altromin Spezialfutter GmbH & Co. KG

Im Seelenkamp 20
32791 Lage (Germany)

P.O. Box 1120
32770 Lage (Germany)

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Value added tax identification number: DE 124 596 384
Location of the company Lage, Local court Lemgo HRA 3113
Partner liable to unlimited extent:
altromin Spezialfutter Verwaltung GmbH
Location of the company Lage, Local court Lemgo HRB 3672

Managing director: Hans-Leopold Altrogge
(authorized representative)
I. COMPANY PORTRAIT

Altromin Spezialfutter GmbH & Co. KG is a family-run feeding stuff company and one of the leading internationally-active manufacturers of laboratory animal diets. Our passion is to produce high-level standardized diets for laboratory animals used in the field of experimental biomedical research and development.

Company’s origin was a mill mentioned for the first time in documents dated back to the 14th century. In 1882, the Altrogge family took over the baronial mill. In 1952, Hans Altrogge founded the independent feeding stuff production sector and started with the manufacturing of feeding stuff for productive livestock breeding and husbandry. In the middle of the Fifties, the company was confronted with the difficulties in standardizing the nutrition of laboratory animals. Collaborating with specialized scientists from universities and the pharmaceutical industry, Altromin developed the first standard diets for laboratory animals. Comprehensive scientific essays were published in 1961 and marked the start of laboratory animal nutrition on a scientific basis.

Thus, having more than 50 years of experience in laboratory animal nutrition, Altromin is able to provide the highest level of scientific and technological know-how as well as valuable professional expertise.

Beside the supply of high-standardized animal diets, Altromin supports customers with competent scientific consultancy and capacious professional customer advisory service. Our outstanding competence is the development and production of customized nutritional solutions for laboratory animals, which comprises the conceptual design of special diets and GMP-compliant manufacturing in our laboratory (“Technikum”).

I.A HISTORY OF ALTROMIN

1370 First reference of a mill by historic document
1882 The mill was taken over by Altrogge family
1945 New construction of the mill and of a production site for concentrated feeding stuffs
1956 First ideas of Professor Brock (Asta Bielefeld) and H. Altrogge (Lage) to develop complete feeding stuffs for laboratory animals
1957 Start of the development of complete feeding stuffs for laboratory animals in a close cooperation with Professor Brock
1961 Completion of the development and start of production of the Standard Diet "Altromin-R" for rats and mice
1962 Completion of the development and start of production of the Standard Diet "Altromin-K" for guinea pigs and rabbits
1963 Foundation of Altromin Company for lab animal diets
1965 Completion of the development and start of production of the Standard Diet "Altromin-H" for dogs
1966 Inauguration of the first special plant for the production of laboratory animal feeding stuffs; Development and production of "Purified Diets"
1967 Completion of the development and start of production of a Standard Diet for primates. Production of first diets with a low germ count
1971 Completion of the development and start of production of a Standard Diet for tree shrews
1975 First edition of "Altromin Kontakt Inform", an informative leaflet about current questions regarding laboratory animal nutrition
1976 Completion of the development and start of production of a Standard Diet for cats
1979  Organization of a symposium about laboratory animal science in Barcelona (Spain); Completion of the development and start of production of a Standard Diet for nude mice and nude rats; Publication of the 10th "Altromin Kontakt Inform"

1981  1st Altromin-Symposium: "Thymusaplastic Hairless Mouse (nu/nu) and Hairless Rat (mu/ mu). Breeding, Keeping, Diet, and Test Models"

1984  2nd Altromin-Symposium: "Minipig - Breeding, Maintenance, Alimentation and Test Models".

1987  Publication of the 20th "Altromin Kontakt Inform"

1988  3rd Altromin-Symposium: "Breeding, Maintenance and Alimentation of Rabbits - the Rabbit as a Model in Biomedical Research"

1990  4th Altromin-Symposium: "Hamster and Gerbil - Breeding, Maintenance, Alimentation, Test Models"

1992  5th Altromin-Symposium: "The dog as a Model in Biomedical Research and Possibilities of its Replacement"

1994  6th Altromin-Symposium in cooperation with GV-SOLAS: “Requirements for Test Animal Diets in the Experiment and Generation and Use of Transgene Animals"

1995  Certification according to ISO 9001:2001 by German TÜV; Publication of the 30th "Altromin Kontakt Inform"

1997  7th Altromin-Symposium in cooperation with GV-SOLAS: "Feeding Stuff Hygiene and Feeding Stuff Treatment -- The Rat as a Model in Experimental Surgery"

1998  Recertification according to ISO 9001 by German TÜV.

1999  8th Altromin-Symposium in cooperation with the Genetics Committee of GV-SOLAS: "Classic Breeding (Genetics) -- Transgene Technology" -- Do they contradict or complement each other?"

2004  Purchase of new property “Im Seelenkamp”

2005  Move of office to the new property

2006  Construction of new facility for Special Diet production

2007  Opening of new special diet production

2009  New permit and certification for GMP-production

2010  Begin of construction of new Standard Diet production

2011  Opening of new manufacturing plant for Standard Diet production; recertification ISO 9001:2008 for the new production site

2012  9th Altromin-Symposium “Principles of Laboratory Animal Science – Breeding, Housing, Hygiene, Nutrition”

2013  50th Anniversary of Altromin; GMP-recertification

I.B  LOCATION AND MANUFACTURING SITE

All company activities (management, administration, logistics, scientific staff, manufacture of standard and special diets) are located at one place, Im Seelenkamp 20, 32791 Lage, Eastern-Westphalia, Germany. All Altromin diets are produced at this location, Altromin does not have any subcontract production. This results in hands-on control of all stages of developing, manufacturing and handling of high-quality laboratory animal diets and in a maximum flexibility in order to meet customers’ special requirements. Storage of raw materials and end-products is also located at Im Seelenkamp 20, 32791 Lage.

The manufacturing site has a dimension of 11.000 m2 and is completely enclosed by a fence.
I.C SPECIAL CUSTOMIZED CAPABILITIES

In addition to standard diets for laboratory animals, Altromin’s most valuable know-how is the formulation and manufacture of special customized diets, exactly adjusted to the customers’ requirements. Altromin provides purified diets for all kinds of scientific aims: e.g. diets for induction of deficiency/excess symptoms, diets with adjusted nutritional values, high-fat diets, test diets with added substances/drugs. All purified diets are available with the adequate control diet (picture 1). A dying of purified diets in different colours is also available (picture 2).

Moreover, Altromin has the official permission to manufacture medicated diets for laboratory animals. Thus, a treatment of Oxyuriasis in an animal facility is possible by using the medicated form of Altromin Standard Diets and therefore avoiding a diet change during treatment. Manufacturing of medicated diets takes place in an extra manufacturing plant (dedicated equipment) and is strictly separated from the manufacturing of other, non-medicated diets.

All special diets as well as medicated diets are handmade by our experienced staff. The strictly on demand manufacturing takes place in our laboratory (“Technikum”) under strict hygiene requirements.
We are also able to provide customized packaging solutions: All kinds of packaging, from simple untreated paperbags to double vacuumed and irradiated plastic packages in different sizes are available. For autoclaving-specific packaging, Altromin provides consulting and tailored packaging solutions.

II. QUALITY MANAGEMENT AND QUALITY ASSURANCE

QM-SYSTEM

In 1999, Altromin established a quality management system according to DIN EN ISO 9001:2008, certified by the TÜV Rhineland within the same year. Since then, several yearly regular control and supervision audits as well as recertifications followed, in which Altromin was certified as running a well-functioning, continuously improving quality management system.

In 2004, the company established a HACCP-system, which is also yearly audited by TÜV Rhineland during the ISO 9001-audit.

Additionally, Altromin is GMP-certified for the manufacture of special diets in the Altromin laboratory production (“Technikum”) and has also the permission to produce medicated diets for laboratory animals.

Please find attached all corresponding certificates (Annex I-III).

QM-MANUAL

All company processes, including the HACCP-system and most Standard Operation Procedures (SOPs), are gathered in the quality manual. Processes have been subdivided into management, core and supporting processes. Responsibilities are determined, process interfaces are shown and communication channels are defined.

The quality manual is versioned and controlled via a document directory. At least one time a year, the whole manual is checked during an internal audit with the collaboration of an external expert. Only the CEO is authorized to release new versions.

RESPONSIBILITIES

Responsibilities and authorizations have been clearly defined in the quality manual in the form of a responsibility matrix and an organization chart. Responsibilities can only be determined by the managing director. The competences delegated by management authorization have been clearly defined within the scope of job descriptions.
DOCUMENT CONTROL

All quality-relevant documents such as the quality manual, all quality records, process and work instructions as well as product specifications, are subject to fixed control rules: For each document versioning is documented in a directory. Access to all QM-documents is given via the company’s intranet to ensure easy and efficient version management. Electronically stored documents and records are regularly saved. The quality manager is responsible for the publication and exchange of documents and records.

All quality-relevant records are basically retained for at least 10 years after their creation. All other documents have to be stored for 6 years. Commercial documents and personnel documents are retained for the legally fixed 30-year term. The storage period is mentioned in the header of each document.

QUALIFIED STAFF

All of our employees have undergone a qualified vocational education and have been extensively trained for their activities. Altromin is an official practical training company, continuously providing official apprenticeship positions: Apart from industrial businessmen, Altromin trains specialists for food technology (state certified three-year-training occupation), which are retained in the company after their successful training if possible. Through this we ensure that our employees are familiar with all internal activities and understand Altromin’s quality policy from the start of their professional career. Beside further education on international conferences, training courses and trade fairs, Altromin carries out internal trainings regarding quality management and quality assurance, HACCP, workplace hygiene, production processes and occupational safety according to a yearly training schedule. Employees have to join at least one QM-, Hygiene-, HACCP-, and occupational safety training per year and their participation is documented. Apart from oral instructions, all newly engaged employees are trained in quality management and hygiene rules and are informed about the company’s policy.

HYGIENE REGIME

Our production rooms are exclusively cleaned by our own employees according to a defined cleaning schedule. The responsible persons of the individual departments ensure the correct cleaning of their sector and document all cleaning and disinfection work. Internal and external training regarding hygiene takes place regularly.

PEST CONTROL

To exclude any opportunity for rodents to get inside the buildings, Altromin ensures that all doors and gates are closed all the time and installed rodent barriers and plastic curtains. Altromin engaged an official authority-certified contract pest control company monitoring all storage and manufacturing areas, both inside and outside areas. Pest control is done via visibly numbered traps against rodents and insects which act as both control and fight measure: Beside classic Cumarine baits against rodents and light/pheromonal traps against insects, Altromin also uses aversive
ultrasonic sound sources against rodents. All traps are regularly checked (4/8-week-interval) by the pest controller regarding functionality, possible bait consumption (rodents) or infestation status (insects). For each check, a detailed protocol including a site plan with all traps is provided to Altromin. Beside the professional pest control measures, Altromin carries out internal routine controls to be able to immediately react to any possible infestations. The pest controller is quickly reachable and will react to unexpected incidents very quickly with appropriate professional corrective actions.

SUPPLIERS OF RAW MATERIAL

For Altromin diets, raw materials in food quality condition are used. Cereals come from certified (e.g. GMP+, ISO) German suppliers of surrounding countryside of Lage, near to Altromin site. We buy our raw materials exclusively from efficient suppliers with whom we have had successful business relations for many years. We evaluate our suppliers within the scope of specifications, external audits and regular controls. Through this we can recognize any deviations quickly and reliably.

QUALITY CONTROL

Neither any raw material nor end-product is allowed to be used or shipped before having been released by our qualified staff. All raw materials and end products are sensory checked by trained employees. In addition, end-products are checked for pellet hardness and humidity. Our products are regularly examined with respect to nutritional value, microbiological status as well potential content of undesirable substances. For this purpose, we send samples to specialized accredited test laboratories. Beside routine controls, batch-based examinations are carried out upon request.

MONITORING TESTING AND MEASURING EQUIPMENT

All our measuring instruments such as weighing scales are registered and numbered and subject to regular and documented test equipment supervisions. Regularly checks (internal/external/official calibration) are done according to a defined schedule and calibration protocols are archived as QM-documents.

STORAGE

All Altromin goods are exclusively produced based on incoming orders and are packaged, palletized and shipped directly after production. Therefore, stock keeping has been minimized. For all raw materials, packaging materials and end-products Altromin works according to the FIFO(- First-In, First-Out)-principle. Main raw materials are directly blown from trucks into storage silos and do not have contact with the floor. A hygiene regimen for all storage areas has been established.
TRACEABILITY

Altromin uses a specific software program for the manufacturing of standard and special diets. Thus, we are able to ensure the easy traceability of our several products. When raw materials are received, they get an internal batch number, regenerated by the software. Storage is carried out strictly according to the FIFO-principle. The batch numbers are absolutely allocated to a certain delivery and accompany the product in all production processes. This data is stored in the IT-mixing instructions and is archived for 10 years. All the products that leave our company are marked with a batch number which shows the expiry date and the time of the production process. For each produced batch a batch protocol from mixing to bagging is saved in the software. Through this, a complete marking is provided enabling identification of every single added and mixed component even after many years (complete up- and downstream).

A retention sample is taken from each produced batch and from each raw material and is stored for 12 months from the production date. This ensures that the product is available in our company for up to 3 months succeeding the expiration date.

COMPLAINT MANAGEMENT

Altromin has extensive verified mechanisms for dealing with complaints, possible product recalls or even emergency cases. In every case, we can ensure that incidents are efficiently handled immediately after their notification. Faulty goods can be completely traced back within a very short time, not only within our company, but also up to the customer or supplier (see traceability). Communication with the customers will be realized very quickly. Any relevant recalls are made immediately, necessary analyses can be ordered in the short term.

In case of faulty products or customer complaint, Altromin has a written schedule about how to act. Elements in complaint management are clarification of the exact problem, assessment/analysis of retention sample(s), identification of causes (e.g. check of mixing protocol, analysis), trace back, required reactions (e.g. customer information, product recall), internal measures/changes in order to prevent and QM-statement for the customer. All complaints are documented in detail and are statistically evaluated once a year.

INTERNAL AUDITS

In addition to regularly audits regarding ISO 9001 and GMP, regularly internal audits are carried out by the quality manager in cooperation with the management. At least once a year, an internal audit is performed by an external QM-expert and the QM-manual is carefully reviewed. The QM-expert lists all deviations and determines appropriate measures including deadlines for their implementation.

Furthermore, the management assesses the QM-system during a yearly management review: Yearly quality goals, intended innovations and measures are checked as well as results of previous audits. The yearly review particularly takes into account deviations and customer complaints, does a detailed statistical analysis of complaints and determines measures for improvement.
Certificate

Certificate Regist. No.: 01 100 059936

Certificate Holder: Altromin Spezialfutter GmbH & Co. KG
Im Seelenkamp 20
D - 32791 Lage

Scope: development, production and distribution of animal diets

Proof has been furnished by means of an audit that the requirements of ISO 9001:2008 are met.
The due date for all future audits is 29.03.

Validity: The certificate is valid from 02.05.2014 until 01.05.2017.
First certification 2007

22.04.2014

TÜVRheinland Cert GmbH
Am Grauen Stein - 51105 Köln

www.tuv.com
<table>
<thead>
<tr>
<th>Teil 1</th>
<th>Part 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BESTÄTIGUNG DER ÜBEREINSTIMMUNG EINES HERSTELLERS MIT GMP</strong></td>
<td><strong>CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER</strong></td>
</tr>
<tr>
<td>Ausgestellt nach einer Inspektion gemäß Art. 80 (5) der Richtlinie 2001/82/EG</td>
<td>Issued following an inspection in accordance with Art. 80 (5) of Directive 2001/82/EC</td>
</tr>
<tr>
<td>Die zuständige deutsche Überwachungsbehörde bestätigt.</td>
<td>The competent authority of GERMANY confirms the following:</td>
</tr>
<tr>
<td>Der Hersteller</td>
<td>The manufacturer</td>
</tr>
<tr>
<td>Altromin Spezialfutter GmbH &amp; Co. KG</td>
<td>Altromin Spezialfutter GmbH &amp; Co. KG</td>
</tr>
<tr>
<td>Anschrift der Betriebsstätte</td>
<td>Site address</td>
</tr>
<tr>
<td><strong>Im Seelenkamp 20</strong></td>
<td><strong>Im Seelenkamp 20</strong></td>
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<tr>
<td><strong>32791 Lage</strong></td>
<td><strong>32791 Lage</strong></td>
</tr>
<tr>
<td>wurde im Rahmen der nationalen Arzneimittelüberwachung inspiziert in Verbindung mit der Herstellungserlaubnis Nr. 8.82.40.22.19-HE01 gemäß Art. 44 der Richtlinie 2001/82/EG umgesetzt in deutsches Recht durch:</td>
<td>has been inspected under the national inspection programme in connection with manufacturing authorisation no. 8.82.40.22.19-HE01 in accordance with Art. 44 of Directive 2001/82/EC/ transposed in the following national legislation:</td>
</tr>
<tr>
<td>§ 13 Abs. 1 und § 72a Arzneimittelgesetz</td>
<td>Sect 13 para 1 and sect 72a Arzneimittelgesetz (German Drug Law)</td>
</tr>
<tr>
<td>Auf Grund der aus der letzten Inspektion vom 03.04.2013 gewonnenen Erkenntnisse wird für die oben genannte Betriebsstätte des Herstellers die Übereinstimmung mit den Grundsätzen und Leitlinien der Güten Herstellungspraxis gemäß Artikel 51 der Richtlinie 2001/82/EG bestätigt.*</td>
<td>From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 2013/04/03, it is considered that it complies with the The principles and guidelines of Good Manufacturing Practice laid down in Directive article 51 of Directive 2001/82/EC.*</td>
</tr>
<tr>
<td>Dieses Zertifikat bestätigt den Status der Betriebsstätte zum Zeitpunkt der oben genannten Inspektion. Es sollte nicht zur Bestätigung der Übereinstimmung herangezogen werden, wenn seit der genannten Inspektion mehr als drei Jahre vergangen sind. Nach Ablauf dieser Zeit sollte mit der zuständigen Behörde Kontakt aufgenommen werden.</td>
<td>This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection, after which time the issuing authority should be consulted.</td>
</tr>
<tr>
<td>Die Echtheit dieses Zertifikates kann ggf. durch die ausstellende Behörde bestätigt werden.</td>
<td>The authenticity of this certificate may be verified with the issuing authority.</td>
</tr>
</tbody>
</table>
Annex III: Permit Medicated Diet Production

HERSTELLUNGSERLAUBNIS

1. Nummer der Erlaubnis
   8.82.40.22.19-HE01

2. Name des Erlaubnisinhabers
   Altromin Spezialfutter GmbH & Co. KG

3. Anschriften der Betriebsstätten des Herstellers
   Im Seelenkamp 20
   32791 Lage

4. Eingetragene Anschrift des Erlaubnisinhabers
   Im Seelenkamp 20
   32791 Lage

5. Umfang der Erlaubnis sowie Darreichungsformen
   siehe ANLAGE 1

6. Rechtsgrundlage der Erlaubniserteilung
   ☑ § 13 Absatz 1   ☐ § 72 Absatz 1

des Gesetzes über den Verkehr mit Arzneimitteln (Arzneimittelgesetz – AMG)
in gültiger Fassung

7. Name des verantwortlichen Bearbeiters der zuständigen Behörde des
   Mitgliedstaates, der die Erlaubnis erteilt.
   Dr. Matthies

8. Unterschrift

9. Datum
   15. Dezember 2009

10. Beigefügte Anlagen
    Anlage 1 Umfang der Erlaubnis