

| | |
|--------------------------|-------------------------------------|
| Name Manufacturer | MEDITES PHARMA, spol. s r.o. |
| Department | Quality Control |
| Certificate | Certificate of Analysis |

We MEDITES PHARMA, spol. s r.o. hereby declare that:

1. Product identification



| | |
|---------------------------|--|
| Product name: | CITRASOL 4% |
| REF: | 601031 |
| Lot Number | A0045221 |
| Manufacturing Date | 2021 07 09 |
| Expiry Date | 2023 06 |
| Packaging type | 18 x 250 ml in a cardboard box |
| Packaging material | non – PVC bag; connectors: Tulip red cap, injection connector secondary packaging |
| Unit volume | 250 ml |

2. Finished product Analysis Compliance


Each production batch was sampled, tested and released to MEDITES PHARMA in accordance with specification NR - C115 CITRASOL.

| <i>Parameter</i> | <i>Specification</i> | <i>Result</i> | <i>Reference</i> |
|---|---|---------------|------------------|
| <i>Physical and Chemical parameters</i> | | | |
| Identification of Active Compound | Identity test for presence of Sodium (Na ⁺) and Citrates has to be satisfactory (passed). | Comply | PRG6841 |
| Clarity | The product must be clear. | Comply | PRG6841 |
| Actual acidity – pH | 6.7 – 7.4 | Comply | PRG6841 |
| Aluminium | < 30 µg/L | Comply | PRG6841 |
| Available volume | The volume of the solution in the bag must not be lower than the volume printed on the PP bag. | Comply | PRG6841 |
| Assay of sodium | 9.08 - 9.54 g/L | Comply | PRG6841 |
| Assay of citrates | 24.3 - 26.8 g/L | Comply | PRG6841 |
| Contamination by particles under the visibility level | Particles of size ≥ 10 µm max. 25/ml. Particles of size ≥ 25 µm max. 3/ml. | Comply | P/298/21 |
| <i>Microbiological parameters</i> | | | |
| Limit test for bacterial endotoxins | < 0.25 IU/ml | Comply | 1516/21 |
| Sterility | The product has to be sterile. | Comply | T105195 |

3. QC Final Approval

| Designated Authority | Name | Job title | Signature | Date |
|----------------------|---------------------|--------------------|---|-----------|
| Prepared By | Daniela Mateřánková | QA / QC Specialist |  | 12.8.2021 |
| Reviewed By | Radmila Doleželová | QA /QC Manager |  | 12.8.2021 |

4. Final Release Approval

| Designated Authority | Name | Job title | Signature | Date |
|----------------------|--------------------|----------------|--|-----------|
| Reviewed By | Radmila Doleželová | QA /QC Manager |  | 12.8.2021 |



Certificate of Analysis

| | | | |
|-------------|--|------------------|---|
| Project No: | PRG6841 | Issue Date: | 28/07/2021 |
| Client: | MEDITES PHARMA, spol. s r.o., Rožnov pod Radhoštěm | Laboratory: | ALS Czech Republic, s.r.o. Pharmaceutical |
| Address: | 1. máje 2625 Rožnov pod Radhoštěm 756 61 Czech Republic | | Na Harfe 336/9 - Prague 9 - Vysocany Czech Republic 190 00 |
| Contact: | Radmila Dolezelova | Contact: | F&P Client Service |
| Email: | radmila_dolezelova@meditespharma.cz | Email: | czsupport.pharma@alsglobal.com |
| Telephone: | 571115905 | Telephone: | +420 226 226 998 |
| Order No: | | Page: | Page 1 of 2 |
| Sampled By | | Date of test: | 19/07/2021 - 27/07/2021 |
| | | Certificate No.: | TPRG006763-1 Final |

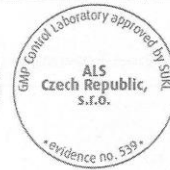
General Comments:

This report shall not be reproduced except in full, without prior written approval from the laboratory.
The laboratory declares that the test results relate only to the listed samples.
The information about sample representativity is not mentioned.
The sample expiry date is not mentioned.

Responsible person:

Responsible for accuracy of reported results are persons listed below. The results were approved and authorized for reporting according to the procedures specified in the document CZ_SOP_D06_GMP_02 Processing of GMP Project which is in accordance with the procedures specified in FDA document CFR Title 21, Part 11.

| Name/Position | Authorization Date |
|--|--------------------|
| Eva Hudečková, Pharma Section Supervisor | 28/07/21 13:57 |
| Martina Malkova, Section Supervisor | 28/07/21 09:07 |



Issue Date: 28/07/2021
Page: Page 2 of 2
Project: PRG6841
Client: MEDITES PHARMA, spol. s r.o., Rožnov pod Radhoštěm



Client Sample ID
Prod: CITRASOL 4% Citrasol 4% 250 ml
Rcvd Dt: 19/07/2021
Sched Dt: 19/07/2021
Sample Date: 19/07/2021
Description: Citrasol 4% 250 ml, č.č. A0045221
Date / Time Sampled: 19/07/2021

Laboratory Sample ID
PRG10360

Client Sampling Date/Time
19/07/2021 00:00

| Test | Method | Result | Units | Specification | Eval | Flag |
|---------------------|----------------------|----------------------|-------|----------------------|------|------|
| Al | METL-ALMSFXVJ0-PRG | <10 | µg/L | <30 µg/L | Pass | §2 |
| Na | METL-NAMSFVC2-PRG | 9.15 | g/L | 9.08 - 9.54 g/L | Pass | §2 |
| Na - ID | METL-IDENOE5-NA-PRG | Pass | - | Pass | Pass | §2 |
| Citrates | PHAR-CITRA2#M1-PRG | 25.2 | g/L | 24.3 - 26.8 g/L | Pass | §1 |
| Actual acidity (pH) | PHAR-PHP2-ELE#M1-PRG | 6.9 | - | 6.7 - 7.4 | Pass | §1 |
| Citrates | PHAR-CITR2-ID#MC-PRG | Complies to test | - | Complies to test | Pass | §1 |
| Clarity | PHAR-SENZL1#MC-PRG | The sample is clear. | - | The sample is clear. | Pass | §1 |
| Available volume | PHAR-AVOLUM1#M0-PRG | 250 | mL | min. 250 ml | Pass | §1 |

§2 Analysis was performed by ALS testing site Na Harč 336/9, Prague 9, 190 00
§1 Analysis was performed by ALS testing site Poděbradská 540/26, Prague 9, 190 00

If the client does not specify the date and time of sample collection, the laboratory will specify the date on sample delivery in parentheses, instead. If the time of sample collection is specified as 0:00 it means that the client did specify the date but not the time.

The end of result part of the certificate of analysis

Brief Method Summaries

| Analytical Methods | Method Descriptions |
|----------------------|---|
| METL-ALMSFXVJ0-PRG | Metals by ICP-MS - fixation |
| METL-IDENOE5-NA-PRG | Metals by ICP-OES-A - fixation |
| METL-NAMSFVC2-PRG | Metals by ICP-MS - fixation |
| PHAR-AVOLUM1#M0-PRG | Volume; G184 |
| PHAR-CITR2-ID#MC-PRG | Identification; G174 |
| PHAR-CITRA2#M1-PRG | Assay of citric acid / citrate; Medites |
| PHAR-PHP2-ELE#M1-PRG | pH; G183 - Medites |
| PHAR-SENZL1#MC-PRG | Clarity/Coloration; G182 |

LAL TEST
Limit test for bacterial endotoxins (BET)
in CITRASOL 4%...

The test was carried out using work equipments and procedure in accordance with *SOP:10.05.06.02 LAL test*.

Controlled product: CITRASOL 4% 250 ml Lot No.: A0045221

Endotoxin limit: 0,25 EU/ml Analysis No.: 1516/21

LAL Reagent: Pyrotell (ACC) Declared sensitivity λ 0,03 EU/ml

Lysate: --- Lot No.: 519-08-932

- dissolved in reconstitution buffer

Endotoxin: --- Lot No.: 171

Validation of the kit (confirmation of sensitivity) carried out on : 27.5.2021

Preparation of the product:

Dilution:

Quantity of undiluted product in ml: 1,0 Initial pH: 6,97

Quantity of buffer (Tris 1) in ml: 7,0

Quantity of water for BET in ml: ---

Test result CITRASOL 4%:

| Determination | Sample | Positive control | Negative control |
|---------------|--------|--|---------------------------|
| | | 1. 50 μ l 0,125 IU endotoxin/ml + 50 μ l buffer TRIS 1 2. 50 μ l 0,125 IU endotoxin/ml + 50 μ l sample 1:3 buffer TRIS 1 | 100 μ l buffer TRIS 1 |
| 1. | - | + | - |
| 2. | - | + | - |

Test result CITRASOL CPD50 -/ACD-A:

| Determination | Sample | Positive control | Negative control |
|---------------|--------|--|---------------------------|
| | | 1. 50 μ l 0,125 IU endotoxin/ml + 50 μ l water for BET 2. 50 μ l 0,125 IU endotoxin/ml + 50 μ l sample 1:3 buffer TRIS 2 | 100 μ l water for BET |
| 1. | | --- | --- |
| 2. | | --- | --- |

Test result CITRASOL 0,5%:

| Determination | Sample | Positive control | Negative control |
|---------------|--------|---|---------------------------|
| | | 1. 50 μ l 0,5 IU endotoxin/ml + 50 μ l water for BET 2. 50 μ l 0,5 IU endotoxin/ml + 50 μ l sample | 100 μ l water for BET |
| 1. | | --- | --- |
| 2. | | --- | --- |

Evaluation:

The sample complies test for BET according to Ph.Eur. 10: yes no

QC: *Handwritten signature* **MEDITES PHARMA** Date of execution: 27.7.2021
spol. s r.o.
QP: *Handwritten signature* 756 61 Rožnov pod Radhoštěm Date of control: 27.7.2021

Particle Sizing Systems, Inc.
Santa Barbara, Calif., USA

Particle Analysis Report

CITRASOL 4% (250 ml) A0045221 P/298/21
 File Name = A0045221.1CB Time Date = 11:54:36 7/27/2021
 Sensor Model: LE400-0.5 EXT S/N: 9811901 Cal. File: 9811901S.sns
 Date of Calibration: 06-23-21
 Control File: C:\PSS\SWS788\sws788.rcp

Elapsed Time of Data Collection = 40 Sec.
 Background File = NONE

Number of Pulls = 4 Volume of Pull = 5.0 ml

Large Volume Injectables

Cumulative Number of Particles Per Pull Volume

| PULL | CH1 10.0 | CH2 25.0 (um) |
|------|-------------|------------------|
|------|-------------|------------------|

| | | |
|-----|---|---|
| 1 * | 8 | 2 |
| 2 | 5 | 1 |
| 3 | 3 | 0 |
| 4 | 6 | 0 |

| | | |
|--------|--------|--------|
| MEAN # | 4 | 0 |
| #/ml | 0 | 0 |
| LIMIT | 25 | 3 |
| TEST | Passed | Passed |

* First pull was not included.

Operator's Name: Materankova

Operator's Signature *Materankova* Date 27.7.2021

Supervisor's Approval *[Signature]* Date 27.7.2021

MEDITES PHARMA
 spol. s r.o.
 756 61 Rožnov pod Radhoštěm



ITEST plus s.r.o. biological tests, laboratory diagnostics

Kontrolní laboratoř ITEST plus
Kladská 1032,
500 03 Hradec Králové 3
místo provedení zkoušky
Kontrolní laboratoř BV
Bílé Vchynice 10
533 16 Vápno u Přelouče
tel/fax: 466 937 106, mail: itestbv@itest-plus.cz

MEDITES PHARMA , spol. s.r.o.

1. máje 2625

75661 Rožnov pod Radhoštěm

ATEST č. T105195 o zkoušce na sterilitu

Testovaný vzorek:

| č. testu | název přípravku (vzorku) * | číslo šarže * | obal | ml * |
|----------|----------------------------|---------------|--------|------|
| T105195 | CITRASOL 4% | A0045221 | PP vak | 250 |

*vzorky číslo: 10ks TZHALV210:č.š.:F1BB43962 TR:č.š.:090721B

Datum přijetí vzorku: 21.07.2021

Test provedl: Perduňáková K.

Datum zahájení zkoušení: 21.07.2021

Datum posledního hodnocení: 04.08.2021

Metoda: Ph.Eur.10, SOP-K.1.01, membránová filtrace-steritest

Výsledky:

| | |
|--|----------|
| Thioglykolanová půda, 30°C až 35°C | STERILNÍ |
| TSB /půda z hydrolyzátů soji a kaseinu/ 20°C až 25°C | STERILNÍ |

ZÁVĚR

Vzorek přípravku VYHOVUJE zkoušce na sterilitu
provedené podle Ph.Eur.10

Datum vystavení: 04.08.2021



Hodnotil a uvolnil:


RNDr. Otakar Beneš
zástupce vedoucí kontrolní laboratoře

Bez písemného souhlasu laboratoře se nesmí atest reprodukovat jinak než celý. Data dodaná zákazníkem jsou označena*.
Za správnost údajů dodaných zákazníkem, které mají vliv na výsledek zkoušky, laboratoř nenesse odpovědnost.
Nejistotu měření nelze na tuto zkoušku aplikovat. Výsledky se týkají pouze vzorků, které byly předmětem zkoušení.
Vzorky byly zpracovány tak, jak byly přijaty.

IZ: SOP-K.1.01/3/5

----- Konec výsledkové části atestu -----

Výtisk číslo: 1

strana 1/1



plus s.r.o. biological tests laboratory diagnostics

TEST s.r.o.
Raková 102
250 03 Hradec Králové 2
Královské náměstí
Královské náměstí 1
250 03 Hradec Králové 2
Královské náměstí 1
Královské náměstí 1
Královské náměstí 1

Komunikace: TEST s.r.o.
Králové 102
250 03 Hradec Králové 2
Královské náměstí
Královské náměstí 1
250 03 Hradec Králové 2
Královské náměstí 1
Královské náměstí 1
Královské náměstí 1

TEST 5. T102195
o sterilitě na sterilní

| Č. řádku | Popis | Objem (ml) | Číslo série | Podpis | Podpis |
|----------|-----------------|------------|-------------|--------|--------|
| 1 | TEST 5. T102195 | 100 | A004321 | PRV | PRV |
| 2 | TEST 5. T102195 | 100 | A004321 | PRV | PRV |

STERILNÍ
STERILNÍ

ZÁVĚR

Podle výsledků zkoušek je sterilita
prokázána.



Podpis ředitele
Podpis vedoucího
Podpis laboranta