NEW ZEALAND- EUROPEAN COMMUNITY

MUTUAL RECOGNITION AGREEMENT

OF

CONFORMITY ASSESSMENT, CERTIFICATES AND

MARKINGS

SECTORAL ANNEX

MEDICINAL PRODUCTS GMP INSPECTION AND BATCH CERTIFICATION

NEW ZEALAND- 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 New Zealand and the European Community, and to which Good Manufacturing Practice (GMP) requirements apply.

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

   In addition, the manufacturer's certification of the conformity of each batch to its specifications will 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 New Zealand 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, stable 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 will 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 supervising manufacturers of medicinal products will 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 will 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 will 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 will 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 will attest that the batch meets its specifications and will 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 will take account of the provisions of the current WHO certification scheme on the quality of pharmaceutical products moving in international commerce. The certificate will detail the agreed specifications of the product, the reference of the analytical methods and the analytical results. It will contain a statement that the batch processing and packaging records were reviewed and found in conformity with GMP. The batch certificate will 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 New Zealand, the responsible persons are:

   – for pharmaceuticals for human use: the authorised person responsible for Quality Assurance named on the licence to manufacture (Medicines Act 1981); and

   – for animal remedies (veterinary medicines): the authorised person responsible for Quality Assurance named on the manufacturers licence (Animal Remedies Act 1967).

SECTION I: LEGISLATIVE, REGULATORY AND ADMINISTRATIVE REQUIREMENTS

Subject to Section III "Operational provisions", general GMP inspections will be carried out against the GMP requirements of the exporting Party. The legislative, regulatory and administrative requirements are listed in the Appendix 1.

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

SECTION II: OFFICIAL INSPECTION SERVICES

For New Zealand:

for medicines for human use:
Ministry of Health
Therapeutics Section
P.O. Box 5013
Wellington
New Zealand
Tel.: 64-4-496-2081
Fax: 64-4-496-2229

for veterinary medicines:
Ministry of Agriculture
Agricultural Compounds Unit
P.O. Box 40063
Upper Hutt
New Zealand
Tel.: 64-4-528-0126
Fax : 64-4-528-1378

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 Φαρμάκου
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 Servicio 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 5406
NL-2280 HW RIJSWIJK
Tel. : 31-70-340 7911
Fax : 31-70-340 5177

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 will forward a copy of the last inspection report of the manufacturing site or control site, in the case where analytical operations are contracted out. The request may concern a "full inspection report" or a "detailed report" (see item 2 below). Each Party will 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 will be inspected against the applicable GMP of the exporting country (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 will inspect against its own GMP or, in the absence of specific GMP requirements, against the applicable GMP of the importing country. 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) will 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 except as provided for in paragraph 6 below.

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 will exchange any information necessary for the mutual recognition of inspections.

In addition, the relevant Authorities in New Zealand and in the European Community will keep each other informed of any new technical guidance or inspection procedure. Each Party will 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 mutual recognition of official batch releases. However, when an official batch release procedure applies, the manufacturer will 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 New Zealand, 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, will be accessible to inspectors of the other Party. The Parties to the Agreement will keep each other informed on 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 will 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 will be agreed.

The Parties will 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 New Zealand:
for medicinal products for human use:
Ministry of Health
Therapeutics Section
PO Box 5013
Wellington
New Zealand
Tel.: 64-4-496-2000
Fax: 64-4-496-2340

for medicinal products for use in animals:
Ministry of Agriculture
Agricultural Compounds Unit
PO Box 40063
Upper Hutt
New Zealand
Tel.: 64-4-528 4794
Fax: 64-4-528 6089

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 will 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.

SECTION IV : TRANSITIONAL ARRANGEMENTS FOR VETERINARY MEDICINAL PRODUCTS

In respect of veterinary medicinal products, the European Community will, subject to satisfactory verification of New Zealand's GMP inspection programme, recognise the conclusions of New Zealand GMP inspections and of New Zealand Manufacturers' certifications of batch conformity, three years after the entry into force of the Agreement. New Zealand will, subject to satisfactory verification of the European Community's GMP inspection programme, recognise the conclusions of the European Community's inspections and of the European Community's Manufacturers' certifications of batch conformity three years after the entry into force of the Agreement. During this three year period, joint inspections, carried out in accordance with Section III, item 10 of this Sectoral Annex, may be authorised as a means to build further confidence between the Parties regarding the application and interpretation of their respective requirements.

The terms of any existing recognition arrangements concerning imports into New Zealand will remain valid during this three year period.

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 New Zealand:

Medicines Act 1981

Medicines Regulations 1984

New Zealand Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods, Parts 1, 2, 4 and 5

Animal Remedies Act 1967

Animal Remedies Regulations 1980

Code of GMP for Animal Remedies 1994

APPENDIX 2

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

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

The company .....,
whose legally registered address is: .....
.....
.....
has been authorised, under the Medicines Act 1981 and Medicines Regulations 1984 / 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 New Zealand 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