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CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 1 of 18

Effective Date:

Annexure-4
Calculation of Contamination Limit



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 2 of 18

Effective Date:

Equipment Name	Surface area of equipment	Cefixime	Cephalexin	Cefixime & Ofloxacin	Cefpodoxime Proxetil
	Sq.cm				
Vibro Sifter 36"	16600	√	√	√	√
Multimill	9600	X	X	√	√
Roll Compactor	10200	X	X	√	√
Octagonal Blender (600 Ltr)	25400	√	√	√	√
Octagonal Blender (250 Ltr)	22000	√	√	√	√
Tray Dryer	8400	X	X	X	X
Compression Machine-16 Station	7480	√	X	X	X
Compression Machine-27 Station	7700	√	√	√	√
Auto Coater	38150	X	X	√	X
Strip Packing Machine	10500	X	√	X	X



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 3 of 18

Effective Date:

Blister Packing Machine	7820	X	X	X	X
Alu-Alu Packing Machine	8790	√	X	√	√
Total Surface Area of contact parts	172640	87970	82200	138440	100290

Product contact surface area of equipment's for each product:



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 4 of 18

Effective Date:

1.0 10 ppm criteria:

**MAR (mg/swab)= 10 X Min. batch size of next product B (in kg) X swab surface area (in cm²)
1 x Total surface area of equipment (in cm²)**

S.No.	Product	MAR calculation:
1.	Cefixime	MAR = $\frac{10 \times 50 \times 100}{1 \times 89970} = 0.555 \text{ mg/swab} = 555 \text{ } \mu\text{g/swab}$
2.	Cephalexin	MAR = $\frac{10 \times 90 \times 100}{1 \times 82200} = 1.094 \text{ mg/swab} = 1094 \text{ } \mu\text{g/swab}$
3.	Cefixime & Ofloxacin	MAR = $\frac{10 \times 77.55 \times 100}{1 \times 138440} = 0.560 \text{ mg/swab} = 560 \text{ } \mu\text{g/swab}$
4.	CefpodoximeProxetil	MAR = $\frac{10 \times 55 \times 100}{1 \times 100290} = 0.548 \text{ mg/swab} = 548 \text{ } \mu\text{g/swab}$

2.0 Dose Criteria:

Calculation of the maximum allowable residue:

MAR ($\mu\text{g/swab}$) = $\frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA}}{1000 \times 1000 \times 1000}$
 $\times 1000 \times \text{MRDD of next product (B)} \times \text{TSA}$

LRDD: Lowest Recommended Daily Dose (in mg)

MRDD: Maximum Recommended Daily Dose (in mg)

SBS: Smallest Batch Size of next product (in kg)

SSA: Swab surface area (in cm²)



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 5 of 18

Effective Date:

TSA: Total Surface area of equipment (product contact part) (in cm²)

S.No. Maximum Allowable Residual Concentration (MAR)

1 **Maximum Allowable Residual Concentration (MAR) of Cefixime in a batch of Cephalexin is calculated as follows:**

Product	Cefixime Tablets(Product A)	Cephalexin Tablets (Product B)
Strength	100 mg	125 mg
Batch size	50.00 kg	50.00 kg
Lowest recommended daily dose (LRDD)	100 mg	125 mg
Maximum recommended daily dose (MRDD)	400 mg	250 mg
Common total surface area of equipments	87970 cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	

$$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 250 \times 87970} = 22735 \mu\text{g/swab}$$



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 6 of 18

Effective Date:

2 **Maximum Allowable Residual Concentration (MAR) of Cefixime in a batch of Cefixime & Ofloxacin is calculated as follows:**

Product	Cefixime Tablets (Product A)	Ofloxacin in Cefixime & Ofloxacin Tablets (Product B)
Strength	100 mg	200 mg
Batch size	50.00 kg	50.00 kg (Smallest batch size is 50.0 kg)
Lowest recommended daily dose (LRDD)	100 mg	200 mg
Maximum recommended daily dose (MRDD)	400 mg	800 mg
Common total surface area of equipments	87970 cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	
$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA} \times 1000 \times 800 \times 87970} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 800 \times 87970} = 7105 \mu\text{g/swab}$		



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 7 of 18

Effective Date:

3

Maximum Allowable Residual Concentration (MAR) of Cefixime in a batch of Cefpodoxime Proxetil calculated as follows:

Product	Cefixime Tablets (Product A)	Cefpodoxime Proxetil Tablets (Product B)
Strength	100 mg	100 mg
Batch size	50.00 kg	50.00 kg (Smallest batch size is 50.0 kg)
Lowest recommended daily dose (LRDD)	100 mg	100 mg
Maximum recommended daily dose (MRDD)	400 mg	400 mg
Common total surface area of equipments	87970 cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	
$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 87970}$ $= 14209 \mu\text{g/swab}$		



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 8 of 18

Effective Date:

4 **Maximum Allowable Residual Concentration (MAR) of Cephalexin Tablet in a batch of Cefixime Tablet is calculated as follows:**

Product	Cephalexin Tablet (Product A)	Cefixime Tablets (Product B)
Strength	125 mg	100 mg
Batch size	90 kg	50.00 kg
Lowest recommended daily dose (LRDD)	125 mg	100 mg
Maximum recommended daily dose (MRDD)	250 mg	400 mg
Common total surface area of equipments	82200cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	
$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}}$ $= \frac{125 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 82200}$ $= 19008 \mu\text{g/swab}$		



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 9 of 18

Effective Date:

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PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 10 of 18

Effective Date:

5 **Maximum Allowable Residual Concentration (MAR) of Cephalexin Tablet in a batch of Cefixime in Cefixime & Ofloxacin Tablet is calculated as follows:**

Product	Cephalexin Tablet (Product A)	Cefixime Tablets (Product B)
Strength	125 mg	200 mg
Batch size	90 kg	50.00 kg (Smallest batch size is 28.0 kg)
Lowest recommended daily dose (LRDD)	125 mg	100 mg
Maximum recommended daily dose (MRDD)	250 mg	400 mg
Common total surface area of equipments	82200 cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	

$$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{125 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 82200}$$

$$= 19008 \mu\text{g/swab}$$



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 11 of 18

Effective Date:

6 **Maximum Allowable Residual Concentration (MAR) of Cephalexin Tablet in a batch of Cefpodoxime Proxeil Tablet is calculated as follows:**

Product	Cephalexin Tablet (Product A)	Cefpodoxime Proxeil Tablets (Product B)
Strength	125 mg	200 mg
Batch size	90 kg	50.00 kg
Lowest recommended daily dose (LRDD)	125 mg	100 mg
Maximum recommended daily dose (MRDD)	250 mg	400 mg
Common total surface area of equipments	82200cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	

$$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{125 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 82200} = 19008 \mu\text{g/swab}$$



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 12 of 18

Effective Date:

7 **Maximum Allowable Residual Concentration (MAR) of Cefixime & Ofloxacin Tablet in a batch of Cefixime Tablet is calculated as follows:**

Product	Ofloxacin Tablet (Product A)	Cefixime Tablets (Product B)
Strength	200 mg	100 mg
Batch size	77.55 kg	50.00 kg
Lowest recommended daily dose (LRDD)	100 mg	100 mg
Maximum recommended daily dose (MRDD)	400 mg	400 mg
Common total surface area of equipments	138440cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	

$$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 138440} = 9029 \mu\text{g}/\text{swab}$$



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 13 of 18

Effective Date:

8 **Maximum Allowable Residual Concentration (MAR) of Cefixime & Ofloxacin Tablet in a batch of Cephalexin Tablet is calculated as follows:**

Product	Ofloxacin Tablet (Product A)	Cephalexin Tablet (Product B)
Strength	200 mg	125 mg
Batch size	77.55 kg	50 kg
Lowest recommended daily dose (LRDD)	100 mg	100 mg
Maximum recommended daily dose (MRDD)	400 mg	400 mg
Common total surface area of equipments	138440cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	

$$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 138440} = 9029 \mu\text{g/swab}$$



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 14 of 18

Effective Date:

9 **Maximum Allowable Residual Concentration (MAR) of Cefixime & Ofloxacin Tablet in a batch of Cefpodoxime Proxetil Tablet is calculated as follows:**

Product	Ofloxacin Tablet (Product A)	Cefpodoxime Proxetil Tablets (Product B)
Strength	200 mg	500 mg
Batch size	77.55 kg	50.00 kg
Lowest recommended daily dose (LRDD)	100 mg	100 mg
Maximum recommended daily dose (MRDD)	400 mg	400 mg
Common total surface area of equipments	138440cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	

$$\text{MAR (mcg/swab)} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 138440} = 9029 \mu\text{g/swab}$$



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 15 of 18

Effective Date:

10 **Maximum Allowable Residual Concentration (MAR) of Cefpodoxime Proxetil Tablet in a batch of Cefixime Tablet is calculated as follows:**

Product	Cefpodoxime Proxetil Tablets (Product A)	Cefixime Tablets (Product B)
Strength	200 mg	100 mg
Batch size	50.00 kg	50.00 kg
Lowest recommended daily dose (LRDD)	100 mg	100 mg
Maximum recommended daily dose (MRDD)	400 mg	400 mg
Common total surface area of equipments	100290cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	

$$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 400 \times 100290} = 12463 \mu\text{g/swab}$$



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 16 of 18

Effective Date:

11 **Maximum Allowable Residual Concentration (MAR) of Cefpodoxime Proxetil Tablet in a batch of Cephalexin Tablet is calculated as follows:**

Product	Cefpodoxime Proxetil Tablets (Product A)	Cephalexin Tablet (Product B)
Strength	200 mg	125 mg
Batch size	50.00 kg	50.00 kg
Lowest recommended daily dose (LRDD)	100 mg	125 mg
Maximum recommended daily dose (MRDD)	400 mg	250 mg
Common total surface area of equipments	100290cm ²	
Swab surface area (cm ²)	100 cm ²	
Safety factor	1/1000	
$\text{MAR} = \frac{\text{LRDD of previous product (A)} \times \text{SBS of next product (B)} \times \text{SSA} \times 1000 \times 1000 \times 1000}{1000 \times \text{MRDD of next product (B)} \times \text{TSA}} = \frac{100 \times 50 \times 100 \times 1000 \times 1000 \times 1000}{1000 \times 250 \times 100290}$ $= 19942 \mu\text{g/swab}$		



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No.:

Rev No.: 00

Page 17 of 18

Effective Date:

S.No.	Possible product changeovers	Common surface area (Sq.cm)	MAR
1	Cefixime-Cephalexin	87970	22735 µg/swab
2	Cefixime- Cefixime & Ofloxacin	87970	7105 µg/swab
3	Cefixime-CefpodoximeProxetil	87970	14209 µg/swab
4	Cephalexin-Cefixime	82200	19008 µg/swab
5	Cephalexin - Cefixime & Ofloxacin	82200	19008 µg/swab
6	Cephalexin -CefpodoximeProxetil	82200	19008 µg/swab
7	Cefixime & Ofloxacin- Cefixime	138440	9029 µg/swab
8	Cefixime & Ofloxacin - Cephalexin	138440	9029 µg/swab
9	Cefixime & Ofloxacin -CefpodoximeProxetil	138440	9029 µg/swab
10	CefpodoximeProxetil- Cefixime	100290	12463 µg/swab
11	CefpodoximeProxetil - Cephalexin	100290	19942 µg/swab
12	CefpodoximeProxetil -CefpodoximeProxetil	100290	6232 µg/swab

Limit to follow:

Calculate the final results for residual contamination using following formula:



PHARMADEVILS

QUALITY ASSURANCE

CLEANING VALIDATION PROTOCOL

Document Name: Cleaning Validation Protocol for Cefixime-100 DT Tablets

Document No:

Rev No.: 00

Page 18 of 18

Effective Date:

Analyte area from swab x Weight of standard x 2 x 5 (solution taken for swab) x Potency x 1000

Amount of API in ppm = -----

Average area of standard x 100 x 100 x 1 x 100 x Recovery factor (0.89)

Conclusion: _____

Checked By:

Verified By:

Approved By:

(Signature/Date)(Signature/Date)(Signature/Date)