French National Agency for Medicines and Health Products Safety

CERTIFICATE NUMBER: ***2019/HPF/FR/067***

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER [1, 2]

Part 1

Issued following an inspection in accordance with :
Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of France confirms the following:
The manufacturer: ***CIS BIO INTERNATIONAL***
Site address: ***Route Nationale 306, Saclay BP 32, GIF SUR YVETTE, 91192, France***

Has been inspected under the national inspection programme in connection with manufacturing authorisation no. ***MM 14/58*** in accordance with Art. 40 of Directive 2001/83/EC transposed in the following national legislation:
Art. L.5124-3 of Public Health Code

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2018-12-14*** , it is considered that it complies with :

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC [3]

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

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[1] *The certificate referred to in paragraph 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/EC, shall also be required for imports coming from third countries into a Member State.*

[2] *Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.*

[3] *These requirements fulfil the GMP recommendations of WHO.*

Part 2

Human Medicinal Products

1 MANUFACTURING OPERATIONS	
1.1	**Sterile products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.2 Lyophilisates 1.1.1.4 Small volume liquids Special Requirements 5 Radiopharmaceuticals
	1.1.2 Terminally Sterilised (processing operations for the following dosage forms) 1.1.2.3 Small volume liquids Special Requirements 5 Radiopharmaceuticals 1.1.2.5 Other: column of molybdenum-99 for radionuclide generator of technetium(en)
	1.1.3 Batch certification
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1 Capsules, hard shell Special Requirements 5 Radiopharmaceuticals 1.2.1.6 Liquids for internal use Special Requirements 5 Radiopharmaceuticals 1.2.1.10 Radionuclide generators Special Requirements 5 Radiopharmaceuticals
	1.2.2 Batch certification

1.3	**Biological medicinal products (list of product types)**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.1 Blood products Special Requirements 5 Radiopharmaceuticals 1.3.1.2 Immunological products Special Requirements 5 Radiopharmaceuticals 1.3.1.5 Biotechnology products Special Requirements 5 Radiopharmaceuticals 1.3.1.6 Human or animal extracted products Special Requirements 5 Radiopharmaceuticals
	1.3.2 Batch Certification (list of product types) 1.3.2.1 Blood products Special Requirements 5 Radiopharmaceuticals 1.3.2.2 Immunological products Special Requirements 5 Radiopharmaceuticals 1.3.2.5 Biotechnology products Special Requirements 5 Radiopharmaceuticals 1.3.2.6 Human or animal extracted products Special Requirements 5 Radiopharmaceuticals
1.5	**Packaging**
	1.5.1 Primary Packing 1.5.1.1 Capsules, hard shell 1.5.1.6 Liquids for internal use 1.5.1.10 Radionuclide generators
	1.5.2 Secondary packing
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.2 Microbiological: non-sterility* *1.6.3 Chemical/Physical* *1.6.4 Biological*

2 IMPORTATION OF MEDICINAL PRODUCTS	
2.1	**Quality control testing of imported medicinal products**
	2.1.1 Microbiological: sterility *2.1.2 Microbiological: non-sterility* *2.1.3 Chemical/Physical* *2.1.4 Biological*
2.2	**Batch certification of imported medicinal products**
	2.2.1 Sterile products 2.2.1.1 Aseptically prepared 2.2.1.2 Terminally sterilised
	2.2.2 Non-sterile products
	2.2.3 Biological medicinal products 2.2.3.1 Blood products 2.2.3.2 Immunological products 2.2.3.5 Biotechnology products 2.2.3.6 Human or animal extracted products
2.3	**Other importation activities**
	2.3.1 Site of physical importation
	2.3.2 Importation of intermediate which undergoes further processing

Clarifying remarks (for public users)

This pharmaceutical site is the subject of the injunction n° 2018MEDCHIM234-INJ dated February 20th 2019 published on the ANSM website. This good manufacturing practice certificate is valid until June 30th 2020 --- Manufacture : 1.1.2.5 : the sterilization of the column of molybdenum-99 is followed by an aseptic connexion with a receiving recipient for radionuclide generator of technetium. The site is allowed to manufacture radiopharmaceutical medicines, generators, kits and precursors stipulated in paragraph 7°, 8°, 9°, 10° of Article L.5121 of the French Public Health Code --- Signatory: Mrs Dominique Debourges, deputy head of pharmaceutical product inspection and counterfeiting fight department --- The ANSM does not issue hardy copies of good practice certificates

2019-02-25

Name and signature of the authorised person of the Competent Authority of France

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Confidential
French National Agency for Medicines and Health Products Safety
Tel: ***Confidential***
Fax: ***Confidential***

Health and Youth Care Inspectorate – Pharmaceutical Products

CERTIFICATE NUMBER: ***NL/H 20/2016374***

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER [1, 2]

Part 1

Issued following an inspection in accordance with :
Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of Netherlands confirms the following:
The manufacturer: ***Curium Netherlands B.V.***
Site address: ***Westerduinweg 3, PETTEN, 1755LE, Netherlands***

Has been inspected under the national inspection programme in connection with manufacturing authorisation no. ***108988 F*** in accordance with Art. 40 of Directive 2001/83/EC transposed in the following national legislation:
Art. 100 of the Medicines Act

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2020-01-16*** , it is considered that it complies with :

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC [3]

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

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[1] *The certificate referred to in paragraph 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/EC, shall also be required for imports coming from third countries into a Member State.*

[2] *Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.*

[3] *These requirements fulfil the GMP recommendations of WHO.*

Part 2

Human Medicinal Products

1 MANUFACTURING OPERATIONS	
1.1	**Sterile products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.2 Lyophilisates Special Requirements 5 Radiopharmaceuticals 1.1.1.6 Other: radionuclide generator(en)
	1.1.2 Terminally Sterilised (processing operations for the following dosage forms) 1.1.2.3 Small volume liquids Special Requirements 5 Radiopharmaceuticals
	1.1.3 Batch certification
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1 Capsules, hard shell Special Requirements 5 Radiopharmaceuticals 1.2.1.10 Radionuclide generators Special Requirements 5 Radiopharmaceuticals
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1.5	**Packaging**
	1.5.1 Primary Packaging 1.5.1.1 Capsules, hard shell Special Requirements 5 Radiopharmaceuticals 1.5.1.10 Radionuclide generators Special Requirements 5 Radiopharmaceuticals
	1.5.2 Secondary packaging

1.6	**Quality control testing**
	1.6.1 Microbiological: sterility
	1.6.2 Microbiological: non-sterility
	1.6.3 Chemical/Physical
	1.6.4 Biological

2 IMPORTATION OF MEDICINAL PRODUCTS	
2.1	**Quality control testing of imported medicinal products**
	2.1.1 Microbiological: sterility
	2.1.3 Chemical/Physical
	2.1.4 Biological
2.2	**Batch certification of imported medicinal products**
	2.2.1 Sterile products 2.2.1.1 Aseptically prepared 2.2.1.2 Terminally sterilised
2.3	**Other importation activities**
	2.3.1 Site of physical importation
	2.3.2 Importation of intermediate which undergoes further processing

Clarifying remarks (for public users)

1.6.4 and 2.1.4 are only applicable for endotoxine test

2020-03-12

Name and signature of the authorised person of the Competent Authority of Netherlands

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Confidential
Health and Youth Care Inspectorate – Pharmaceutical Products
Tel: ***Confidential***
Fax: ***Confidential***

HANDELSVERGUNNING

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN/ MEDICINES EVALUATION COLLEGE

CBG MEB

MEDICINES EVALUATION BOARD

Registration Nr.	RVG 16136
Name of the medicine	Ultra-TechneKow FM, radionuclide generator 2, 15-43,00 GBq/stuk
Pharmaceutical form	Radionuclide generator
Active substances and quantity per dosage unit or concentration	TECHNETIUM TC 99M, 2.15-43.0 GBq/st
Name and address of the marketing authorization holder	Curium Netherlands B.V. Westerduinweg 3 1755 LE Petten
Date of issue	1 7 December 1996
Date of renewal indefinitely	17 December 2016
Delivery status	Prescription only

Utrecht, 13 november2019

(Signature)

mw. dr. A.J. de Vries-van der Weij

This page(s) together with the last approved version of the summary of product characteristics constitute(s) the marketing authorisation.

«MEDEFERENT GRUP» S.R.L. IDNO 1002600053289

HANDELSVERGUNNING

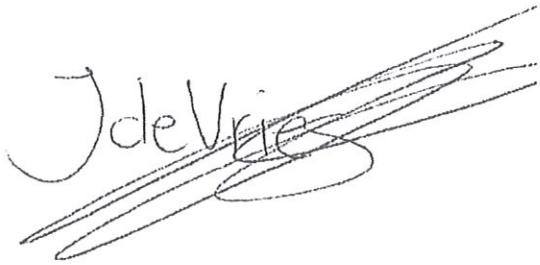
COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

CBG MEB

MEDICINES EVALUATION BOARD

registratienummer	**RVG** 16136	
naam van het geneesmiddel	Ultra-TechneKow FM, radionuclide generator 2,15-43,00 GBq/stuk	
farmaceutische vorm	Radionuclide generator	
werkzame stoffen en hoeveelheid per doseringseenheid of de concentratie	TECHNETIUM TC 99M	2.15-43.0 GBq/st
naam en adres houder van de handelsvergunning	Curium Netherlands B.V. Westerduinweg 3 1755 LE Petten	
datum van afgifte	17 december 1996	
datum van verlenging voor onbepaalde tijd	17 december 2016	
afleverstatus	Uitsluitend recept	

Utrecht, 13 november 2019



mw. dr. A.J. de Vries-van der Weij

Deze pagina('s) vormt (vormen) samen met de laatst goedgekeurde versie van de samenvatting van de productkenmerken de handelsvergunning.

HANDELSVERGUNNING

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN/ MEDICINES EVALUATION COLLEGE

CBG MEB

MEDICINES EVALUATION BOARD

Registration Nr.	RVG 35162
Name of the medicine	Technescan Sestamibi 1 mg, kit for radiopharmaceutical preparation
Pharmaceutical form	kit for radiopharmaceutical preparation
Active substances and quantity per dosage unit or concentration	[Tetrakis(2-methoxy-2-methylpropyl-1 isocyanide)copper(I)] tetrafluoroborate 1.0mg/vial
Name and address of the marketing authorization holder	Mallinckrodt Medical B.V. Westerduinweg 3 1755 LE Petten
Date of issue	28 April 2009
Date of renewal indefinitely	24 july 2013
Delivery status	Prescription only

Utrecht, 05 june 2013

(Signature)

mw. dr. H. Stevenson
deputy secretary

This page(s) together with the last approved version of the summary of product characteristics constitute(s) the marketing authorisation.

HANDELSVERGUNNING

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

CBG MEB

MEDICINES EVALUATION BOARD

registratienummer	**RVG** 35162	
naam van het geneesmiddel	Technescan Sestamibi 1 mg kit voor radiofarmaceutisch preparaat	
farmaceutische vorm	Kit voor radiofarmaceutisch preparaat	
werkzame stoffen en hoeveelheid per doseringseenheid of de concentratie	KOPER(1+),TETRAKIS[1-ISOCYANO-2-METHOXY-2-METHYLPROPYL]TETRAFLUORBORAAT	1.0 mg/flacon
naam en adres houder van de handelsvergunning	Mallinckrodt Medical B.V. Westerduinweg 3 1755 LE Petten	
datum van afgifte	28 april 2009	
datum van verlenging voor onbepaalde tijd	24 juli 2013	
afleverstatus	Uitsluitend recept	
wettelijke grondslag	Art 10(1), Directive 2001/83/EC, generic application	

Utrecht, 05 juni 2013

mw. ir. H. Stevenson

Adjunct-Secretaris

Deze pagina('s) vormt (vormen) samen met de laatst goedgekeurde versie van de samenvatting van de productkenmerken de handelsvergunning.

HANDELSVERGUNNING

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN/ MEDICINES EVALUATION COLLEGE

CBG MEB

MEDICINES EVALUATION BOARD

Registration Nr.	RVG 16133
Name of the medicine	Technescan HDP 3.0 mg, kit for radiopharmaceutical preparation
Pharmaceutical form	kit for radiopharmaceutical preparation
Active substances and quantity per dosage unit or concentration	Sodium Oxidronate 3.0mg/vial
Name and address of the marketing authorization holder	Curium Netherlands B.V. Westerduinweg 3 1755 LE Petten
Date of issue	14 November 1996
Date of renewal indefinitely	14 November 2016
Delivery status	Prescription only

Utrecht, 18 march 2020

(Signature)

dr. M.B. Scholten

This page(s) together with the last approved version of the summary of product characteristics constitute(s) the marketing authorisation.

HANDELSVERGUNNING

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

CBG MEB

MEDICINES EVALUATION BOARD

registratienummer	**RVG** 16133	
naam van het geneesmiddel	Technescan HDP 3,0 mg kit voor radiofarmaceutisch preparaat	
farmaceutische vorm	Kit voor radiofarmaceutisch preparaat	
werkzame stoffen en hoeveelheid per doseringseenheid of de concentratie	OXIDRONAAT DINATRIUM	3.0 mg/flacon
naam en adres houder van de handelsvergunning	Curium Netherlands B.V. Westerduinweg 3 1755 LE Petten	
datum van afgifte	14 november 1996	
datum van verlenging voor onbepaalde tijd	14 november 2016	
afleverstatus	Uitsluitend recept	

Utrecht, 18 maart 2020

M. Scholten

dhr. M.B. Scholten

Deze pagina('s) vormt (vormen) samen met de laatst goedgekeurde versie van de samenvatting van de productkenmerken de handelsvergunning.

ANEXA NOI. RUSENI, SOCIETATEA CU RĂSPUNDERE LIMITATĂ A REPREZENTANȚILOR MEDEFERENT GRUP
IDNO 1002600053289
«MEDEFERENT GRUP»
S.R.L.

Petten, The Netherlands

Date: 03 August 2020

I, Sandra van Leeuwen, certify that the following is, to the best of my knowledge and belief, a true and accurate translation ofthe document with registration number RVG 16139 from Dutch into English.

Sandra van Leeuwen
Head of Regulatory Affairs
Curium Netherlands B.V.

Curium Netherlands B.V.
Visit: Westerduinweg 3, 1755 LE Petten, The Netherlands
Mail: P.O. Box 3, 1755 ZG Petten, The Netherlands

T +31 (0)224 56 78 90
W curiumpharma.com
Trade register Alkmaar: 37042281

Medicines Evaluation Board

CBG
MEB
MEDICINES EVALUATION BOARD

registration number	**RVG** 16139
name of the medicinal product	Technescan DTPA, 20,8 mg, kit for radiopharmaceutical preparation
active substances and quantity per unit of dose or the concentration	PENTETIC ACID 20.8 mg/vial
name and address of the marketing authorization holder	Curium Netherlands B.V. Westerduinweg 3 1755 LE Petten
Date of registration	29 October 1996
Date of renewal indefinitely	29 October 2016
Channeling	prescription only

Utrecht, 12 March 2020

[signature]
Mr. M.B. Scholten

These page(s) forms (form) together with last approved version of summary of product characteristics the marketing authorization.

FRENCH REPUBLIC

MEDICINAL PRODUCTS AGENCY
Evaluation Department

Saint-Denis, **25 June 1997**

The Marketing Authorization Holder
Laboratoires **CIS bio International**
B.P. 32
91192 GIF SUR YVETTE Cedex
FRANCE

Our reference n°s: NL 18 548
GTRA N°63
YMC/BL

THE DIRECTOR GENERAL OF THE MEDICINAL PRODUCTS AGENCY,

IN VIEW OF book V of the Public Health Code, particularly Articles L. 601, and R. 5128 to R. 5140 and R 5143-5-1 to R 5143-5-5;

IN VIEW OF book VI of the Public Health Code, particularly Articles L. 670-1

IN VIEW OF the marketing authorization application submitted by Laboratoires **CIS bio International, FRANCE**

for the proprietary medicinal product named: **PULMOCIS, kit for the preparation of technetium [^{99m}Tc] human albumin macroaggregates - MAA**

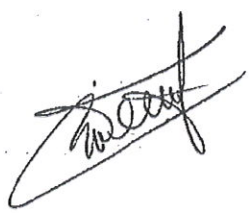
IN VIEW OF the opinion of the Commission mentioned in Article R.5140 of the Public Health Code;

HAS DECIDED

ARTICLE 1 - The marketing authorization as set out in Article L. 601 of the Public Health Code is granted for the proprietary medicinal product named:

PULMOCIS, kit for the preparation of technetium [^{99m}Tc] human albumin macroaggregates - MAA

TRADUCTION CERTIFIÉE
CONFORME A L'ORIGINAL



NL 18 548.CIS:

ARTICLE 2 – The raw material (human plasma) used for the fractionation has to be compliant with the biological characterictics (including detection tests) stated in the dossier. These characteristics must be updated according to the evolution of regulation in this field. Draft modifications must be submitted for approval.

ARTICLE 3 – Compliance with the manufacturing and control methods of the proprietary medicinal product stated in the dossier is required. The methods are to be updated to keep pace with scientific and technical progress. The draft modifications are to be submitted for approval.

ARTICLE 4 - The information intended for the medical and health care professions must comply with the provisions of appendix I (SUMMARY OF PRODUCT CHARACTERISTICS) and appendix IIA (KIT USER PACKAGE LEAFLET) of this decision.

The information intended for the public should conform to the provisions of appendices IIB (PATIENT PACKAGE LEAFLET) and appendix III (LABELLING) of this decision.

ARTICLE 5 – As an exception to article R 5144-26, taking into account the possible use for several patients, all the detachable labels corresponding to the number of patients are included in the secondary packaging.

ARTICLE 6 - The validity of this marketing authorization is limited to five years from the date of this decision. It may be renewed under the conditions set out in Article R.5137 of the Public Health Code.

ARTICLE 7 – Blood donations are compliant with articles L. 666-1 to L. 666-7 of the Public Health Code.

ARTICLE 8 - This decision has been notified to the party concerned.

Decision made in Saint-Denis, 25 June 1997

Certified copy
The Inspecting Pharmacist

A. NORTH

THE DIRECTOR GENERAL OF THE
MEDICINAL PRODUCTS AGENCY

Didier TABUTEAU

TRADUCTION CERTIFIÉE
CONFORME A L'ORIGINAL

Enclosed: 4 annexes

NL 18 548.CIS

AGENCE DU MEDICAMENT
Direction de l'Evaluation

RÉPUBLIQUE FRANÇAISE

SAINT DENIS, le 25 JUIN 1997

Monsieur le Titulaire de
l'Autorisation de Mise sur le Marché
Laboratoires **CIS Bio internationale**
B.P. 32
91192 GIF SUR YVETTE Cédex

Références à rappeler : NL 18 548
GTRA 63
YMC/BL

LE DIRECTEUR GENERAL DE L'AGENCE DU MEDICAMENT,

VU le Livre V du code de la santé publique, notamment les articles L. 601, R. 5128 à R. 5140 et R. 5143-5-1 à R. 5143-5-5 ;

Vu le livre VI du code la santé publique, notamment les articles L. 670-1

VU la demande d'autorisation de mise sur le marché présentée par les laboratoires **CIS Bio International**

pour la spécialité pharmaceutique dénommée : **PULMOCIS, Trousse pour la préparation de macroagrégats d'albumine humaine technétiés [^{99m}Tc]MAA**

VU l'avis de la commission prévu à l'article R.5140 du code de la santé publique;

D E C I D E

ARTICLE 1.- L'autorisation de mise sur le marché mentionnée à l'article L. 601 du code de la santé publique est accordée à la spécialité dénommée :

- **PULMOCIS, Trousse pour la préparation de macroagrégats d'albumine humaine technétiés [^{99m}Tc]MAA**

ARTICLE 2.- Le matériel de départ (plasma humain) utilisé pour le fractionnement devra répondre aux caractéristiques biologiques (incluant les tests de dépistage) prévues au dossier. Ces caractéristiques devront être actualisées en fonction de l'évolution des réglementations dans ce domaine. Les projets de modification devront être soumis pour approbation.

«MEDEFERENT GRUP» S.R.L.

143/147, Boulevard Anatole France - 93285 Saint-Denis Cedex - Tél. : 48.13.20.00

ARTICLE 3.- Les méthodes de fabrication et les techniques de contrôle de cette spécialité, prévues au dossier, devront être respectées. Elles devront être modifiées en fonction des progrès scientifiques et techniques. Les projets de modification devront être soumis pour approbation.

ARTICLE 4. - L'information destinée au corps médical et aux professions de santé devra être conforme aux dispositions de l'annexe I (RESUME DES CARACTERISTIQUES DU PRODUIT) et de l'annexe IIA (NOTICE POUR UTILISATEUR DE LA TROUSSE) de la présente décision.

L'information destinée au public devra être conforme aux dispositions des annexes IIB (NOTICE PATIENT) et annexe III (ETIQUETAGE) de la présente décision.

ARTICLE 5.- Par dérogation à l'article R. 5144-26, compte tenu de l'utilisation possible pour plusieurs patients, l'ensemble des étiquettes détachables correspondant au nombre de patients se trouve dans le conditionnement secondaire.

ARTICLE 6. - La validité de cette autorisation de mise sur le marché est limitée à cinq ans à compter de la date de la présente décision. Elle peut être renouvelée dans les conditions prévues à l'article R. 5137 du code de la santé publique.

ARTICLE 7. - Les dons de sang répondent aux critères prévus aux articles L. 666-1 à L. 666-7 du code de la santé publique.

ARTICLE 8. -La présente décision est notifiée à l'intéressé.

FAIT A SAINT-DENIS, le 25 JUIN 1997

Pour ampliation
Le Pharmacien-inspecteur

NORTH

LE DIRECTEUR GENERAL
DE L'AGENCE DU MEDICAMENT

Didier TABUTEAU

P.J : 4 annexes

NL 18 548.CIS