

Emprove[®] Material Qualification Dossier

Documentation to support qualification

103795

Cellvento[®] 4CHO COMP Chemically defined
cell culture medium

Not appropriate for regulatory submission as active pharmaceutical
ingredient. The use of this dossier shall be subject to the terms of
use that can be found at [Emprove.de](https://www.emprove.de)

The life science business
of Merck KGaA, Darmstadt,
Germany operates as
MilliporeSigma in the
U.S. and Canada.

SAFC[®]

Pharma & Biopharma Raw
Material Solutions

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Introduction

The Emprove® dossiers are designed to enable our customers to respond to the regulatory recommendations/requirements easily, quickly, and adequately. As a result of the Emprove® qualification processes, we offer the Emprove® Material Qualification Dossier. This dossier is designed to facilitate qualification of material for application in the pharmaceutical industry. With the Emprove® Quality Management Dossier, we assist in conducting the required risk assessments. With the Emprove® Operational Excellence Dossier, we provide supporting information to optimize processes according to the relevant regulations.

Version history

The dossier version number is indicated in the header of every page. Product quality-relevant content changes result in a full-version increase, for example version 1.0 to 2.0. Editorial or formatting changes result in a sub-version increase, for example 1.0 to 1.1.

Additionally, the Version History Report provides an overview of components which have been updated in this version.

Regulatory Framework

Marketing Authorization Holders are responsible for qualifying the raw and starting materials used in their products and assessing the risk associated with their use. To facilitate qualification and the required risk assessment in line with ICH Q9 and Q11, we provide a set of quality and regulatory documentation free of charge in our Material Qualification Dossier.

The dossier content includes information on applied quality systems, manufacturing processes, product characterization, regulatory certificates and more.

1 General Properties

Characteristics according to

- Declared Specification (see in the following pages)
- Material Safety Data Sheet (can be found in local languages on the corresponding product detail page of our website)



Specification

1.03795.0001 Cellvento® 4CHO COMP Chemically defined cell culture medium

| Specification | | |
|--------------------------------------|---------------------------------|-----------|
| Appearance | white to light pink, compactate | |
| Solubility | well soluble | |
| pH (without Supplement) | 5.1 - 5.6 | |
| pH (with Supplement) | 6.7 - 7.3 | |
| Osmolality (without Supplement) | 250 - 310 | mosmol/kg |
| Osmolality (with Supplement) | 280 - 340 | mosmol/kg |
| Water content | ≤ 3.5 | % |
| Endotoxins | ≤ 1.0 | I.U./ml |
| Mycoplasma | not detectable | |
| TAMC (Total aerobic microbial count) | ≤ 10 ² | CFU/g |
| TYMC (Total yeast and mould count) | ≤ 10 ² | CFU/g |
| Cell growth | conforms | |

Dr. Dennis Binder

Responsible laboratory manager quality control

This document has been produced electronically and is valid without a signature.

Merck KGaA, Frankfurter Straße 250, 64293 Darmstadt (Germany): +49 6151 72-0
 EMD Millipore Corporation - a subsidiary of Merck KGaA, Darmstadt, Germany
 400 Summit Drive, Burlington, MA 01803, USA, Phone +1 (781) 533-6000
 SALSA Version 1005381/000000000000// Date: 13.10.2020

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2 Manufacture

2.1 Manufacturer

original manufacturer see below

address:

Merck KGaA
Frankfurter Str. 250
64293 Darmstadt
Germany

Please find attached a DIN ISO 9001 Certificate and a description of our QA-System applied at Merck KGaA, Darmstadt, Germany in the following pages.



CERTIFICATE



This is to certify that

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

with the organizational units/sites as listed in the annex

has implemented and maintains a **Quality Management System**.

Scope:

Development, manufacture and distribution of basic chemicals, special chemical products and analytical systems.

Through an audit, documented in a report, it was verified that the management system fulfills the requirements of the following standard:

ISO 9001 : 2015

| | |
|------------------------------|-------------|
| Certificate registration no. | 005356 QM15 |
| Valid from | 2020-11-24 |
| Valid until | 2023-11-23 |
| Date of certification | 2020-11-18 |



DQS GmbH

Markus Bleher
Managing Director



Accredited Body: DQS GmbH, August-Schanz-Straße 21, 60433 Frankfurt am Main, Germany

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Annex to certificate
Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

005356
Merck KGaA
Frankfurter Straße 250
64293 Darmstadt

Including:
Real Estate GmbH
Merck Performance Materials Germany
GmbH

With regional offices at:
Roesslerstrasse 96
64293 Darmstadt

Gutenbergstrasse 10
64331 Weiterstadt

519160
Merck S. A.
Tronador 4890
C1430DNN Buenos Aires
Argentina

And regional warehouse at
Marconi 877 – B1812CDE Carlos
Spegazzini
Pcia. de Buenos Aires
Argentina

496580
Merck Pty. Limited
885 Mountain Highway
Bayswater VIC 3153
Australia

531364
Sigma-Aldrich Handels GmbH
Marchettigasse 7 / 2
1060 Vienna
Austria

Scope

Development, manufacture and distribution of basic chemicals, special chemical products and analytical systems.

Import, warehousing, trading and distribution of chemical products, lab equipment and IVD's.

Distribution of chemicals, laboratory equipment and consumables, filtration, separation, Life Science and purification products.

Sales of laboratory and industrial chemicals.

This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

531355
Sigma-Aldrich BVBA SPRL
Brusselsesteenweg 288
3090 Overijse
Belgium

Sales of laboratory and industrial chemicals.

527487
Merck Bulgaria EAD
48 Sitnyakovo Blvd.
1505 Sofia
Bulgaria

Sales and distribution of chemicals and reagents, raw materials, microbiological products, mixtures for analysis of foods, water and environment, chromatographic consumables, products used in laboratories and laboratory equipment. Service and maintenance. Training.

541664
Merck S.A. (Brazil)
Alameda Xingu, 350, 5º andar - Alphaville
Barueri
06455-030
Brazil

Administrative process of importation and local purchase of finished products, equipment and raw materials for industries: pharmaceutical, chemical, food, beverages and research, development and analysis laboratory.

541662
Sigma Aldrich Brazil LTDA
Alameda Xingu, 350, 5º andar - Alphaville
Barueri
06455-030
Brazil

Administrative process of importation and local purchase of finished products, equipment and raw materials for industries: pharmaceutical, chemical, food, beverages and research, development and analysis laboratory.

527768
Sigma Aldrich Brazil LTDA
Rua Torre Eiffel, 100
Cotia - SP
06705-481
Brazil

Importation, receiving, storage and distribution of finished products, equipment and raw materials for industries: pharmaceutical, chemical, food, beverages and research, development and analysis laboratory.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

541661

Merck S.A. (Brazil)
Rua Torre Eiffel, 100
Cotia - SP
06705-481
Brazil

Importation, receiving, storage and distribution of finished products, equipment and raw materials for industries: pharmaceutical, chemical, food, beverages and research, development and analysis laboratory.

527756

Sigma-Aldrich Canada Co.
2149 Winston Park Drive
Oakville L6H 6J8
Canada

Sales and distribution of biochemical and organic chemical products and kits.

450241

Merck & Cie
Weisshausmatte
6460 Altdorf
Switzerland

Manufacture and distribution of active pharmaceutical ingredients, chromatography resins and other Life Science products

527490

Sigma-Aldrich Chemie GmbH
Industriestrasse 25
9470 Buchs SG
Switzerland

Development, manufacturing and distribution of reagents and chemicals for research, development, production and analytical purposes.

530377

Sigma-Aldrich Production GmbH
Industriestrasse 25
9470 Buchs SG
Switzerland

Development, manufacturing and distribution of reagents and chemicals for research, development, production and analytical purposes.

496582

Merck S.A.
Francisco de Paula Taforó 1981 - Ñuñoa
7780349 Santiago
Chile

Distribution of chemical products and pharmaceutical ingredients, instruments and laboratory equipment.
Service of installation, maintenance, repair and technical assist of instruments and equipment of laboratory.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|--|--|
| 527755 Sigma-Aldrich (Wuxi) Life Science & Technology Co., Ltd. 99 Ximei Road Wuxi New District Wuxi City 214028 P.R. China | Packaging of bio-chemical reagent products (non-medicinal) and manufacture of disposal bio processing bags. |
| 519308 Merck Limited FLAT/RM 601-2, Li Po Chun Chambers, 189 Des Voeux Road Central Hongkong P.R. China | Sales, supply and innovation of Life Science chemical products and solutions. |
| 547589 Versum Materials, US LLC Shanghai Wai Wai Gao Qiao (Warehouse) No. 238 Fenju Road Wai Gaoqiao, Free Trade Zone Shanghai P.R. China | Assembly of equipment to control limited distribution of gases and chemicals as well as storage and distribution of specialty gases and chemicals. |
| 533161 Sigma Aldrich (Shanghai) Trading Co., Ltd #10 Building,509 Renqing Road Pudong District 201201 Shanghai P.R. China | Distribution and warehousing of Life Science chemicals. |

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

507106

**Merck Chemicals (Shanghai) Co., Ltd.
(Sales Office)
Room 908, Tomson-Trade Building,
No.01 Joring Rd,
Waigaoqiao Free Trade Zone
201203 Shanghai
P.R. China**

Sales Office: Sales and supply of Life Science chemicals, materials, reagent, equipment and consumable.

China BioReliance Validation Services Lab:
Provision of laboratory testing and validation service for filtration products and Single Use Assemblies.

System and Solutions Operations China:
Design and provision of filtration and ultrafiltration products, system and related solution.

514696

**Merck Display Materials (Shanghai) Ltd.
First Floor and Second Floor Area B of
14th Building East Side and 15th building,
No. 211 Qinqiao Road, Free Trade Zone
201206 Shanghai
P.R. China**

Design, development, manufacture and distribution of liquid crystal materials; distribution of other chemical materials.

521709

**Merck Electronic Materials (Suzhou) Ltd.
Shanghai sales office
First Floor and Second Floor Area B of
14th Building East Side and 15th building,
No. 211 Qinqiao Road,
201206 Shanghai
P.R. China**

Sale of photoresist products, edge bead rinse thinner and remover used for the electronic industry. Distribution of ancillary chemicals and additives used for electronic industry, including anti-reflective coating, developer and adhesion promoter.

518298

**Merck Electronic Materials (Suzhou) Ltd.
No. 70, Longpu Road, Industrial Park
215021 Suzhou City, Jiangsu Province
P.R. China**

Production and sale of photoresist products, edge bead rinse thinner and remover used for electronic industry. Distribution of ancillary chemicals and additives used for electronic industry, including anti-reflective coating, developer and adhesion promoter.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|--|---|
| <p>542618 Merck Life Science Technologies (Nantong) Co., Ltd No.39 Jianggang Road Nantong Economic & Technological Development Area 226017 Jiangsu P.R. China</p> | <p>Manufacturing of cell culture media, ready-to-use products and inorganic salts.</p> |
| <p>531357 Sigma-Aldrich spol. s.r.o. Na Hřebenech II 1718/10 140 00 Praha 4 Czech Republic</p> | <p>Sales, customer and technical service for laboratory and industrial chemicals.</p> |
| <p>092560 Merck spol. s.r.o. Na Hřebenech II. 1718 / 10 140 00 Praha 4 Czech Republic</p> | <p>Marketing, sales and distribution (including after sales service) of laboratory chemicals, instruments, equipment and consumables; chemicals for production; analytical systems.</p> |
| <p>273047 Biochrom GmbH Leonorenstrasse 2 - 6 12247 Berlin Germany</p> | <p>Sales, customer and technical service for cell culture products and sterile liquids.</p> |
| <p>527728 Sigma-Aldrich Biochemie GmbH Georg-Heyken-Strasse 14 21147 Hamburg Germany</p> | <p>Development, procurement, production, sales and distribution of reagents and chemicals for research, development, production and analytical purpose.</p> |
| <p>240237 Merck KGaA Mainzer Strasse 41 64579 Gernsheim Germany</p> | <p>Development, manufacture and sales of chemical products.</p> |

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

518299

Merck Performance Materials GmbH
Rheingaustrasse 190 - 196
65203 Wiesbaden
Germany

Design and development, production and supply of photoresist, liquid crystals and process chemicals for the electronic and printing industry.

505611

Merck Life Science GmbH
Lilienthalstrasse 16
69214 Eppelheim
Germany

Development, manufacture and distribution of culture media and systems for microbiology.

531362

Sigma-Aldrich Chemie GmbH
Eschenstrasse 5
82024 Taufkirchen
Germany

Sales, customer and technical service for laboratory and industrial chemicals.

002955

Merck Schuchardt OHG
Eduard-Buchner-Strasse 14 - 20
85662 Hohenbrunn
Germany

Manufacture, sales and distribution of chemicals for widespread applications in Pharma, Cosmetics and Technical Industry.

527503

Sigma-Adrich Chemie GmbH
Riedstrasse 2
89555 Steinheim
Germany

Development, procurement, production and distribution of reagents and chemicals for research, development, production and analytical purpose.

Incl. Sigma Aldrich Production GmbH
Riedstrasse 2
89555 Steinheim

527729

Sigma-Aldrich Chemie GmbH
Kappelweg 1
91625 Schnelldorf
Germany

Storage, packaging and shipping of chemicals.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|--|--|
| <p>531349 Merck Life Science A/S Vandtårnsvej 62A, 5. A 2860 Søborg Denmark</p> | Sales and Services. |
| <p>450321 Merck S.L.U. Poligono Industrial Merck 08100 Mollet del Valles (Barcelona) Spain</p> | Manufacture and distribution of chemicals for regulated markets and special applications. |
| <p>531363 Merck Life Science S.L.U Calle de Maria de Molina, 40 28006 Madrid Spain</p> | Sales and Services. |
| <p>531352 Merck Life Science OY Keilaranta 6 02150 Espoo Finland</p> | Sales and Services. |
| <p>527727 Sigma-Aldrich Chimie S.a.r.l. 80 Rue de Luzais 38297 St. Quentin-Fallavier France</p> | Sales and distribution of reagents and chemicals for research, development and production. |
| <p>518302 Merck Performance Materials SAS L'Usine de la Motte 1 Rue du Flottage 60350 Trosly Breuil France</p> | Design, manufacturing and distribution of colloidal silica. |

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

492648
Millipore S.A.S.
39, Route Industrielle de la Hardt
67120 Molsheim
France

Design, development, production engineering, manufacturing and distribution of devices, media and equipment for fluid analysis and purification. Production engineering, manufacturing and distribution of water purification systems for laboratories. Deliver engineered systems and technical solutions. Validation and scientific support to users. Maintenance and repair for biomonitoring and process solution equipment. Technical and commercial support to customers.

534721
Merck Chimie SAS
10 Avenue de Lattre de Tassigny
69330 Meyzieu
France

Development, production and sale of polymer microspheres mainly used as solid supports in diagnostic kits and marketed under the brand estapor.

506585
Millipore S.A.S.
1, rue Jacques Monod
Rond-Point des Sangliers
78280 Guyancourt
France

Design, development of and field service for water purification systems for laboratories.

527501
Sigma-Aldrich Co. Ltd.
Fancy Road
Poole, Dorset
BH12 4QH
United Kingdom

Technical service for reagents and chemicals for research, development, production and analytical purposes.

527761
Sigma-Aldrich Co. Ltd.
Homefield Road
Haverhill, Suffolk
CB9 8QP
United Kingdom

Manufacture of custom oligonucleotides. Sales and support of custom biomolecules and Life Science research products.

This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

505626

Millipore (UK) Ltd.
3 Fleming Road
Kirkton Campus
Livingston
EH54 7BN
United Kingdom

Development, manufacture and sale of clinical diagnostic products derived from biological sources.

527496

Sigma-Aldrich Co. Ltd.
T/A SAFC
Second Avenue
Heatherhouse Industrial Estate
Irvine
KA12 8NB
United Kingdom

Manufacture of cell culture related critical raw materials for the global health care industry.

527730

Sigma-Aldrich Co. Ltd.
The Old Brickyard, New Road
Gillingham, Dorset
SP8 4XT
United Kingdom

Procurement, sales and distribution of reagents and chemicals for research, development, production and analytical purposes.

501978

Merck A.E. Hellas
41-45 Kifissias ave.
15123 Maroussi / Attica
Greece

Trade and distribution of pharmaceutical and chemical products and medical devices.

505613

Merck Kft.
Október huszonharmadika utca 6 - 10
1117 Budapest
Hungary

Distribution of laboratory and specialty chemicals and lab equipment. Servicing of distributed equipment.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

531351

Sigma-Aldrich Kft.
Október huszonharmadika utca 6 - 10
1117 Budapest
Hungary

Sales, customer and technical service for laboratory and industrial chemicals.

540290

PT Merck Chemicals and Life Sciences
Jl. TB. Simatupang No. 8
Pasar Rebo
Jakarta 13760
Indonesia

Sales (including Customer Excellence) Supply Chain and Distribution of Life Science and Performance Material products.

450286

P.T. Merck Tbk.
Jl. TB. Simatupang no. 8
Pasar Rebo
Jakarta 13760
Indonesia

Sales, marketing and distribution of Pharmaceutical Raw Material Products.

510831

Merck Life Science Private Limited
Godrej One, 8th floor, Pirojshanagar,
Eastern Express Highway, Vikhroli - East
Mumbai, Vikhroli 400 079
India

Development, manufacturing and marketing of microbiology products. Manufacturing and marketing of laboratory reagent. Marketing of laboratory products.

518300

Merck Performance Materials Pvt. Ltd.
Khopoli Site
Survey No 109, 110, 112 Savroli Village,
Taluka Khalapur, Dist. Raigad
Maharashtra 410 203
India

Design, development, manufacturing, marketing and sales of silicon resins (polysilazanes and silazanes) and formulations.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

501956

Merck Life Science Private Limited
50 A & 51, 2nd Phase, Ring Road, Peenya
Bangalore 560 058
India

Design, manufacture, assembly, testing and supply of filtration equipment and related products for biopharm process solutions, biomonitoring, lab water, ASP (Analytical Sample Preparation), and provision of laboratory testing and validation service for filtration and single use products.

And regional offices in New Delhi, Ahmedabad, Bangalore, Kolkata, Mumbai and Hyderabad

530393

Sigma Aldrich Chemicals Private Limited
12, Bommasandra Jigani Link Road
Bangalore, Karnataka State 560100
India

Development, manufacturing, sales and distribution of specialty and fine chemicals.

547726

SIGMA ALDRICH SBS (subsidiary of Merck)
7th FLOOR, TOWER-2, ELECTRONIC CITY PHASE-1
Bangalore District 560100
India

Global support services in Accounting, Commercial, Financial Analytics, HR Information System, New Product Introduction, Product Management Operations, Regulatory Affairs, Strategic Marketing and Innovation, Studio M, Supply Chain Operations, Quality Services and Trade Compliance for the Merck Group.

505619

Merck Millipore Ltd.
Tullagreen
Carrigtwohill
T45 KD29 County Cork
Ireland

Design and manufacture of filtration products for the pharmaceutical, food, beverage, electronic and analytical industries. Manufacture of chromatography adsorbents, immobilized enzymes and other ligands for modification and purification of biomolecules.

527495

Sigma-Aldrich Ireland Ltd.
Vale Road
Arklow, County Wicklow
Ireland

Procurement, sales and distribution of reagents and chemicals for research, development, production and analytical purposes.

This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

527758

Sigma-Aldrich Israel Ltd.
3 Plaut St., Park Rabin
Rehovot 7670603
Israel

Development, manufacture, marketing, sales and distribution of biochemicals, organic chemicals and reagents for research, production and analytical purposes.

527759

Sigma-Aldrich Israel Ltd.
13-15 Kiryat Hamada St., Har Hotzvim
Jerusalem 9777613
Israel

Development and manufacture of biochemicals, organic chemicals and reagents for research, development, production and analytical purposes.

531353

Merck Life Science S.r.l.
Via Monterosa 93
20149 Milano
Italy

Sales and Services.

518301

Merck Performance Materials Ltd.
Shizuoka Site
3330 Chihama,
Kakegawa-shi,
Shizuoka 437-1412
Japan

Development and production of photoresists and other electronics materials related to chemical product, functional coating.

527752

Sigma Aldrich Japan G.K.
Ichikawa Site
368 O-Machi
Ichikawa-Shi
Chiba
Japan

Distribution of Life Science Products.

This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.

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Annex to certificate
Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

532377

Merck Performance Materials Ltd.
Atsugi Site
4084, Nakatsu, Aikawa-machi, Aiko-gun
Kanagawa Pref. 243-0303
Japan

Design, development and manufacture of chemical products.

497387

Merck Ltd.
Atsugi Site
4084, Nakatsu, Aikawa-machi, Aiko-gun
Kanagawa Pref. 243-0303
Japan

Distribution of Life Science products.

532379

Merck Performance Materials Ltd.
Arco Tower 5F, 1-8-1
Shimomeguro, Meguro-ku
Tokyo 153-8927
Japan

Sales of chemical products.

453292

Merck Ltd.
Arco Tower 5F, 1-8-1
Shimomeguro, Meguro-ku
Tokyo 153-8927
Japan

Supply chain and Quality for sales support of chemical products and life science products.

497388

Merck Ltd.
Baraki Technical Center
Nippon Express Baraki Air Cargo Center,
2526-26 Baraki Ichikawa,
Chiba Pref. 272-0004
Japan

Stock holding and provision of repair for filtration products and analytical instrumentation.

This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

497390
Merck Ltd.
Yokohama Technical Center
YBP West Tower 2F, 134 Godo-cho,
Hodogaya-ku
Yokohama, Kanagawa Pref. 240-0005
Japan

With units
BioReliance Validation Services, Process
solutions
Life Science

Scope

Laboratory testing, validation and compliance
services.

426640
Merck Performance Materials Ltd.
Onahama Site
51-15 Izumimachi Kurosuno Aza Egoshi
Iwaki-shi, Fukushima 971-8184
Japan

Development and manufacture of chemical
products.

505622
Merck Performance Materials Ltd.
306, Pyeongtaekhang-Ro, Poseung-eup
Pyeongtaek-shi,
Gyeonggi-do 451-822
Republic of Korea

Development, manufacture, marketing, sales
and servicing of chemicals.

518304
Merck Electronic Materials Ltd.
50-14 Hyupdongdanji-gil, Miyang-myeon
Anseong-si, Gyeonggi-do 17600
Republic of Korea

Research, development, production,
inspection and testing of light-sensitive
materials and related processing chemicals for
semiconductor industry.

505621
Merck Ltd. Korea
Haesung-Building 15F
508 Teheran-ro, Gangnam-gu
Seoul 06178
Republic of Korea

Marketing, sales and distribution of
pharmaceuticals and chemical products
including central functions (HR and finance
administration).

This annex (edition: 2020-11-18) is only valid in connection
with the above-mentioned certificate.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|---|---|
| <p>536979 Sigma Aldrich Korea Ltd. 113, Songdo Kukje-daero 343 beon-gil Yeon-Su Gu, Incheon 21991 Republic of Korea</p> | Marketing, sales and distribution of reagents for research purposes. |
| <p>547576 Versum Materials, Banwol Jangjagol Ro, 82, Danwon-gu Ansan-si, Gyeonggi-do 425-833 Republic of Korea</p> | Manufacture and transfill of specialty gases and chemicals. |
| <p>547582 Versum Materials, US LLC Ansan #283, Haebong-Ro, Danwon-gu Ansan-Si 425-839 Republic of Korea</p> | Design and assembly of equipment to control limited distribution of gases and chemicals |
| <p>547591 Versum Materials, US LLC Shihwa Shiwa Ind., Complex 143, Hyeomnyeok-ro Siheung-si 429-450 Republic of Korea</p> | Manufacture and transfill of specialty gases and chemicals. |
| <p>547580 Versum Materials, US LLC 88-19, Sandan-ro Pyeongtaek-si, Gyeonggi-do 459-040 Republic of Korea</p> | Manufacture of high purity chemicals. |
| <p>547595 Versum Materials, US LLC Ulsan 48, Yonyeon-ro 98 beon-gil Nam-gu 680-150 Republic of Korea</p> | Manufacture and transfill of specialty gases and chemicals. |

This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|--|---|
| <p>507107 Merck S.A. de C.V. Calle 5 No. 7 Fracc. Ind. Alce Blanco 53370 Naucalpan de Juárez, Estado de México, Mexico</p> | Sales, distribution and after sales of products and equipment of Life Science and Performance Materials business sectors. |
| <p>506583 Merck Chemicals B.V. Haarlerbergweg 21 - 23 1101 CH Amsterdam Zuidoost Netherlands</p> | Customer orders and cash processing. |
| <p>531365 Sigma-Aldrich Chemie BV Stationsplein 4E 3331 LL Zwijndrecht Netherlands</p> | Sales of laboratory and industrial chemicals. |
| <p>531354 Merck Life Science AS Drammensveien 123 0277 Oslo Norway</p> | Sales and Services. |
| <p>506584 Merck, Inc. 24/F GT Tower International, 6813 Ayala Avenue 1227 Makati City, Metro Manila Philippines</p> | Marketing, sales and distribution of chemical products, laboratory supplies and equipment. |
| <p>531356 Sigma-Aldrich Sp. z o. o., ul. Szelągowska 30 61-626 Poznań Poland</p> | Sales, customer and technical service for laboratory and industrial chemicals. |

This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|---|---|
| <p>531358 Merck Life Science S.L.U Sucursal em Portugal Edifício DUO Miraflores, Alameda Fernão Lopes, 12 - 4ºB 1495-190 Algés Portugal</p> | Sales of laboratory and industrial chemicals. |
| <p>528833 Merck Romania SRL Str. Gara Herastrau 4D, Sector 2 020334 Bucharest Romania</p> <p>Warehouse Localitatea Rudeni, Oras Chitila, Soseaua Rudeni nr. 74 A, Hala C2, 077045 Judetul Ilfov Romania</p> | Marketing and sales of specialty chemicals and high purity preparations, equipment analysis technology filtration equipment, installation and service of equipment sold. Storage of chemicals, medical devices and equipment. |
| <p>496590 Merck Pte Ltd. (Life Science) Merck Millipore 2 Science Park Drive # 05-01/12 Ascent Building Singapore 118222 Singapore</p> <p>Warehouse: 5 Tuas Ave 3, #03-00 Warehouse B Singapore 639405</p> | Sales, marketing and distribution of chemicals, laboratory equipment and consumables, filtration, separation, Life Science and purification products. |
| <p>540293 Sigma Aldrich Pte Ltd 2 Science Park Drive #05-01/12 Ascent Building Singapore 118222 Singapore</p> | Provision of warehouse related logistics services from goods receiving delivery to customers. |

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|--|--|
| 547594 Versum Materials, US LLC Tuas (Warehouse) 8 Tuas Basin Link 638762 Tuas Singapore | Storage and distribution of specialty gases and chemicals. |
| 527484 Merck d.o.o. Serbia Omladinskih brigada 90v 11070 Belgrade Serbia | Wholesale trade of medicines and medical devices. |
| 531348 Sigma-Aldrich spol. s r.o. Dvořákovo nábřežie 4 810 06 Bratislava Slovakia | Sales, customer and technical service for laboratory and industrial chemicals. |
| 531360 Sigma-Aldrich Sweden AB Solkraftsvägen 14C 135 70 Stockholm Sweden | Sales and distribution of laboratory and industrial chemicals. |
| 527491 SAFC Hitech Taiwan Co., Ltd. No. 15, Luke 3rd Rd. Kaohsiung Science Park Luzhu Dist. 82151 Kaohsiung City Taiwan | Manufacture of chemicals for industrial applications (for optoelectronics and semiconductor devices). |
| 518305 Merck Performance Materials Ltd. No. 458-6, 8 & 11, Xinxing Rd., Hu Kuo Township Hsinchu County Taiwan | Development and manufacture of photo-resist products, top-layer anti-reflective coating materials and other chemical products. |

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**Annex to certificate
Registration No. 005356 QM15**

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

| Location | Scope |
|--|--|
| <p>547592 Versum Materials, US LLC Taichung Branch Office No. 6, Dachen S. Road Wuci District Taichung City 43541 Taiwan (R.O.C.)</p> | Storage and distribution of specialty gases and chemicals. |
| <p>547587 Versum Materials, US LLC Nanke No. 772, Singnong Road Shanhua District 74160 Tainan Taiwan (R.O.C.)</p> | Manufacture and transfill of specialty gases and chemicals |
| <p>542621 Merck Ltd. 6F, No.89,Sec.2, Tiding Blvd., Taipei Taiwan</p> | Sales and distribution of Life Science Chemicals. |
| <p>426643 Merck Performance Materials Ltd. No. 39, 39-1, Ching Chien 1st Road Kuan Yin Industrial Park Taoyuan Taiwan</p> | Development, manufacture and distribution of chemical products. |
| <p>547596 Versum Materials, US LLC Vultee 1919 Vultee Street Allentown, 18103 United States of America</p> | Design and assembly of equipment to control limited distribution of gases and chemicals. |
| <p>547577 Versum Materials, US LLC Hometown 357 Marian Avenue Tamaqua, 18252 United States of America</p> | Manufacture and transfill of specialty gases and chemicals |

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**Annex to certificate
Registration No. 005356 QM15**

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

547585

Versum Materials, US LLC Catoosa
1115 West Keystone
Catoosa, OK 74015
United States of America

Manufacture and transfill of specialty gases and chemicals.

547586

Versum Materials, US LLC Dallas
8201 S. Central Express Way
Dallas, TX 75241
United States of America

Manufacture and distribution of specialty chemicals.

547588

Versum Materials, US LLC Samsung Austin Semiconductor
Samsung Austin Semiconductor
12100 Samsung Boulevard
Austin, TX 78754
United States of America

Servicing chemicals distribution systems

547593

Versum Materials, US LLC Tempe
8555 South River Parkway
Tempe, AZ 85284
United States of America

Manufacture Chemical Mechanical Planarization and Polishing Solutions.

547584

Versum Materials, US LLC Carlsbad
1969 Palomar Oaks Way
Carlsbad, CA 92011
United States of America

Manufacture of high purity chemicals and assembly of glass and stainless steel chemical containers.

547725

MilliporeSigma Corp.
8511 W Riggan Ave
Visalia, 93291
United States of America

Distribution.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

534975
EMD Performance Materials - Ormet
Circuits, Inc
6555 Nancy Ridge Drive Suite 200
San Diego, CA 92121
United States of America

The design, development and manufacture of conductive pastes, inks and other materials for electronic applications.

505627
EMD Millipore Corp.
28820 Single Oak Drive
Temecula, CA 92590
United States of America

Design and development, manufacture and distribution of chemical and biological reagents

With associated organization:
26578 Old Julian Highway
Ramona, CA 92065

505631
EMD Millipore Corp.
28820 Single Oak Drive
Temecula, CA 92590
United States of America

Design and development, manufacture, technical support and distribution of research use only immunoassay kits. Bioscience global technical and sales support organization.

450330
EMD Performance Materials Corp.
110 EMD Blvd.
Savannah, GA 31402
United States of America

Design and development, manufacture and distribution of pigments.

496589
EMD Millipore Corp.
195 W. Birch Street
Kankakee, IL 60901
United States of America

Design, development, manufacturing and distribution of highly purified blood proteins and biologically active factors.

With associated organization:

2407 Eastgate Industrial Parkway
Kankakee, IL 60901

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

527747
Sigma-Aldrich
1302 West Anthony Drive
Urbana, IL 61802
United States of America

Manufacture of reagents and chemicals for research, development, production and analytical purposes.

527748
SAFC Biosciences, Inc.
13804 West 107th Street
Lenexa, KS 66219
United States of America

Design, control, procurement, manufacturing and distribution of sera, dry powder media, as well as repackaging of raw materials.

527749
SAFC Biosciences, Inc.
11296 Renner Boulevard
Lenexa, KS 66219
United States of America

Design, control, procurement and distribution of sera and dry powder media.

496583
EMD Millipore Corp.
80 Ashby Road
Bedford, MA 01730
United States of America

Development & customer support for purification and separation media for life science applications, expression technology cell culture products; Service & repair for instruments.

496285
EMD Millipore Corp.
400 Summit Drive
Burlington, MA 01803
United States of America

Finished Goods, biological and compliance testing, reagents and kits, filter equipment, field service.

532231
Sigma Aldrich Research Biochemicals, Inc.
("Sigma- RBI)
600 Summit Drive
Burlington, MA 01803
United States of America

Design, development, manufacturing, contract manufacturing of reagents, raw materials, components and kits.

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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

527489

EMD Performance Materials Corp.
1429 Hilldale Avenue
Haverhill, MA 01832
United States of America

Manufacturing high purity chemicals for optoelectronics and semiconductor devices.

496587

EMD Millipore Corp.
17 Cherry Hill Drive
Danvers, MA 01923
United States of America

Danvers single-use manufacturing.

With associated organizations:

- 54 Cherry Hill Drive, Danvers, MA 01923, USA
- 75 Sylvan Street, Warehouse, Danvers, MA 01923, USA

527745

Sigma-Aldrich
2425 South Second Street (Barton)
St. Louis, MO 63104
United States of America

Storage and distribution of chemical reagents, raw materials, media, components and kits.

546398

Sigma-Aldrich, Inc.
3300 South Second Street (Cherokee)
St. Louis, MO 63118
United States of America

Buffers: manufacturing, packaging, QA, QC



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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

527743

Sigma-Aldrich Corporation
3500 Dekalb Street
St. Louis, MO 63118
United States of America

Design, development, manufacturing, testing, QA, warehouse, maintenance of chemical reagents, raw materials and components. Customer processes.

With associated organizations:

- 545 South Ewing Street, St. Louis, MO 63103
- 3300 South Second Street, XY Building, St. Louis, MO 63118
- 2909 Laclede Street, St. Louis, MO 63101
- 3050 Spruce Street, St. Louis, MO 63103

527744

Sigma-Aldrich, Inc.
3506 South Broadway (Broadway)
St. Louis, MO 63118
United States of America

Cell Culture Media: manufacturing, packaging, QA, QC

492647

EMD Millipore Corp.
11 Prescott Road
Jaffrey, NH 03452
United States of America

Manufacture of membrane and filtration products.

518306

EMD Performance Materials Corp.
70 Meister Avenue
Branchburg, NJ 08876
United States of America

Design and manufacture of photoresist and related chemical products.

527764

Research Organics LLC., dba SAFC
4353 East 49th Street
Cleveland, OH 44125
United States of America

Manufacturing of high purity biochemicals.

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**Annex to certificate
Registration No. 005356 QM15**

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

505606
EMD Millipore Corp.
2828 Highland Avenue
Norwood, OH 45212
United States of America

Design and development, manufacture and distribution of high purity organic solvents, organic chemicals/ reagents, acids and chemical specialities.

527733
Sigma-Aldrich Corporation
3858 Benner Road
Miamisburg, OH 45342
United States of America

Development, procurement, production, testing and sales of chemicals, reagents and laboratory equipment for research, development, production and analytical purposes.

527767
Supelco, Inc.
595 North Harrison Rd.
Bellefonte, PA 16823
United States of America

The design, development, manufacture, distribution and technical support of chromatography products for analysis and purification.

527734
Aldrich Chemical Co., LLC
Ironrun Industrial Park
6950 Ambassador Drive
Allentown, PA 18106
United States of America

Distribution of chemicals, reagents and laboratory equipment for research, development, production and analytical purposes.

527751
SAFC Biosciences, Inc.
5 Dutch Court (Reading)
Sinking Spring, PA 19608
United States of America

Distribution of dry powder media and repackaging of raw materials.



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Annex to certificate Registration No. 005356 QM15

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

Scope

518307
EMD Performance Materials Corp.
788 Chert Quarry Rd.
Martin, SC 29836
United States of America

Design and manufacture of colloidal silica.

With associated organization:

8604 Cliff Cameron Drive, Suite 105
Charlotte, NC 28269
United States of America

527766
Sigma-Genosys of Texas LLC
Db a Sigma Custom Products
9186 Six Pines Drive, Suite 100
The Woodlands, TX 77380
United States of America

Manufacture of DNA, siRNA, AQUA and
PEPscreen peptides for the research and
applied science markets.

527762
Cerilliant Corporation
811 Paloma Drive, Suite A
Round Rock, TX 78665
United States of America

Design and manufacturing of certified
reference materials, analytical reference
standards, analytes and chemical reagents.

527738
Aldrich Chemical Co., LLC
6000 North Teutonia Avenue
Milwaukee, WI 53209
United States of America

Development, procurement, production,
testing, sales and distribution of chemicals,
reagents and laboratory equipment for
research, development, production and
analytical purposes.

With associated organizations at
Milwaukee Emmer Lane, Sheboygan Falls
and Port Washington.

527765
Sigma Aldrich RTC, Inc.
2931 Soldier Springs Road
Laramie, WY 82070
United States of America

Design, manufacturing, certify and distribute,
certified reference materials and proficiency
testing materials and to conduct laboratory
proficiency testing program.

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with the above-mentioned certificate.

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**Annex to certificate
Registration No. 005356 QM15**

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Germany

Location

**505624
Merck (Pty) Ltd.
Modderfontein & Wadeville
1 Friesland Drive
Longmeadow Business Estate
Modderfontein
1645
South Africa**

Scope

Sales, marketing and distribution of locally produced and imported goods for Life Science industry, pigments and cosmetics, and laboratory consumables.
This includes installing, maintaining, repairing and validating Lab Water-, Bioscience-, Biomonitoring- and Third Party systems.



This annex (edition: 2020-11-18) is only valid in connection with the above-mentioned certificate.



To whom it may concern

Good manufacturing practice for products of the GMP cell culture media portfolio

Recognized principles of GMP manufacturing of APIs and excipients are well established in the industry. However, this is not the case for cell culture media used in the production of therapeutic proteins and other metabolites that undergo extensive purification prior to patient exposure. Due to the extensive purification steps downstream of use of cell culture media, the patient risk posed by such cell culture media is generally lower than that of excipients. Therefore, principles of excipient GMP can be safely considered an appropriate level of GMP for cell culture media.

The recognized principles of GMP for pharmaceutical excipients are described in the current "IPEC-PQG Joint GMP Guide for Pharmaceutical Excipients", which is applied for the manufacture of the GMP cell culture media portfolio at our facilities. Catalogue products within this portfolio have been assigned the *M-Clarity*[™] MQ500 marker demonstrating compliance to IPEC-PQG GMP. Customized cell culture products follow the same principles when requested. In addition, for sterile filtered liquid media, we apply appropriate elements of Annex 1 of the EU Guidelines to Good Manufacturing Practice for Medicinal Products.

Processes are performed on the basis of excipient GMP guidelines and/or a certified ISO 9001 Quality Management System standard. They are verified to comply with an adequate quality level of manufacturing and quality control according to the aforementioned IPEC-PQG GMP Guide.

Sincerely,
Merck KGaA, Darmstadt, Germany

ppa.
Dr. Robert Nass
Senior Vice President
Head of Quality and Regulatory Management
Life Science

ppa.
Dr. Matthias Bucerius
Vice President
Head of Actives & Formulation
Process Solutions
Life Science

Date: February 5, 2021

Merck KGaA, Darmstadt, Germany
Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

EMD Millipore Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 01803, USA
Phone +1 (781) 533-6000

Page 1 of 1

2.2 Description of Manufacturing Process



Manufacturing Procedure

Cellvento® Cell Culture Media Portfolio- Compaction

The required components are weighed, sieved and undergo homogenization, interval mixing and milling. After compaction, the target product is filled and packaged.

Flow diagram see next page.

Dr. Katharina Hollmann
LS-QSI-SP

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Merck KGaA, Darmstadt, Germany

Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

EMD Millipore Corporation

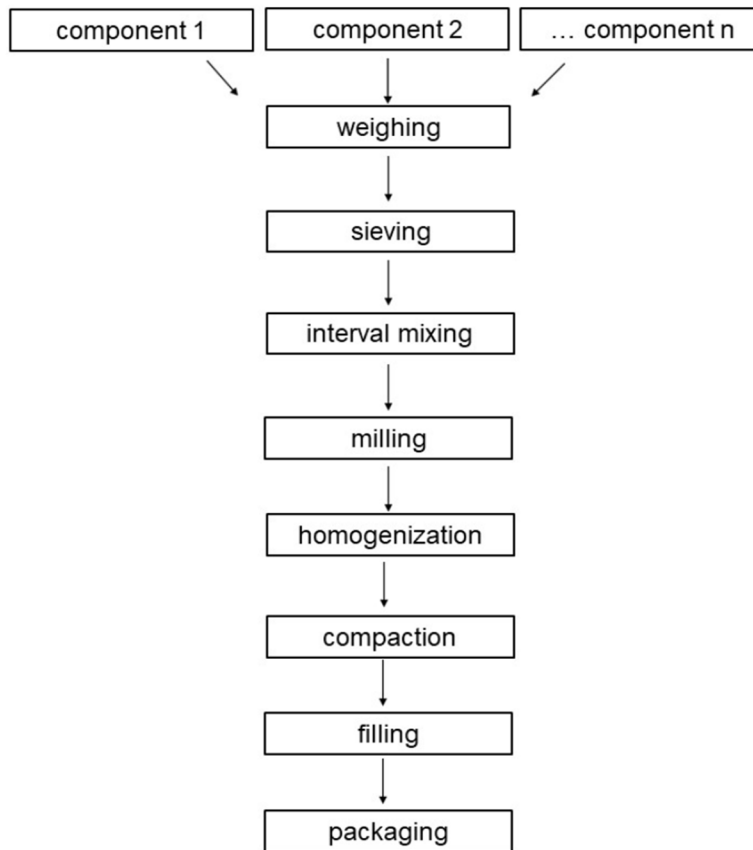
A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 1803, USA
Phone +1 (781) 533-6000

Page : 1 of 2



Manufacturing Procedure - Flow Diagram

Cellvento® Cell Culture Media Portfolio- Compaction



Merck KGaA, Darmstadt, Germany

Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

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Page : 2 of 2

2.3 Control of Materials

The raw materials are suitably controlled before use in production. The control of each component encompasses supplier qualification, quality control and formal release. A comprehensive supplier qualification process is in place.

The specification and amount of the raw materials used in the process is confidential, as it presents detailed production know-how.

2.4 Control of Manufacturing Process

The manufacturing process is performed under conditions such that the quality of the product is at all times in accordance with the specification.

The detailed in-process controls in this process are confidential, as they represent detailed production know-how.

The manufacturing process is capable of consistently meeting product specifications. This is based on knowledge of process parameters, product attributes and their inter-relationship. After significant changes, the impact on process capability is assessed and documented.



Homogeneity Statement

Cellvento® Cell Culture Media Portfolio

Each cell culture media product contains a defined mix of components for the specified formulation. Homogeneity is ensured by various manufacturing steps including mixing and milling, as described in the Manufacturing Flowchart. Control parameters have been established to ensure the effectiveness of the process.

Following packaging, samples are selected from the beginning, middle, and end of the packaging process and are submitted to Quality Control for release testing.

Additionally, homogeneity verification studies have been performed on representative cell culture media formulations, including Cellvento® product batches, for each production line at minimum and maximum batch sizes.

Multiple samples were taken for evaluation, and quantitative analysis for various components was performed, including amino acids, vitamins, and metals. All results were consistent across the batches, meeting acceptance criteria and demonstrating homogeneity. Homogeneity studies are available to be viewed by our customers during on-site audits.

Sarah Nell
Quality Services

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Date: June 30, 2020

Merck KGaA, Darmstadt, Germany
Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

EMD Millipore Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 01803, USA
Phone +1 (781) 533-6000

3 Impurities

Based on evaluation of the manufacturing process and to the best of our knowledge, the following declarations have been established to support the assessment of potential contamination risks in the intended application.



TSE/BSE-Certificate

103795 Cellvento® 4CHO COMP Chemically defined cell culture medium

The note for guidance EMA/410/01 Rev. 3 of the EC considers the requirements of raw materials used for human and veterinary medicinal products. The document introduces risk assessment into the regulatory compliance process for products derived from TSE/BSE-relevant animal species.

We certify that this product is manufactured without the use of raw materials of animal or human origin.

Therefore, the product does not fall under the scope of the above-mentioned guideline and is not concerned by the TSE/BSE issue.

Dr. Katharina Hollmann
Quality Services

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Date: 01-Sep-2020

Merck KGaA, Darmstadt, Germany

Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

EMD Millipore Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 01803, USA
Phone +1 (781) 533-6000

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Viral Safety Statement

Cellvento® Cell Culture Media Portfolio

Chapter 5.1.7. of the European Pharmacopeia provides general requirements concerning the viral safety of medicinal products whose manufacture has involved the use of materials of human or animal origin.

It demands that a risk assessment with respect to viral safety is carried out where materials of human or animal origin are being used as ingredients of medicinal products or in the manufacture of active substances, excipients or medicinal products.

We certify that this product is manufactured without the use of raw materials of animal or human origin.

The viral risk possibly arising from above-mentioned product is reduced to an utmost minimum.

Dr. Tobias Hertzig

Regulatory Management - Biological Materials Europe
Life Science | Quality and Regulatory Management

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Date: July 9, 2020

Merck KGaA, Darmstadt, Germany
Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

EMD Millipore Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 01803, USA
Phone +1 (781) 533-6000



Genetically Modified Organisms (GMO)

Cellvento® Cell Culture Media Portfolio

The European Regulations (EC) 1829/2003 and (EC) 1830/2003 and the US regulation Public Law 114-216 concern the labeling and traceability of genetically modified organisms (GMO) and of food and feed produced from GMO.

The abovementioned products are not intended to be used as food or feed nor consist of genetically modified organisms. Hence, to the best of our knowledge, aforementioned regulations are not applicable for the abovementioned products.

Additionally, we hereby can confirm:

- Our Cellvento® Cell Culture Media Portfolio use raw materials of vegetable origin which might be genetically modified depending on country origin (e.g. soy or corn). In general, these materials are highly processed.
- The raw materials can be derived from these GMO but do not contain any self-replicating organisms
- Inorganic chemicals (salts and trace elements) are unlikely to be GMO-derived raw materials

Sarah Nell
Quality Services

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Date: June 30, 2020*

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Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

EMD Millipore Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 01803, USA
Phone +1 (781) 533-6000



Components of Interest

Cellvento® Cell Culture Media Portfolio

Process-related impurities encompass those that are derived from the manufacturing process, i.e. cell substrates, cell culture media components, or downstream processing (compare ICH Q6B).

In order to assist our customers' need to assess the presence of process-related impurities in their biotechnology-derived products (drug substance or drug product) using the principles of *ICH Q9 Quality Risk Management* to set-up their specifications according to *ICH Q6B Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products*, we would like to inform you whether following components of interest are part of our Cellvento® Cell Culture Media formulations:

| Component | Part of Cellvento® raw material portfolio |
|---|---|
| Antibiotics | not intentionally added |
| Inducers | not intentionally added |
| Serum | not intentionally added |
| Animal Origin | not intentionally added, refer to BSE/TSE declaration |
| Cholesterol | not intentionally added |
| Hormones/recombinant proteins/entities, like <ul style="list-style-type: none"> • LongR3 • IGF • EGF | not intentionally added |
| Insulin | Concentration within typical range for cell culture use: 0.5 - 10 mg/L |
| Vegetable / Plant Origin | refer to Raw Material Origin statement |
| Fermentation Origin | refer to Raw Material Origin statement |

Sarah Nell
Quality Services

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Date: June 30, 2020

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64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

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400 Summit Drive
Burlington, MA 01803, USA
Phone +1 (781) 533-6000

4 Quality Control of Product

4.1 Specification

See section 1

4.2 Analytical Procedures

See product monograph in the Operational Excellence Dossier.

4.3 Validation of Analytical Procedure

Please find the Validation report – open part on the following page.

30.09.2020

Validation report – open part

Cellvento® 4CHO COMP

| Parameter | Specification | Analytical Method | Origin of the Method | Cross Validation |
|--------------------------------------|---------------------------------|---------------------------|----------------------|------------------|
| Appearance | White to light pink, compactate | Visual inspection | In-house | Validated |
| Solubility | Well soluble | Visual inspection | In-house | Validated |
| pH (without Supplement) | 5.1 – 5.6 | pH Meter | In-house | Validated |
| pH (with Supplement) | 6.7 – 7.3 | pH Meter | In-house | Validated |
| Osmolality (without Supplement) | 250 – 310 mosmol/kg | Freezing-point depression | In-house | Validated |
| Osmolality (with Supplement) | 280 – 340 mosmol/kg | Freezing-point depression | In-house | Validated |
| Water Content | ≤ 3.5 % | Karl-Fischer | In-house | Validated |
| Endotoxins | ≤ 1.0 I.U./ml | LAL assay | Ph Eur | Verified |
| Mycoplasma | Not detectable | qPCR | In-house | Not validated |
| TAMC (Total aerobic microbial count) | ≤ 10 ² CFU/g | Pour-plate assay | Ph Eur | Verified |
| TYMC (Total yeast and mould count) | ≤ 10 ² CFU/g | Pour-plate assay | Ph Eur | Verified |

4.4 Batch Analysis

The attached certificates of analysis show typical results obtained in our analytical testing.

Please find also a description of our batch numbering system in the following pages.



Certificate of Analysis

1.03795.0100 Cellvento® 4CHO COMP Chemically defined cell culture medium
Batch F2009195

| | Spec. Values | | Batch Values | |
|--------------------------------------|---------------------------------|-----------|---------------------------------|-----------|
| Amino acid profile | conforms | | conforms | |
| Identity (IR-spectrum) | for information | | for information | |
| Appearance | white to light pink, compactate | | white to light pink, compactate | |
| Solubility | well soluble | | well soluble | |
| pH (without Supplement) | 5.1 - 5.6 | | 5.2 | |
| pH (with Supplement) | 6.7 - 7.3 | | 6.9 | |
| Osmolality (without Supplement) | 250 - 310 | mosmol/kg | 272 | mosmol/kg |
| Osmolality (with Supplement) | 280 - 340 | mosmol/kg | 315 | mosmol/kg |
| Water content | ≤ 3.5 | % | 1.8 | % |
| Endotoxins | ≤ 1.0 | I.U./ml | ≤ 1.0 | I.U./ml |
| Mycoplasma | not detectable | | not detectable | |
| TAMC (Total aerobic microbial count) | ≤ 10 ² | CFU/g | ≤ 10 ² | CFU/g |
| TYMC (Total yeast and mould count) | ≤ 10 ² | CFU/g | ≤ 10 ² | CFU/g |
| Cell growth | conforms | | conforms | |

Date of release (DD.MM.YYYY) 27.04.2018
Minimum shelf life (DD.MM.YYYY) 30.04.2019

Dr. Benjamin Hirschi
Responsible laboratory manager quality control

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Certificate of Analysis

1.03795.0100 Cellvento® 4CHO COMP Chemically defined cell culture medium
Batch F2070795

| | Spec. Values | | Batch Values | |
|--------------------------------------|---------------------------------|-----------|---------------------------------|-----------|
| Appearance | white to light pink, compactate | | white to light pink, compactate | |
| Solubility | well soluble | | well soluble | |
| pH (without Supplement) | 5.1 - 5.6 | | 5.3 | |
| pH (with Supplement) | 6.7 - 7.3 | | 6.9 | |
| Osmolality (without Supplement) | 250 - 310 | mosmol/kg | 274 | mosmol/kg |
| Osmolality (with Supplement) | 280 - 340 | mosmol/kg | 325 | mosmol/kg |
| Water content | ≤ 3.5 | % | 2.0 | % |
| Endotoxins | ≤ 1.0 | I.U./ml | ≤ 1.0 | I.U./ml |
| Mycoplasma | not detectable | | not detectable | |
| TAMC (Total aerobic microbial count) | ≤ 10 ² | CFU/g | ≤ 10 ² | CFU/g |
| TYMC (Total yeast and mould count) | ≤ 10 ² | CFU/g | ≤ 10 ² | CFU/g |
| Cell growth | conforms | | conforms | |

Date of release (DD.MM.YYYY) 03.06.2019

Minimum shelf life (DD.MM.YYYY) 30.06.2020

Dr. Dennis Binder

Responsible laboratory manager quality control

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Merck KGaA, Frankfurter Straße 250, 64293 Darmstadt (Germany): +49 6151 72-0
EMD Millipore Corporation - a subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive, Burlington, MA 01803, USA, Phone +1 (781) 533-6000
SALSA Version 846550 /990000645234// Date: 03.06.2019

Page 1 of 1



Certificate of Analysis

1.03795.0100 Cellvento® 4CHO COMP Chemically defined cell culture medium
Batch F2115795

| | Spec. Values | | Batch Values | |
|--------------------------------------|---------------------------------|-----------|---------------------------------|-----------|
| Appearance | white to light pink, compactate | | white to light pink, compactate | |
| Solubility | well soluble | | well soluble | |
| pH (without Supplement) | 5.1 - 5.6 | | 5.4 | |
| pH (with Supplement) | 6.7 - 7.3 | | 6.9 | |
| Osmolality (without Supplement) | 250 - 310 | mosmol/kg | 270 | mosmol/kg |
| Osmolality (with Supplement) | 280 - 340 | mosmol/kg | 315 | mosmol/kg |
| Water content | ≤ 3.5 | % | 2.2 | % |
| Endotoxins | ≤ 1.0 | I.U./ml | ≤ 1.0 | I.U./ml |
| Mycoplasma | not detectable | | not detectable | |
| TAMC (Total aerobic microbial count) | ≤ 10 ² | CFU/g | ≤ 10 ² | CFU/g |
| TYMC (Total yeast and mould count) | ≤ 10 ² | CFU/g | ≤ 10 ² | CFU/g |
| Cell growth | conforms | | conforms | |

Date of release (DD.MM.YYYY) 17.04.2020
Minimum shelf life (DD.MM.YYYY) 30.04.2021

Dr. Dennis Binder
Responsible laboratory manager quality control

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Information to the batch numbering System

The batch number consists usually of 1 or 2 letters and a 6-9 digits number. In some cases the date of filling is listed additionally. (For some special products groups different rules exist.)

Letter/s: Indicating the production site

Temperature storage conditions

6-9 digits number: 4 to 7 digits as a running number for identification, the last two digits are identical with the last two digits of the product code number, here 60 (out of 1.00160)

F2105840
1.03840.0010
261.96 g

Cellvento®

4CHO-X COMP

Expansion Medium

PKL371460

Made in Germany

Merck KGaA, 64271 Darmstadt
Germany, Tel. +49(0)6151 72-2440
EMD Millipore Corporation
290 Concord Road, Billerica MA 01821
USA, Tel. +1-978-715-4321

Warning. Causes serious eye irritation. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. * Contains Pyruvic acid sodium salt. May produce an allergic reaction. | **Canada only:** Sigma-Aldrich Canada Co. or Millipore (Canada) Ltd. 2149 Winston Park Dr. Oakville, Ontario, L6H 6J8 Phone: +1 800-565-1400.

Achtung. Verursacht schwere Augenreizung. BEI KONTAKT MIT DEN AUGEN: Einige Minuten lang behutsam mit Wasser spülen. Eventuell vorhandene Kontaktlinsen nach Möglichkeit entfernen. Weiter spülen. * Enthält Natriumpyruvat. Kann allergische Reaktionen hervorrufen.

Atención. Provoca irritación ocular grave. EN CASO DE CONTACTO CON LOS OJOS: Enjuagar con agua cuidadosamente durante varios minutos. Quitar las lentes de contacto cuando estén presentes y pueda hacerse con facilidad. Proseguir con el lavado. * Contiene Ácido pirúvico, sal sódica. Puede provocar una reacción alérgica.

Attention. Provoque une sévère irritation des yeux. EN CAS DE CONTACT AVEC LES YEUX: Rincer avec précaution à l'eau pendant plusieurs minutes. Enlever les lentilles de contact si la victime en porte et si elles peuvent être facilement enlevées. Continuer à rincer. * Contient Sodium pyruvate. Peut produire une réaction allergique. | **Seulement pour le Canada:** Sigma-Aldrich Canada Co. or Millipore (Canada) Ltd. 2149 Winston Park Dr. Oakville, Ontario, L6H 6J8 Phone: +1 800-565-1400.

4 054839 754043

2D data matrix bar code (incl. GS1)

Tülay Schollmeier
Quality Services

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Date: July 9, 2020

Merck KGaA Darmstadt, Germany

Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt
Phone +49 6151 72-0

Sigma Aldrich Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, U.S.A.
Phone +1 (800) 521-8956 (314) 771-5765

EMD Millipore Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 1803, U.S.A.
Phone +1 (781) 533-6000

5 Packaging Material

The packaging materials with which the article can come into contact are:

Plastic bottle made of HDPE

Screwcap made of PP

Plastic bag made of LDPE

Plastic bag made of LDPE with integrated desiccant

Packaging materials are inspected for physical condition upon receipt. The packaging materials fulfill the requirements of the framework regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food and other EU regulation having regard to this regulation, including regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food, if applicable.

6 Stability

6.1 Stability Summary and Conclusions

Stability data were obtained by investigation of samples in simulated packaging under long-term storage conditions, in accordance with ICH guideline Q1A Stability Testing of New Drug Substances and Drug Products, and is also in accordance with long-standing product knowledge.

The samples used for the stability study are obtained from production-scale batches. Parameters monitored during the stability studies are quality-indicating, and are those that may show variation during storage. Analytical procedures for stability testing are the same as those applied for product release.

6.2 Postapproval Stability Protocol and Stability Comment

Assigned temperature storage conditions can be found on the corresponding product label and/or the product detail page of our website.

These recommended temperature storage conditions have been defined based on stability studies following the principles of ICH Q1A as well as operational experience.

If stored at declared storage conditions and in original closed containers, the shelf life applies as indicated in our certificate of analysis.

6.3 Stability Data

Stability Data are available in the Quality Management Dossier.

SAFC®

Pharma & Biopharma Raw
Material Solutions

For additional information,
please visit

Emprove.de

We provide information and advice to our customers on application technologies and regulatory matters to the best of our knowledge and ability, but without obligation or liability. Existing laws and regulations are to be observed in all cases by our customers. This also applies in respect to any rights of third parties. Our information and advice do not relieve our customers of their own responsibility for checking the suitability of our products for the envisaged purpose.