3.2.S.4.4 Batch Analyses

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3.2.S.4.4.1 Batch analysis

A tabulated summary of 3 progesterone batches issued from the manufacturers Pharmacia & Upjohn and Bim Sifram Group is provided overleaf.

Table 3.2.S.4.4.-1 Non-micronized progesterone batches from Bim Sifram group and Pharmacia & Upjohn

Manufacturer	Batch number	Manufacturing date	Localisation
BIM SIFRAM	Pro-150301	March 2015	Zhejiang Shenzhou Chine
	Pro-150302		
	Pro-150303		
Pharmacia & Upjohn	L37467	January 2015	Pharmacia & Upjohn
	L37468		
	L37586		

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Table 3.2.S.4.4.-2 Non-micronized progesterone batches from Bim Sifram group

		Batch number (date of manufacture)		
Tests	**Specifications**	**Pro-150301 (17-03-2015)**	**Pro-150302 (18-03-2015)**	**Pro-150303 (19-03-2015)**
Characters	White or almost white, crystalline powder or colourless crystals.	Complies	Complies	Complies
A – IR spectrum	Comparable to the reference	Complies	Complies	Complies
B - TLC	Comparable to the reference	Complies	Complies	Complies
Tests				
Specific optical rotation (2.2.7)	+186° to +194°	+187.5°	+187.2°	+192.6°
Loss on drying (2.2.32)	≤ 0.5 %	0.1%	0.1%	0.1%
Related substances (HPLC 2.2.29)				
Impurity I	≤0.6%	Not found	Not found	Not found
Impurity B	≤0.2%	0.13%	0.14%	0.12%
Impurity C	≤0.3%	0.28%	0.26%	0.24%
Sum of impurities D and E	≤0.15%	0.01%	0.01%	0.01%
Impurity G	≤0.15%	0.09%	0.07%	0.06%
Impurity J	≤0.15%	Not found	Not found	Not found
Impurity K	≤0.15%	Not found	Not found	Not found
Impurity L	≤0.15%	Not found	Not found	Not found
Impurity M	≤0.15%	0.08%	0.07%	0.06%
Impurity H	≤0.15%	0.04%	0.04%	0.04%
Any unspecified impurity	≤0.10%	<0.10%	<0.10%	<0.10%
Sum of impurities other than H	≤1.0%	0.59%	0.55%	0.53%
Assay (HPLC method)	97.0% to 102.0%	99.6%	99.4%	99.4%

(N° R1-CEP 2001-218-Rev 03)

Table 3.2.S.4.4.-3 Non-micronized progesterone batches from Pharmacia & Upjohn

		Batch number (date of manufacture)		
Tests	**Specifications**	**L37467 (09/01/2015)**	**L37468 (09/01/2015)**	**L37586 (09/01/2015)**
Characters	White or almost white, crystalline powder or colourless crystals. Practically insoluble in water, freely soluble in ethanol, sparingly soluble in acetone and in fatty oils.	Complies	Complies	Complies
Identification				
A - IR spectrum	Comparable to the reference	Complies	Complies	Complies
B - TLC	Comparable to the reference	Complies	Complies	Complies
Tests				
Specific optical rotation (2.2.7)	+186° to +194°	+ 190°	+ 190°	+ 191°
Loss on drying (2.2.32)	≤ 0.5 %	0.2%	0.2%	0.1%
Related substances (HPLC 2.2.29)				
Impurity I	≤ 0.6 %	0.2	0.2	0.3
Impurity C	≤ 0.3 %	-	-	-
Impurity B	≤ 0.2 %	-	-	-
Sum of impurities D and E	≤ 0.15 %	-	-	-
Impurity G	≤ 0.15 %	-	-	-
Impurity J	≤ 0.15 %	< 0.05	< 0.05	< 0.05
Impurity K	≤ 0.15 %	0.06	0.06	0.06
Impurity L	≤ 0.15 %	< 0.05	< 0.05	< 0.05
Impurity M	≤ 0.15 %	-	-	-
Impurity H	≤ 0.15 %	-	-	-
Unspecified impurities	≤ 0.10 %	< 0.05	< 0.05	0.05
Sum of impurities other than H	≤ 1.0%	0.3	0.3	0.4

3.2.S.4.4 Batch Analyses

Residual solvent Methylene Chloride Isooctane	 ≤ 300ppm ≤ 1000ppm	 < 100ppm < 250ppm	 < 100ppm < 250ppm	 < 100ppm < 250ppm
Assay (UV 2.2.29)	97.0% to 102.0% (dried substance)	99.8%	101.1%	99.9%
Granulometry (In-house, laser)	Particle size average 53-249 µm	103µm	92µm	88µm

(N° R1-CEP 2005-299-Rev 01)

3.2.S.4.4.2 BIM SIFRAM

Certificates of analysis of 3 batches are provided

Batch number	Date of production	Re-test date
PRO-150301	17 March 2015	16 March 2019
PRO-150302	18 March 2015	17 March 2019
PRO-150303	19 March 2015	18 March 2015

(batch numbers: PRO-150301, PRO-150302, PRO-150303) (N° R1-CEP 2001-218-Rev 03)

Figure 3.2.S.4.4 - 1 Batch Analysis Pro-150301

ZHEJIANG SHENZHOU PHARMACEUTICAL CO., LTD.

Address: NO.14 Chuancheng Nan Road
Xianju, Zhejiang, China
Tel: 0576-87784451
Fax: 0576-87774559
E-mail: senshan@shenzhoupharma.com
Http:// www. shenzhoupharma.com

CERTIFICATE OF ANALYSIS

PRODUCT: PROGESTERONE	
BATCH NO.: PRO-150301	C.O.A. NO.: PRO-E1503-1
MFG.DATE: MAR 17, 2015	RETEST DATE: MAR 16, 2019
PACKING: 20kg/DRUM	BATCH SIZE: 212.0kg

ITEM	SPECIFICATION	RESULTS
Characters	White or almost white, crystalline powder or colourless crystals	White crystalline powder
Identification	A: I.R.	Complies
	B: TLC	Complies
Specific optical rotation	+186°~+194°	+187.5°
Related substances	Impurity I: ≤0.6%	Not found
	Impurity B: ≤0.2%	0.13%
	Impurity C: ≤0.3%	0.28%
	Sum of impurities D and E: ≤0.15%	0.01%
	Impurities G: ≤0.15%	0.09%
	Impurities J: ≤0.15%	Not found
	Impurities K: ≤0.15%	Not found
	Impurities L: ≤0.15%	Not found
	Impurities M: ≤0.15%	0.08%
	Impurity H : ≤0.15%	0.04%
	Any unspecified impurity: ≤0.10%	<0.10%
	Sum of impurities other than H: ≤1.0%	0.59%
Loss on drying	≤0.5%	0.1%
Assay	HPLC method: 97.0 ~ 102.0%	99.6%
Conclusion: The product complies with EP current edition and following R1-CEP 2001-218-Rev 03		

Kegang Chen

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Figure 3.2.S.4.4 - 2 Batch Analysis Pro-150302

ZHEJIANG SHENZHOU
PHARMACEUTICAL CO., LTD.

Address: NO.14 Chuancheng Nan Road
Xianju, Zhejiang, China
Tel: 0576-87784451
Fax: 0576-87774559
E-mail: senshan@shenzhoupharma.com
Http:// www. shenzhoupharma.com

CERTIFICATE OF ANALYSIS

PRODUCT: PROGESTERONE	
BATCH NO.: PRO-150302	C.O.A. NO.: PRO-E1503-2
MFG.DATE: MAR 18, 2015	RETEST DATE: MAR 17, 2019
PACKING: 20kg/DRUM	BATCH SIZE: 221.1kg

ITEM	SPECIFICATION	RESULTS
Characters	White or almost white, crystalline powder or colourless crystals	White crystalline powder
Identification	A: I.R.	Complies
	B: TLC	Complies
Specific optical rotation	+186°~+194°	+187.2°
Related substances	Impurity I: ≤0.6%	Not found
	Impurity B: ≤0.2%	0.14%
	Impurity C: ≤0.3%	0.26%
	Sum of impurities D and E: ≤0.15%	0.01%
	Impurities G: ≤0.15%	0.07%
	Impurities J: ≤0.15%	Not found
	Impurities K: ≤0.15%	Not found
	Impurities L: ≤0.15%	Not found
	Impurities M: ≤0.15%	0.07%
	Impurity H : ≤0.15%	0.04%
	Any unspecified impurity: ≤0.10%	<0.10%
	Sum of impurities other than H: ≤1.0%	0.55%
Loss on drying	≤0.5%	0.1%
Assay	HPLC method: 97.0 ~ 102.0%	99.4%
Conclusion: The product complies with EP current edition and following R1-CEP 2001-218-Rev 03		

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QUALITY ASSURANCE DEPT.

Figure 3.2.S.4.4 - 3 Batch Analysis Pro-150303

ZHEJIANG SHENZHOU
PHARMACEUTICAL CO., LTD.

Address: NO.14 Chuancheng Nan Road
Xianju, Zhejiang, China
Tel: 0576-87784451
Fax: 0576-87774559
E-mail: senshan@shenzhoupharma.com
Http:// www. shenzhoupharma.com

CERTIFICATE OF ANALYSIS

PRODUCT: PROGESTERONE	
BATCH NO.: PRO-150303	C.O.A. NO.: PRO-E1503-3
MFG.DATE: MAR 19, 2015	RETEST DATE: MAR 18, 2019
PACKING: 20kg/DRUM	BATCH SIZE: 218.8kg

ITEM	SPECIFICATION	RESULTS
Characters	White or almost white, crystalline powder or colourless crystals	White crystalline powder
Identification	A: I.R.	Complies
	B: TLC	Complies
Specific optical rotation	+186°~+194°	+192.6°
Related substances	Impurity I: ≤0.6%	Not found
	Impurity B: ≤0.2%	0.12%
	Impurity C: ≤0.3%	0.24%
	Sum of impurities D and E: ≤0.15%	0.01%
	Impurities G: ≤0.15%	0.06%
	Impurities J: ≤0.15%	Not found
	Impurities K: ≤0.15%	Not found
	Impurities L: ≤0.15%	Not found
	Impurities M: ≤0.15%	0.06%
	Impurity H : ≤0.15%	0.04%
	Any unspecified impurity: ≤0.10%	<0.10%
	Sum of impurities other than H: ≤1.0%	0.53%
Loss on drying	≤0.5%	0.1%
Assay	HPLC method: 97.0 ~ 102.0%	99.4%

Conclusion:
The product complies with EP current edition and following R1-CEP 2001-218-Rev 03

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QUALITY ASSURANCE DEPT.

3.2.S.4.4.3 PHARMACIA & UPJOHN

The certificates of analysis of 3 batches of progesterone from this manufacturer: Pharmacia & Upjohn, Company are provided on next pages (N° R1-CEP 2005-299-Rev 01).

Batch number	Date of production	Re-test date
L37467	09 January 2015	08 January 2018
L37468	09 January 2015	08 January 2018
L37586	09 January 2015	08 January 2018

Figure 3.2.S.4.4 - 10 Batch Analysis L37467

CERTIFICATE OF ANALYSIS

Page: 1 of 2

PHARMACIA & UPJOHN COMPANY
(A SUBSIDIARY OF PFIZER INC)
7000 PORTAGE RD
KALAMAZOO, MI 49001-0199 USA

Generated Date:
06-2015

Item:	H000268735
Title:	PROGESTERONE EP
Retest Date:	08-JAN-2018
Expiration Date:	01-2020
Date Of Manufacture:	09-JAN-2015
Specification:	268735 EU REG
LOT NUMBER:	L37467

TEST NAME	SPECIFICATION	UNITS	RESULTS
PROGESTERONE DRIED BASIS - EP	97.0 - 102.0	%	99.8
CHARACTERS	MEETS TEST	NONE	MEETS TEST
IDENTIFICATION A - EP	POSITIVE	NONE	POSITIVE
IDENTIFICATION B - EP	POSITIVE	NONE	POSITIVE
SPECIFIC OPTICAL ROTATION DRIED BASIS - EP	186-194	Deg	190
LOSS ON DRYING - EP	<=0.5	%	0.2
PARTICLE SIZE AVERAGE	53-249	um	103
METHYLENE CHLORIDE GC	<=300	ppm	< 100
ISOOCTANE GC	<=1000	ppm	< 250
1 DEHYDRO PROGESTERONE - EP IMP J	<= 0.15	%	<0.05
3-OXO-PREGNA-4, 20-DIENE-20-CARBOXALDEHYDE - EP IMP L	<= 0.15	%	<0.05
RELATED SUBSTANCES ANY OTHER DETECTABLE IMP - EP	<=0.10	%	<0.05
RELATED SUBSTANCES TOTAL - EP	<= 1.0	%	0.3

3.2.S.4.4 Batch Analyses

CERTIFICATE OF ANALYSIS

Generated Date:
06-2015

PHARMACIA & UPJOHN COMPANY
(A SUBSIDIARY OF PFIZER INC)
7000 PORTAGE RD
KALAMAZOO, MI 49001-0199 USA

Item:	H000268735
Title:	PROGESTERONE EP
Retest Date:	08-JAN-2018
Expiration Date:	01-2020
Date Of Manufacture:	09-JAN-2015
Specification:	268735 EU REG
LOT NUMBER:	L37467

TEST NAME	SPECIFICATION	UNITS	RESULTS
BISNORALDEHYDE EPIMER A AND B - EP IMP I	<= 0.6	%	0.2
9-DEHYDRO-PROGESTERONE - EP IMP K	<= 0.15	%	0.06

This lot/batch was manufactured and tested according to the standard operating procedures, material specification, and batch records under cGMP's and applicable regulatory guidelines of Pharmacia & Upjohn Company, 7000 Portage Road, Kalamazoo, Michigan, 49001. Telephone: 269-833-4000.

PARENT LOT*: N/A

*Parent Lot is the unique number assigned at time of manufacture. A new unique lot number is assigned each time the material is final packaged.

Electronic Signature: Susan Ahrenholz Lot Release Local Timestamp: 26-MAY-2015 13:18:41

Full Name: Debra H. Pike

Signature: Debra H Pike

Date: 01-Jun-2015

Questions concerning this certificate or requests for additional certificates should be directed to your local Pfizer CentreSource Sales office:
- America's region: 7000 Portage Road, Kalamazoo, Michigan, USA 49001, Tel: 269-833-5844 Fax: 269-833-3604
- Europe/Middle East/Africa Region, Hermesstraat 5, B-1930 Zaventem, Belgium, Tel: +32.2.714.6502, Fax: +32.2.402.3007
- Asia/Pacific Region: 31 Tuas South Avenue 6, Singapore 637578, Tel: +65.6419.0248, Fax: +65.6419.0022

Figure 3.2.S.4.4 - 11 Batch Analysis L37468

CERTIFICATE OF ANALYSIS

Page: 1 of 2

PHARMACIA & UPJOHN COMPANY
(A SUBSIDIARY OF PFIZER INC)
7000 PORTAGE RD
KALAMAZOO, MI 49001-0199 USA

Generated Date:
06-2015

Item:	H000268735
Title:	PROGESTERONE EP
Retest Date:	08-JAN-2018
Expiration Date:	01-2020
Date Of Manufacture:	09-JAN-2015
Specification:	268735 EU REG
LOT NUMBER:	L37468

TEST NAME	SPECIFICATION	UNITS	RESULTS
PROGESTERONE DRIED BASIS - EP	97.0 - 102.0	%	101.1
CHARACTERS	MEETS TEST	NONE	MEETS TEST
IDENTIFICATION A - EP	POSITIVE	NONE	POSITIVE
IDENTIFICATION B - EP	POSITIVE	NONE	POSITIVE
SPECIFIC OPTICAL ROTATION DRIED BASIS - EP	186-194	Deg	190
LOSS ON DRYING - EP	<=0.5	%	0.2
PARTICLE SIZE AVERAGE	53-249	um	92
METHYLENE CHLORIDE GC	<=300	ppm	< 100
ISOOCTANE GC	<=1000	ppm	< 250
1 DEHYDRO PROGESTERONE - EP IMP J	<= 0.15	%	<0.05
3-OXO-PREGNA-4, 20-DIENE-20-CARBOXALDEHYDE - EP IMP L	<= 0.15	%	<0.05
RELATED SUBSTANCES ANY OTHER DETECTABLE IMP - EP	<=0.10	%	<0.05
RELATED SUBSTANCES TOTAL - EP	<= 1.0	%	0.3

3.2.S.4.4 Batch Analyses

CERTIFICATE OF ANALYSIS

Generated Date:
06-2015

PHARMACIA & UPJOHN COMPANY
(A SUBSIDIARY OF PFIZER INC)
7000 PORTAGE RD
KALAMAZOO, MI 49001-0199 USA

Item:	H000268735
Title:	PROGESTERONE EP
Retest Date:	08-JAN-2018
Expiration Date:	01-2020
Date Of Manufacture:	09-JAN-2015
Specification:	268735 EU REG
LOT NUMBER:	L37468

TEST NAME	SPECIFICATION	UNITS	RESULTS
BISNORALDEHYDE EPIMER A AND B - EP IMP I	<= 0.6	%	0.2
9-DEHYDRO-PROGESTERONE - EP IMP K	<= 0.15	%	0.06

This lot/batch was manufactured and tested according to the standard operating procedures, material specification, and batch records under cGMP's and applicable regulatory guidelines of Pharmacia & Upjohn Company, 7000 Portage Road, Kalamazoo, Michigan, 49001. Telephone: 269-833-4000.

PARENT LOT*: N/A

*Parent Lot is the unique number assigned at time of manufacture. A new unique lot number is assigned each time the material is final packaged.

Electronic Signature: Susan Ahrenholz Lot Release Local Timestamp: 26-MAY-2015 13:20:05

Full Name: Debra H. Pike

Signature: Debra H Pike

Date: 01-Jun-2015

Questions concerning this certificate or requests for additional certificates should be directed to your local Pfizer CentreSource Sales office:
- America's region: 7000 Portage Road, Kalamazoo, Michigan, USA 49001, Tel: 269-833-5844 Fax: 269-833-3604
- Europe/Middle East/Africa Region, Hermesstraat 5, B-1930 Zaventem, Belgium, Tel: +32.2.714.6502, Fax: +32.2.402.3007
- Asia/Pacific Region: 31 Tuas South Avenue 6, Singapore 637578, Tel: +65.6419.0248, Fax: +65.6419.0022

Figure 3.2.S.4.4 - 12 Batch Analysis L37586

CERTIFICATE OF ANALYSIS

Page: 1 of 2

PHARMACIA & UPJOHN COMPANY
(A SUBSIDIARY OF PFIZER INC)
7000 PORTAGE RD
KALAMAZOO, MI 49001-0199 USA

Generated Date:
06-2015

Item:	H000268735
Title:	PROGESTERONE EP
Retest Date:	08-JAN-2018
Expiration Date:	01-2020
Date Of Manufacture:	09-JAN-2015
Specification:	268735 EU REG
LOT NUMBER:	L37586

TEST NAME	SPECIFICATION	UNITS	RESULTS
PROGESTERONE DRIED BASIS - EP	97.0 - 102.0	%	99.9
CHARACTERS	MEETS TEST	NONE	MEETS TEST
IDENTIFICATION A - EP	POSITIVE	NONE	POSITIVE
IDENTIFICATION B - EP	POSITIVE	NONE	POSITIVE
SPECIFIC OPTICAL ROTATION DRIED BASIS - EP	186-194	Deg	191
LOSS ON DRYING - EP	<=0.5	%	0.1
PARTICLE SIZE AVERAGE	53-249	um	88
METHYLENE CHLORIDE GC	<=300	ppm	< 100
ISOOCTANE GC	<=1000	ppm	< 250
1 DEHYDRO PROGESTERONE - EP IMP J	<= 0.15	%	<0.05
3-OXO-PREGNA-4, 20-DIENE-20-CARBOXALDEHYDE - EP IMP L	<= 0.15	%	<0.05
RELATED SUBSTANCES ANY OTHER DETECTABLE IMP - EP	<=0.10	%	0.05
RELATED SUBSTANCES TOTAL - EP	<= 1.0	%	0.4

3.2.S.4.4 Batch Analyses

CERTIFICATE OF ANALYSIS

Generated Date:
06-2015

PHARMACIA & UPJOHN COMPANY
(A SUBSIDIARY OF PFIZER INC)
7000 PORTAGE RD
KALAMAZOO, MI 49001-0199 USA

Item:	H000268735
Title:	PROGESTERONE EP
Retest Date:	08-JAN-2018
Expiration Date:	01-2020
Date Of Manufacture:	09-JAN-2015
Specification:	268735 EU REG
LOT NUMBER:	L37586

TEST NAME	SPECIFICATION	UNITS	RESULTS
BISNORALDEHYDE EPIMER A AND B - EP IMP I	<= 0.6	%	0.3
9-DEHYDRO-PROGESTERONE - EP IMP K	<= 0.15	%	0.06

This lot/batch was manufactured and tested according to the standard operating procedures, material specification, and batch records under cGMP's and applicable regulatory guidelines of Pharmacia & Upjohn Company, 7000 Portage Road, Kalamazoo, Michigan, 49001. Telephone: 269-833-4000.

PARENT LOT*: N/A

*Parent Lot is the unique number assigned at time of manufacture. A new unique lot number is assigned each time the material is final packaged.

Electronic Signature: Susan Ahrenholz Lot Release Local Timestamp: 26-MAY-2015 13:23:17

Full Name: Debra H. Pike

Signature: Debra H Pike

Date: 01-Jun-2015

Questions concerning this certificate or requests for additional certificates should be directed to your local Pfizer CentreSource Sales office:
- America's region: 7000 Portage Road, Kalamazoo, Michigan, USA 49001, Tel: 269-833-5844 Fax: 269-833-3604
- Europe/Middle East/Africa Region, Hermesstraat 5, B-1930 Zaventem, Belgium, Tel: +32.2.714.6502, Fax: +32.2.402.3007
- Asia/Pacific Region: 31 Tuas South Avenue 6, Singapore 637578, Tel: +65.6419.0248, Fax: +65.6419.0022