Recourse to this safeguard clause should be an exception. Should such an inspection take place, inspection costs may be recovered.

7. Exchange of information between authorities and approximation of quality requirements

In accordance with the general provisions of the Agreement, the Parties shall exchange any information necessary for the mutual recognition of inspections.

In addition, the relevant Authorities in Australia and in the European Community shall keep each other informed of any new technical guidance or inspection procedure. Each Party shall consult the other before their adoption and will endeavour to proceed towards their approximation.

8. Official Batch release

The official batch release procedure is an additional verification of safety and efficacy of immunological medicinal products (vaccines) and blood derivatives, carried out by the competent authorities before the distribution of each batch of product. This Agreement does not encompass this mutual recognition of official batch releases. However, when an official batch release procedure applies the manufacturer shall provide, at the request of the importing Party, the official batch release certificate if the batch in question has been tested by the control authorities of the exporting Party.

For the European Community, the official batch release procedure for medicinal products for human use is specified, in document "Administrative EC Batch Release Procedure III/3859/92" and different specific batch release procedures. For Australia, the official batch release procedure is specified in document "WHO Technical Report Series, No. 822, 1992."

9. Inspectors training

In accordance with the general provisions of the Agreement, training sessions for inspectors, organised by the Authorities, shall be accessible to inspectors of the other Party. The Parties to the Agreement will keep each other informed of these sessions.

10. Joint Inspections

In accordance with the general provisions of the Agreement, and by mutual agreement between the Parties, joint inspections may be authorised. These inspections are intended to develop common understanding and interpretation of practice and requirements. The setting up of these inspections and their form shall be agreed through procedures approved by the Joint Committee.

11. Alert system

Contact points will be agreed between the Parties to permit competent authorities and manufacturers to inform the authorities of the other Party with the appropriate speed in case of quality defect, batch recalls, counterfeiting and other problems concerning quality, which could necessitate additional controls or suspension of the distribution of the batch. A detailed alert procedure shall be agreed.

The Parties shall ensure that any suspension or withdrawal (total or partial) of a manufacturing authorisation, based on non compliance with GMP and which could affect the protection of public health, are communicated to each other with the appropriate degree of urgency.

12. Contact points

For the purpose of this Agreement, the contact points for any technical question, such as exchange of inspection reports, inspectors training sessions, technical requirements, will be:

for Australia:
for medicinal products for human use:
the Chief GMP Auditor
Therapeutic Goods Administration
Department of Health and Family Services
PO Box 100
Woden ACT 2606
Australia
Tel: 61-6-232-8632
Fax: 61-6-232-8659

for medicinal products for use in animals:
the GMP Licensing Scheme Manager
National Registration Authority
PO Box E 240
Parkes ACT 2600
Australia
Tel: 61-6-272-5158
Fax: 61-6-272-4753

for the European Community:
the Director of the European Agency for the Evaluation of Medicinal Products
7 Westferry Circus
Canary Wharf
London E14 4HB
United Kingdom
Tel: 44-171-418 8400
Fax: 44-171-418 8416

13. Divergence of views

Both Parties shall use their best endeavours to resolve any divergence of views concerning *inter alia* compliance of manufacturers and conclusions of inspection reports. Unresolved divergences of view will be referred to the Joint Committee.

<p style="text-align: center;">SECTION IV : TRANSITIONAL ARRANGEMENTS FOR VETERINARY MEDICINAL PRODUCTS</p>
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The Parties note that the current GMP requirements for veterinary medicinal products in Australia are not equivalent to those that apply in the European Union. Therefore, Australian veterinary medicinal products manufacturers will be inspected by Therapeutic Goods Administration on behalf of the veterinary National Registration Authority, according to the TGA reference GMP and relevant additional EU GMP for veterinary medicinal products.

During a two year transitional period, TGA inspection reports will be routinely sent to the importing Party, which may accept them or decide to carry out an inspection itself. If

accepted, the European Community will recognise Australian manufacturers' certifications of batch conformity.

Two years after the entry into force of the Agreement, the European Community shall, subject to satisfactory verification of Australia's GMP inspection programme, recognise the conclusions of inspections carried out by the TGA and Australian manufacturers' certifications of batch conformity.

Should the National Registration Authority (NRA) begin to carry out inspections itself, inspection reports will also be routinely transmitted to the importing Party until there has been a satisfactory verification of the NRA GMP inspection programme.

APPENDIX 1

LIST OF APPLICABLE LEGISLATIVE, REGULATORY & ADMINISTRATIVE PROVISIONS

For the European Community:

Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products as extended, widened and amended.

Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products as extended, widened and amended.

Council Directive 81/851/EEC of 6 November 1981 on the approximation of the laws of the Member States relating to veterinary medicinal products as widened and amended.

Commission Directive 91/356/EEC of 13 June 1991 laying down the principles and guidelines of good manufacturing practice for medicinal products for human use

Commission Directive 91/412/EEC of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products

Council Regulation No (EEC) 2309/93 of 23 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products

Council Directive 25/92/EEC of 31 March 1992 on the wholesale distribution of medicinal products for human use & Guide to Good Distribution Practice

Current version of the Guide to Good Manufacturing Practice, Rules Governing Medicinal Products in the European Community, Volume IV

For Australia:

For products for human use:

Therapeutic Goods Act 1989, and regulations, Orders and Determinations thereunder, including Orders setting standards such as labelling, the Determination establishing manufacturing Principles.

- ◆ Therapeutic Goods Act 1989
- ◆ Therapeutic Goods Regulations
- ◆ Therapeutic Goods (Charges) Act 1989
- ◆ Therapeutic Goods (Charges) Regulations
- ◆ Therapeutic Goods (Excluded Goods) Order No. 1 of 1992
- ◆ Therapeutic Goods (Goods that are not Therapeutic Devices) Order No. 1 of 1992
- ◆ Therapeutic Goods (Manufacturing Principles) Determinations.
- ◆ Australian Code of Good Manufacturing Practice for Therapeutic Goods - Medicinal Products, August 1990, including:
 - Appendix A: Guidelines for Sterilisation by Irradiation, October 1993
 - Appendix C: Guidelines on Tests for Sterility, July 1991
 - Appendix D: Guidelines for laboratory Instrumentation, November 1991
 - Appendix E: Guidelines for Industrial Ethylene Oxide Sterilisation of Therapeutic Goods, April 1986
 - Appendix F: Guidelines for Estimation of Microbial Count in Process Water, August 1990
 - Appendix G: Guidelines for Good Manufacturing Practice for Investigational Medicinal Products, June 1993
- ◆ Australian Code of Good Manufacturing Practice - Blood and Blood products (including technical annexes 1-7), July 1992
- ◆ Australian Code of Good Manufacturing Practice for Therapeutic Goods - Sunscreen Products, February 1994
- ◆ Australian Code of Good Manufacturing Practice for Therapeutic Goods - Medicinal Gases, July 1992

and for products for veterinary use:

Legislation - Commonwealth:

- Agricultural and Veterinary Chemicals (Administration) Act, 1992
- Agricultural and Veterinary Chemicals Act, 1993
- Agricultural and Veterinary Chemicals Code Act, 1993
- Agricultural and Veterinary Chemicals (Consequential Amendments) Act, 1993

Legislation - New South Wales:

- Stock Foods and Medicines Act, 1940
- Public Health Act, 1961
- Poison Act, 1966

- Pesticides and Allied Chemicals Act, 1979

Legislation - Victoria:

- Animal Preparations Act, 1987
- Health Act, 1958
- Drugs, Poisons and Controlled Substances Act, 1981

Legislation - Queensland:

- Agricultural Standards Act, 1952-1981
- Stock Act, 1915-1976
- Health Act, 1937-1987

Legislation - South Australia:

- Stock Medicines Act, 1939-1978
- Stock Foods Act, 1941
- Dangerous Drugs Act, 1986
- Controlled Substances Act, 1984
- Stock Diseases Act, 1934

Legislation - Western Australia:

- Veterinary Preparations and Animal Feeding Stuffs Act, 1976–1982
- Poisons Act, 1964-1981
- Health (Pesticides) regulations, 1956

Legislation - Tasmania:

- Veterinary Medicines Act, 1987
- Poisons Act, 1971
- Public Health Act, 1962
- Pesticides Act, 1968

Legislation - Northern Territory:

- Poisons and Dangerous Drugs Act, 1983
- Therapeutic Goods and Cosmetics Act, 1986
- Stock Diseases Act, 1954

**CERTIFICATE OF PHARMACEUTICAL MANUFACTURER IN THE
FRAMEWORK OF THE AGREEMENT ON MUTUAL RECOGNITION IN RELATION
TO CONFORMITY ASSESSMENT, CERTIFICATES AND MARKINGS BETWEEN
AUSTRALIA AND THE EUROPEAN COMMUNITY, SECTORAL ANNEX ON
MEDICINAL PRODUCTS GMP INSPECTION AND BATCH CERTIFICATION**

As requested by the Competent Authorities of Australia / (*) on
.../.../... (date) (reference:), the Competent Authority of
..... confirms the following:

The company,
whose legally registered address is:
.....

has been authorised, under the Therapeutic Goods Act 1989 / Directive 75/319/EEC, Article 16,
and Directive 81/851/EEC, Article 24, transposed in the national legislation of
..... (*), under the authorisation reference number
.....,

covering the following site(s) of manufacture (and contract testing laboratories, if any):

- 1
-
- 2
-
- 3
-

to carry out the following manufacturing operations:

- + complete manufacture (**)
- + partial manufacture (**), i.e. (detail of manufacturing operations authorised):
.....
.....

for the following medicinal product:

for human use / use in animals (**).

From the knowledge gained during inspections of this manufacturer, the latest of which was
conducted on .../.../... (date), it is considered that the company complies with the Good
Manufacturing Practice requirements referred to in the Agreement on Mutual Recognition in
relation to Conformity Assessment, Certificates and Markings between Australia and the
European Community.

.../.../... (date)

For the Competent Authority,

(Name and signature of the officer responsible)

(*) : insert European Community Member State or European Community as required
(**): delete that which does not apply