Jungbunzlauer

Information Package for Pharmaceutical Customers
Xanthan Gum

The following Jungbunzlauer product

- **Xanthan Gum**

is manufactured by fermentation of carbohydrates. The product undergoes several purification steps and is finally obtained in its highly pure form.

The above mentioned product is manufactured in the following Jungbunzlauer plant:

- **Jungbunzlauer Austria AG**
  Werk Pernhofen
  2064 Wulzeshofen
  AUSTRIA

Xanthan Gum is supplied in accordance with the requirements of the European Pharmacopoeia (Ph.Eur.), the United States Pharmacopoeia (USP), the Food Chemicals Codex (FCC) and the European Commission Directive 2008/84/EC, always in their latest version.

Our production plants have set up quality management systems that guarantee that our products meet the requirements of our customers and of all essential international food, drug and other relevant regulations. Fulfilment of the requirements of the ISO 9001:2000 Quality Management System Standards is the logical result of Jungbunzlauer's comprehensive quality commitment. Our factories have been certified according to ISO 9001:2000 criteria.

Since most Jungbunzlauer products are not active pharmaceutical substances per se we do not hold a GMP certificate for these plants. However, Jungbunzlauer as a supplier to various pharmaceutical customers worldwide has manifold proven its capability to fulfil the typical standards required for the manufacture of excipients.

To assist our customers in their assessment of our manufacturing practices, we would like to provide you with the following questionnaire that states the most important details about our quality system, organisation, facilities, processes, documentation, etc.

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ITEM	YES	NO	COMMENT
A. GENERAL			
1. Has your firm been audited by the FDA or other regulatory/health agency or ministry, for any product, during the past three years?	**X**		**The site has never been audited by the FDA. The site is regularly inspected by an official authority hygiene responsible personnel from the government. Moreover, the site is audited by 20-30 customers every year.**
2. Is the facility ISO Certified?	**X**		**There are regular ISO 9001 audits conducted by Lloyd's.**
3. Does the company have a policy on SHE (Safety, Health & Environment)?	**X**		**The site is affiliated to a Responsible Care program.**
B. ORGANIZATION AND PERSONNEL			
1. How many employees are at this site?			**approx. 300**
2. Is there a QA/QC department?	**X**		
3. Who is responsible for responding to recalls?			**Quality Assurance Manager**
4. Are there written job descriptions describing the required qualifications and training needed for each job?		**X**	
5. Is there an SOP for training, addressing both permanent and temporary employees?	**X**		
6. What type of trainings do you perform?			**Typical training topics are: clothing regime, working hygienically, the use of manufacturing records, the use of the equipment, (cross) contamination prevention methods, sampling, the collection of data, correct performing QC testing (QC personnel), SOP Training etc.**
7. Are training and qualifications documented for each employee, including temporary employees?	**X**		
8. Is training performed and documented when SOPs are created or updated?	**X**		**where applicable**
9. Are changes in regulatory requirements tracked and communicated to employees?	**X**		
10. If repackaging or handling of exposed product occurs:			
a. Is there personal hygiene training for personnel handling product so they understand the precautions necessary to prevent contamination of the product?	**X**		

ITEM	YES	NO	COMMENT
b. Are personnel with illness or open skin lesions that may contaminate or otherwise adversely affect the safety or quality of the product allowed to work in any operation that could cause the product to become contaminated?		**X**	
c. If there are parts of an operation where loose and/or unsecured jewelry or other items could fall into the product, is there a policy prohibiting such items?	**X**		
d. Are personnel required to wear clean, intact, and sanitary protective apparel (e.g., outer garments, hair coverings, gloves) where necessary to protect the product from contamination by perspiration, hair, cosmetics, and other foreign substances?	**X**		
11. Is the storage or consumption of foods, beverages, and tobacco ever allowed in the warehouse area?		**X**	
12. Is the storage of clothing and personal belongings, to designated areas?	**X**		
C. FACILITIES			
1. How old are the facilities?			**Start of Xanthan Gum production in 1986**
2. Is a separate facility used for any operations (such as second warehouse)?		**X**	
3. Is there adequate security to assure there is no entry by unauthorized persons?	**X**		
4. Are facilities of suitable size, design, and construction for the operations being performed?	**X**		
5. Are materials stored such that areas under, around, and behind can be easily inspected?	**X**		
6. Are facilities maintained in a clean and orderly manner and in a good state of repair? (Any significant floor cracks, openings in walls, ceiling leaks or openings)?	**X**		
7. Are the surrounding grounds maintained in a clean and orderly manner so as not to attract pests or constitute a potential source of contamination?	**X**		
8. Are separate areas, with appropriate air handling systems, provided for sampling of materials?		**X**	
9. Is the warehouse clean and well-organized, and can materials be easily located?	**X**		
10. Are shipping docks protected from weather where necessary?	**X**		

ITEM	YES	NO	COMMENT
11. Is there appropriate storage for controlled substances?	**X**		
12. Is there adequate lighting and, where appropriate to protect exposed product or machinery, is it equipped with protection against shattering?	**X**		
13. Are there provisions for power backup sources for critical systems if main power should fail, and/or an SOP for recovery from power failure?	**X**		
14. Are there appropriate fire protection measures and alarm systems?	**X**		
15. PEST CONTROL			
a. Is there an SOP for Pest Control?	**X**		
b. Does the facility use an integrated pest-control system, such as electrocutors, hanging partitions at bay doors (to minimize birds, flying insects), sticky traps, etc.?	**X**		
c. Are facilities properly maintained against rodents, birds, insects, and other vermin and are records kept? Are only approved rodenticides and pesticides used?	**X**		
d. If pest control is performed by a licensed pest control contractor, is that company's performance and compliance adequately monitored? Does the company provide a detailed written report of its activities and any rodenticides or pesticides used?	**X**		
e. Are the windows adequately screened, where necessary?	**X**		
f. If raw materials or intermediates are stored in silos, tanks, or other large containers, are the vents adequately protected to prevent entry of water, birds, and insects?	**X**		
D. EQUIPMENT			
1. Is equipment installed with sufficient clearance to allow access to both the equipment and the surrounding area for cleaning and maintenance operations?	**X**		
2. Is there a master list of all equipment that specifies those requiring maintenance and/or calibration?	**X**		
3. Are there SOPs for inspection (monitoring the condition) and maintenance of equipment and of measuring instruments?	**X**		
4. If equipment and instruments malfunction or are determined to be defective, are they immediately taken out of use?	**X**		

ITEM	YES	NO	COMMENT
5. Are there SOPs for calibration of critical equipment and measuring instruments? Do SOPs assign responsibilities; include schedules; describe methods, equipment, and materials to be used, including calibration over actual range of use and standards traceable to national standards; and include specifications and tolerances?	**X**		
6. If calibration operations are performed in-house, do SOPs specify proper handling and storage conditions for the traceable standards?	**X**		
7. Does an SOP specify that equipment cannot be used if it is beyond the calibration due date, and describe actions to be taken if equipment is used that is found to have been beyond the due date or is found to be out of calibration limits?	**X**		
8. Is equipment in use observed to be within calibration dating?	**X**		
9. Are records maintained for maintenance and calibration operations?	**X**		
E. COMPUTERIZED SYSTEMS			
1. Are any computerized systems used in the operation to perform GMP-related functions (e.g. inventory, training, investigation records?)	**X**		**SAP system used for various transactions (e.g. quality control, warehousing, shipping, etc.) or others data base**
2. Is there a system to control changes to systems and programs that can have an effect on the quality of the product?	**X**		
3. Is a formal log of system and program changes maintained?	**X**		
4. Have such computerized systems been validated (demonstrated to consistently function as expected)?		**X**	**Our SAP system has not been validated according to GMP regulations.**
5. Is there appropriate security to limit access to computerized systems, protect records from tampering, and prevent data alteration?	**X**		
6. If passwords are used as a security measure, are there provisions for periodic changing of passwords?	**X**		
7. Does a responsible person (e.g., system administrator) have a list of all passwords in case of emergency?		**X**	**The system administrator has no list of passwords, but he can change them indirectly in the system.**
8. Are suitable backup systems in place, such as copies of programs and files, duplicate tapes, or microfilm?	**X**		

ITEM	YES	NO	COMMENT
9. If anyone leaves the department or company, or otherwise loses authority to access the systems, are there procedures to immediately remove that person's access codes from the system?	**X**		
F. OPERATIONS			
1. RECEIVING			
a. Is there an SOP for receiving shipments, including inspection and verification of material received against the bill of lading, quantity received, lot numbers, etc?	**X**		
b. Are raw materials on an incoming sampling and inspection program?	**X**		**Incoming materials are checked on certificate of analysis and identification (delivery note). There are test plans for incoming products which indicate the frequency of analytical tests.**
c. Briefly describe how discrepancies in incoming shipments are handled.			**In case of defects, the raw material (full trucks, tanks, silos) is clearly labeled as non-approved and returned to the supplier.**
2. STORAGE IN TANKS/SILOS			
a. Are different lots of a material mixed in storage tanks?	**X**		**We mix different lots of raw material for the fermentation process. After fermentation there is a continuous purification process. A selling lot consists of a blend of different production batches mixed to meet specifications and analyzed before the release.**
3. INVENTORY CONTROL			
a. Is there ongoing inventory reconciliation as materials are removed from stock?	**X**		**The stock rotation of finished products and raw materials is done by FIFO (first in first out) system. The stock of finished products is controlled by computerized SAP system.**
b. Is periodic inventory verification performed?	**X**		
c. Has the periodic inventory been done, as scheduled, for all customers in the past year?	**X**		
4. SHIPPING			
a. Briefly describe the system that prevents unapproved materials from being shipped to customers.			**Positive release system, status indicated in SAP system.**

ITEM	YES	NO	COMMENT
b. Are orders that have been packed for shipment verified against the bills of lading before being loaded onto the truck?	**X**		
5. RETURNED GOODS CONTROL			
a. Briefly describe the steps used for processing of returned goods (including segregation from other items, any identification or labeling as returned, any inspection, and documentation). Also identify whether or not items may be reused, and if so, under what circumstances?			**Returned goods are physical segregated (separate storage) and the status is indicated in SAP system. QC decision on further steps. Use is only possible after active release through QC.**
G. QUALITY SYSTEMS			
1. RESPONSIBILITIES AND AUTHORITY			
a. Are the Quality organization's authority and responsibilities clearly defined in writing?	**X**		
b. Does QA have authority to review and approve or reject packaging materials and finished product?	**X**		
c. Does QA assure that packaging and testing records are reviewed before batches are shipped?	**X**		
d. Is there an adequate program for handling complaints, including investigation to determine the causes, corrective actions, verification of the effectiveness of corrective actions, a target time frame for responding; trend analyses, and notification of appropriate parties including management?	**X**		
2. AUDIT PROGRAMS			
a. Briefly describe how management is assured that internal procedures are being followed adequately?			**Internal audit is performed once a year. Records are reviewed by management and a follow up is done by QA.**
b. Is there an internal quality audit program that covers all areas of the operation to verify that SOPs and other procedures and policies are being followed, and to determine effectiveness of the quality systems?	**X**		
c. Are these internal audits documented as formal reports?	**X**		
d. Are results of internal audits trended, and are these trends reviewed and acted on, by management, as part of a continuous improvement effort?	**X**		

ITEM	YES	NO	COMMENT
e. Based on the audit findings and recommendations, are steps taken to correct any areas of noncompliance?	**X**		
f. Are corrective actions, and preventative measures documented?	**X**		
g. Is formal tracking of corrective actions/preventative measures done to assure these items are completed as scheduled?	**X**		
h. Is the effectiveness of corrective and preventative actions evaluated or verified in subsequent audits?	**X**		
3. INVESTIGATION OF NONCONFORMANCES			
a. Is there an SOP for investigation of deviations or events of non-conformance in any area to determine the cause and institute corrective actions to prevent the situation from recurring?	**X**		
b. Are records maintained of nonconforming materials, related investigations and corrective actions?	**X**		
c. Is formal tracking of investigations done to assure these items are completed?	**X**		
4. RECALLS and RETURNS			
a. Is there an SOP for performing recalls?	**X**		
b. Is the quantity of recalled product verified against inventory records?	**X**		
5. CERTIFICATES OF ANALYSIS			
a. Is every lot (received and shipped) accompanied by a certificate of analysis (COA)?	**X**		
b. Does the COA clearly indicate which tests are performed on every lot and which are created via skip lot testing?	**X**		
c. Does the COA indicate the location (company) where the material was manufactured?	**X**		
d. Does the COA clearly indicate which company performed the analysis?	**X**		
e. Is the COA signed by the Responsible Person?		**X**	**The certificate of analysis is electronically issued by SAP system through release from the Quality Control Manger. The certificate contains no signature.**

ITEM	YES	NO	COMMENT
6. SUPPLIER AUDIT PROGRAM			
a. How are your suppliers approved?			**Every potential supplier is tested on the first deliveries on different criteria. If performance, quality etc. are o.k. he gets approval and is added to the supplier list. We perform supplier audits where applicable. We have a long-term relationship with suppliers.**
b. Are all suppliers audited in person? If not, describe under what circumstances suppliers are not audited in person.		**X**	**We perform audits on suppliers where deemed to be applicable.**
c. Are supplier audit observations trended and reviewed by management as part of a continuous improvement effort?	**X**		
7. MATERIALS CONTROL			
a. Is every finished batch sampled according to a plan that assures that the sample is representative of the batch?	**X**		
b. Are sampled containers labeled with sampler's name and date of production? If not, describe how this is captured.	**X**		
c. Are there adequate procedures for controlling product placed on hold for any reason?	**X**		
d. Is ability to change release status in the computer restricted to authorized QA personnel?	**X**		
e. Is every finished batch tested and approved before shipment?	**X**		
f. Are there complete written instructions for testing and releasing finished materials, including methods, equipment, operating parameters, and acceptance specifications?	**X**		
g. If the material is compendial (e.g., USP / EP), are all compendial tests and specifications performed?	**X**		**Not every compendial parameter is tested for each batch but all parameter are tested at different frequencies (from batch testing to random testing).**
h. Stability Program			
1) Is an expiration date assigned to the material? If so, what is it?	**X**		**5 years from the production date. Except xanthan gum DF = 2 year and QH = 1 year**

ITEM	YES	NO	COMMENT
2) If an expiration dating period has been assigned, are stability data available to support the intended period of use of the material?	**X**		
3) Are stability failures investigated and reported to management?	**X**		
i. Are retention samples kept for every batch for at least one year past expiration date or, if no expiration date is assigned, according to a written policy?	**X**		
H. DOCUMENT CONTROL			
1. STANDARD OPERATING PROCEDURES (SOPs)			
a. Are there written SOPs for all areas of the operation? (e.g. receiving, shipping, inventory controls, area cleaning, pest control, returns, etc)	**X**		**where applicable**
b. Is there an SOP for writing, handling, and updating SOPs? Are SOPs periodically reviewed and updated?	**X**		
c. Describe how the history of SOP revisions is maintained?			**There is an overview list stating the actual status of each SOP**
d. Are current SOPs readily available to employees in the areas where operations are performed?	**X**		
e. Is there an adequate system to assure that unneeded or obsolete documents are removed from use?	**X**		
2. TRACEABILITY			
a. Are batch/ lot numbers assigned in such a manner that they are not duplicated and they enable tracing of all processes and batch records for each batch?	**X**		
b. Is there full traceability on the origin of materials?	**X**		

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CERTIFICATE OF APPROVAL

This is to certify that the Quality Management System of:

Jungbunzlauer Austria AG
Werk Pernhofen
Wulzeshofen
Austria

has been approved by Lloyd's Register Quality Assurance
to the following Quality Management System Standard:

ISO 9001:2000

The Quality Management System is applicable to:

Manufacture of citric acid, sodiumcitrates, magnesiumcitrates, zinccitrates, xanthan gum, glucose syrup, citrofeed, gypsum, corngerms, corngold, cornpro, corn fibres, corn steep liquor

Approval
Certificate No: VNA 200628

Original Approval: 26th October 1994

Current Certificate: 5th December 2008

Certificate Expiry: 31st October 2009

Issued by: Lloyd's Register EMEA Niederlassung
Wien for and on behalf of
Lloyd's Register Quality Assurance Limited

UKAS
QUALITY
MANAGEMENT
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Jungbunzlauer

Quality Policy
Jungbunzlauer Austria AG, Plant Pernhofen
(Excerpt from the quality manual)

Within the scope of entrepreneurial responsibility and in view of the quality assurance and the satisfaction of customer expectations the Plant Management of Jungbunzlauer (Plant Pernhofen) has defined the company's policy for quality assurance as follows:

1) The obligation to fulfil specified customer claims and legal respectively governmental requirements.

2) With reference to the customer claims the percentage of justified customer complaints should be continuously improved. The target will be fulfilled, if a) the trend line (observation period of 3 years) has been continuously improved from the actual evaluated percentage, or b) if the minimum target has been achieved from the economical point of view.

3) On the basis of complaints, internal and external audits corrective actions as well as preventive measures are defined, carried out and maintained.

4) With reference to the relevant departments each quality target will be specified into a SOP and the target tracking will be pictured as figures on a monthly basis.

The Quality Assurance Handbook is the tool for the implementation of this quality policy, and it is an appropriate description of the company's quality assurance systems. Its application guarantees that organizational, administrative and technical activities which influence order processing and quality of execution are planned, coordinated and supervised. The Quality Assurance Handbook complies with the requirements of the ISO 9001:2000 system, and with contractually agreed requirements. This Quality Assurance Handbook is valid for the manufacturing of the products Citric Acid, Citrates and Xanthan Gum.

With this declaration the Company Management obligates all employees, who execute quality influencing activities, to fulfil their activities according to the descriptions set forth in this Quality Assurance Handbook or through the corresponding training at the best of their knowledge and ability.

The manager of quality assurance is responsible for the planning, supervision and correction of the quality assurance system and is obligated to inform the Company Management of any significant quality assurance problems.

The assessment of the quality assurance system by the quality assurance management is ensured through an analysis of the above mentioned quality policy and its documentation in the semi-annual management review.

June 2006

CERTIFICATE

WKO DIE INDUSTRIE

FCIO CHEMISCHE INDUSTRIE

The Association of the Austrian Chemical Industry,
after an audit by independent experts, grants to

Jungbunzlauer Austria AG
Wulzeshofen

the right to use the international Responsible Care-Logo complying with the rules set out by CEFIC for a period of three years.

The company name and site are listed
in the Austrian Directory of Certified Members.

Managing products, processes and plants,
the enterprise considers safety as well as the protection
of people and the environment as a primary concern.

Responsible Care

An Initiative for Health, Safety & Environment

Association of the Austrian Chemical Industry

Dr. Peter Untersperger
President

Dr. Wolfgang Eickhoff
Director General

Vienna, 14th December 2006

Jungbunzlauer

Health, Safety and Environmental Policy
Jungbunzlauer Group

Responsibilities
Jungbunzlauer is a leading producer of ingredients and additives mainly for the food, beverage, detergent, pharmaceutical and cosmetic industries. Our products are made by the natural processes of fermentation based on renewable carbohydrate raw materials. They are readily biodegradable and ecologically safe. Most of our by-products are processed and are sold to the construction and agriculture industry or are used to produce biogas.

The Jungbunzlauer Group takes responsibility for the safety and the health of its employees and for the protection of the environment and its natural resources. Therefore, all Jungbunzlauer production sites take part in a Health, Safety and Environmental program. All of our sites have been certified or are in the process to get certified according to recognised standards like "Responsible Care" or "ISO 14001". Furthermore, all our production sites are located in countries that have ratified the Kyoto Protocol on Climate Change, and have thus agreed to reduce their emissions to target levels below their 1990 emission level.

Nevertheless, the Jungbunzlauer Group issues this policy as a guideline for the management of affiliated companies. It is the responsibility of the management of the subsidiaries to take care of the implementation of this policy, always adapted to the local circumstances.

Objective targets
1. All operations must be in accordance with relevant national laws and regulations with regard to health, safety and protection of the environment.
2. All subsidiaries of the Jungbunzlauer Group are in close cooperation with authorities.
3. Health, safety and environmental standards and performance shall be continuously improved.
4. Jungbunzlauer strives for an ongoing reduction of waste and for optimal recycling of waste. If economically possible, as much substance as possible shall be converted into useful by-products.
5. An ongoing reduction of emissions shall be considered.
6. All operations shall be organized in a way to reduce the health and safety risks of employees to a possible minimum.
7. All processes shall be organized in a way that the hazards for the natural environment as well as for the neighbouring communities are reduced to a minimum.
8. Jungbunzlauer aims to reduce the consumption of energy, water, raw material and other sensitive inputs.
9. Safety and ecological compatibility of packaging and transportation shall be continuously considered.

Implementation
The affiliated companies of the Jungbunzlauer Group will take the necessary steps in order to achieve the objectives defined above. These steps are amongst others the following:

- Motivation, information and training of employees
- Risk-analyses and assessments of plants, processes and projects
- Setting of clear and binding standards
- Implementation of fitting, but demanding formal and/or certification systems
- Continuous monitoring of safety, health and environmental performance
- Inclusions of information on performance compared to standards in the standard reporting procedures

This policy has been issued by the Management Committee and by all Jungbunzlauer companies. Compliance with these policy guidelines shall be audited from time to time.

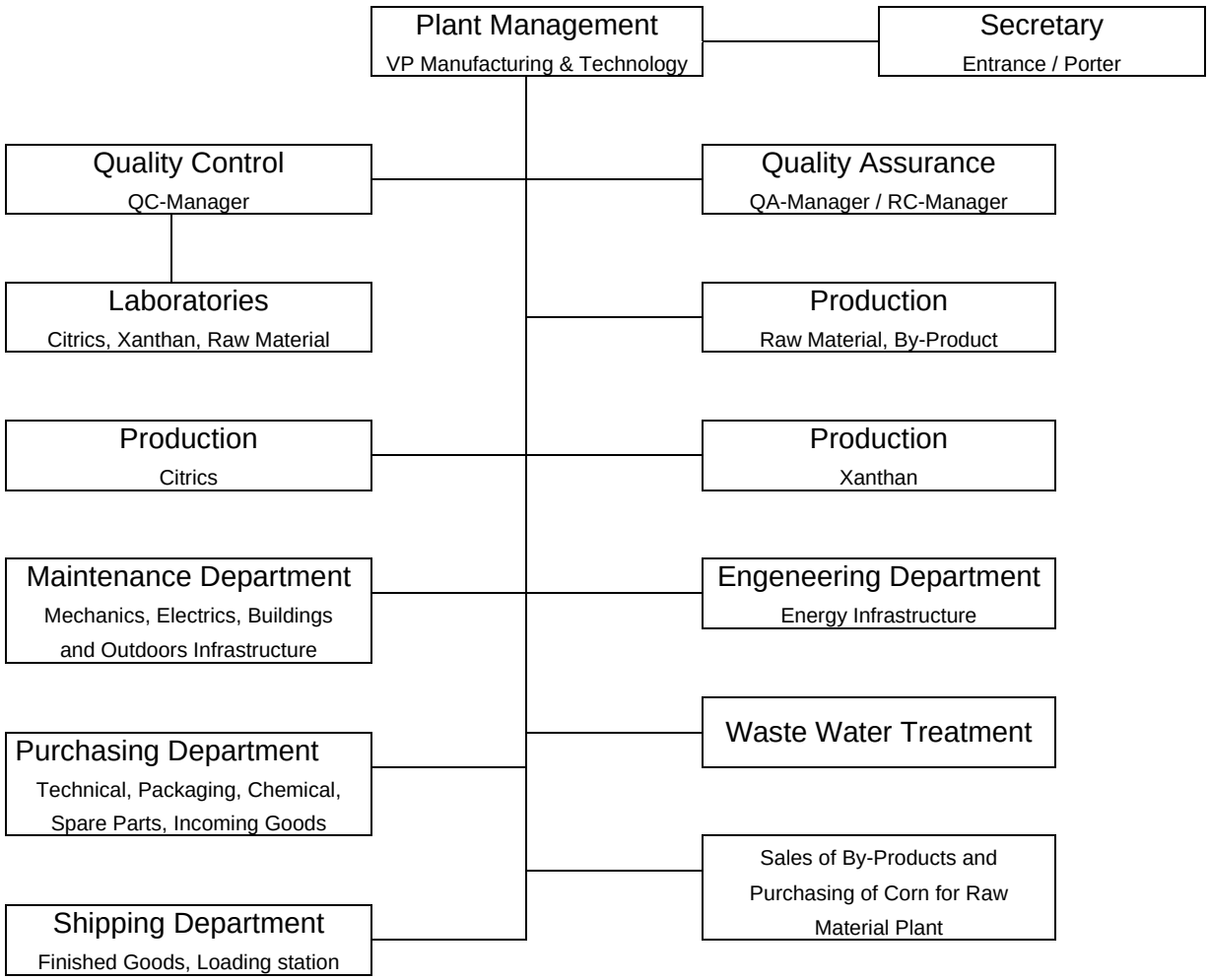
Jungbunzlauer

Organization Chart
Jungbunzlauer Austria AG

The following products are manufactured by Jungbunzlauer Austria AG:

- **Citric Acid**
- **LIQUINAT® (Citric Acid Solution)**
- **Trimagnesium Citrate**
- **Trisodium Citrate**
- **Xanthan Gum**
- **Zinc Citrate**

For your understanding of the scope of responsibilities within our Austrian factory, please find below our organization chart without names that has been adopted from the original organization chart which is part of our ISO manual:



Jungbunzlauer
Technical Service

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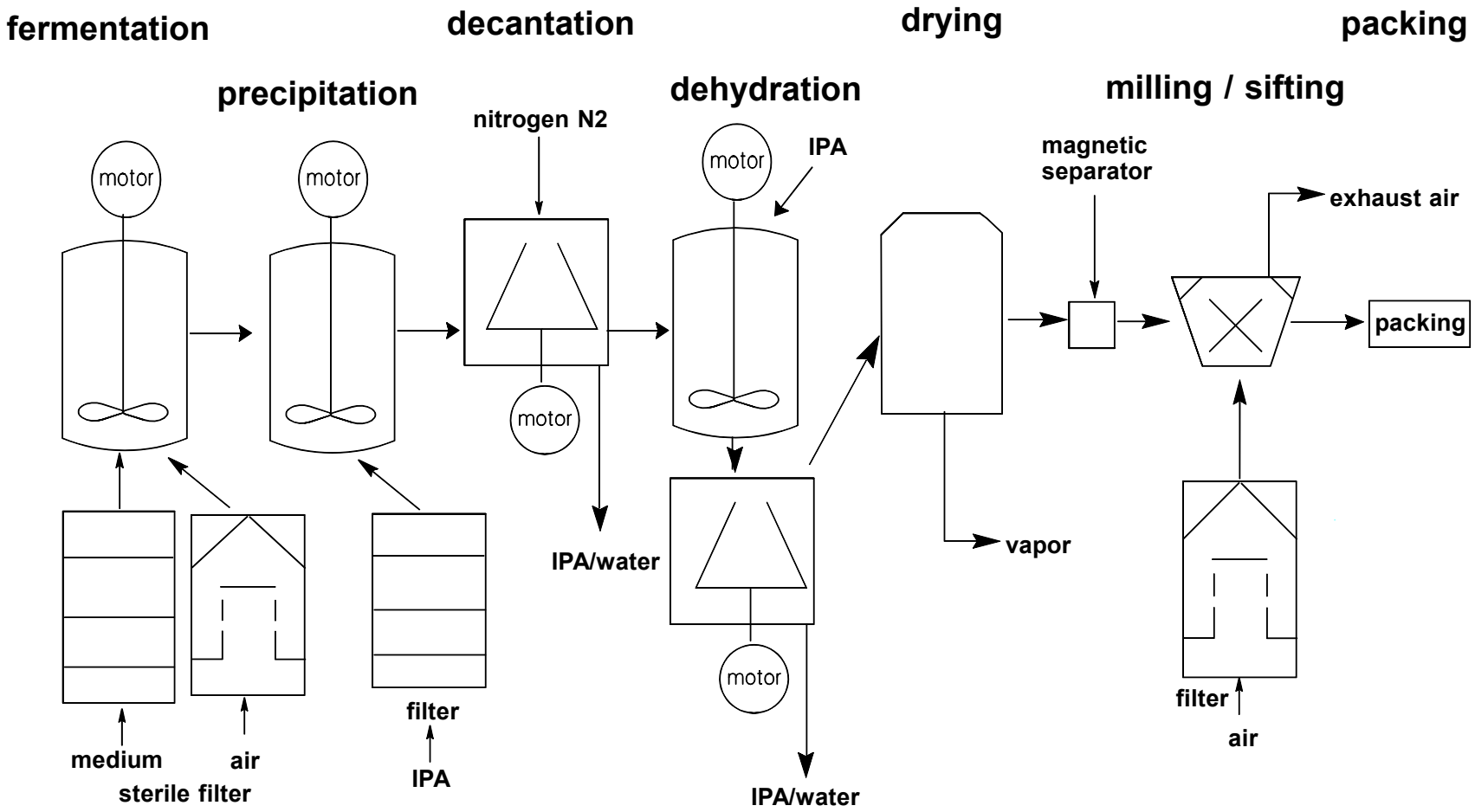
PRODUCTION OF XANTHAN GUM



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Jungbunzlauer

Certificate of Origin

Basel, July 22nd, 2008

Dear customers

The following Jungbunzlauer product

- **Xanthan Gum**

is manufactured by fermentation of carbohydrates containing raw materials like glucose syrup from maize or wheat as well as sugar from sugar beet or sugar cane.

The above mentioned product is manufactured in the following Jungbunzlauer plant:

- **Jungbunzlauer Austria AG**
  Werk Pernhofen
  2064 Wulzeshofen
  AUSTRIA

With best regards

Michael Streit
Technical Service Assistant

Jungbunzlauer

BSE / TSE

The following Jungbunzlauer products

Citric Acid	Citric Acid LIQUINAT® Citric Acid Solution Trisodium Citrate Dihydrate
Gluconates	Glucono-delta-Lactone Sodium Gluconate
Specialities	Citro DC CITROCOAT® and other coated products CITROFOL® ESSICCUM® K Sodium Diacetate sub4salt®
Special Salts	Calcium Lactate Gluconate CITROMA® Monosodium Citrate Potassium Gluconate Tricalcium Citrate Trimagnesium Citrate Tripotassium Citrate Trisodium Citrate Anhydrous Zinc Citrate
Sweeteners	Erythritol
Xanthan Gum	Xanthan Gum

are manufactured by fermentation or synthesis. Above mentioned products do not contain animal derivatives and have never been exposed to animal derivatives.

Due to the fact that Jungbunzlauer does not use animal derived substances in the manufacturing process of above mentioned products existing EC regulations and directives concerning BSE / TSE do not apply.

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Contaminants

The following Jungbunzlauer products

Calcium Lactate Gluconate
Citric Acid
Citro DC
CITROFOL®
Erythritol
ESSICCUM®
Glucono-delta-Lactone
LIQUINAT® Citric Acid Solution
CITROMA®
Monosodium Citrate
Potassium Gluconate
Sodium Diacetate
Sodium Gluconate
sub4salt®
Tricalcium Citrate
Trimagnesium Citrate
Tripotassium Citrate
Trisodium Citrate
Xanthan Gum
Zinc Citrate

are manufactured by fermentation or synthesis. The products undergo several purification steps and are finally obtained in their highly pure form.

Based on the production process as well as on the type of raw materials used, we can exclude to the best of our knowledge that the above mentioned products contain the following contaminants:

3-MCPD (3-monochloropropane-1,2-diol)
Acetaldehyde
Acrylamide
Adsorbable organic halides
Aflatoxins
Antibiotics
Asbestos
Azorubine
Besilates
Bisphenol A
Calcium silicate
Castor oil
Chlorofluorocarbon
CMR substances (carcinogenic, mutagenic or reprotoxic)
Colophonium
Cyanuric acid
Dehydroacetic acid
Deoxynivalenol
Dioxins
Dyes
Ethylene oxide
Ethylhexyl acid
Ethyl-p-hydroxybenzonate
Formaldehyde
Furan
Glycol ether
Herbicides or pesticides
Histamine
(Di)Isetionates
Isoprene (2-Methyl-buta-1,3-diene)
Kaolinite
Latex
Melamine
Mesilates
Mycotoxins
Nickel
Nitrate
Nitrite
Nitrofen
Nitrofuran
Nonylphenol ethoxylates
Perfluorooctane sulfonates
Perfluorooctanoic acid
Phthalates
Phytates
Phytoestrogens
Polycyclic aromatic hydrocarbons
Polybrominated biphenyls
Polybrominated diphenyl ethers
Polychlorinated biphenyls
Propionaldehyde
Radionuclides
Semicarbacide
Silicones
Sodium aluminium silicate
Steroids
Sudan red
Tosilates
Triclosan
Veterinary drugs or hormones

Jungbunzlauer
Technical Service

Residual Solvents

Jungbunzlauer

Xanthan Gum

USP / Ph. Eur. / FCC

Product name	Xanthan Gum
EC No.	234-394-2
CAS No.	11138-66-2
E-No.	E 415

The content of this questionnaire is based on the requirements as defined in:
CPMP/ICH/283/95 Impurities: Guideline for Residual Solvents
CVMP/VICH/502/99 Guideline on Impurities: Residual Solvents
USP General Chapter <467> Residual Solvent requirement

According the above mentioned guidelines, residual solvents were evaluated for their possible risk to human health and placed into one of three classes as follows:

Class 1 solvents: Solvents to be avoided
Known human carcinogens, strongly suspected human carcinogens, and environmental hazards.

Class 2 solvents: Solvents to be limited
Non-genotoxic animal carcinogens or possible causative agents of other irreversible toxicity such as neurotoxicity or teratogenicity. Solvents suspected of other significant but reversible toxicities.

Class 3 solvents: Solvents with low toxic potential
Solvents with low toxic potential to man; no health-based exposure limit is needed.
Class 3 solvents have "permitted daily exposures" (PDE's) of 50 mg or more per day.

Class 1 Solvents

Are class 1 solvents:

- **used in the manufacture or purification of the Product**
- **likely to be produced during manufacture of the Product**
- **impurities of the starting materials used to manufacture the Product**

Yes [ ] **No [X]**

Benzene		Carbon tetrachloride	
1,2-Dichloroethane		1,1-Dichloroethene	
1,1,1-Trichloroethane			

Class 2 Solvents

Are class 2 solvents:

- **used in the manufacture or purification of the Product**
- **likely to be produced during manufacture of the Product**
- **impurities of the starting materials used to manufacture the Product**

Yes [ ] No [x]

Acetonitrile		Chlorobenzene	
Chloroform		Cyclohexane	
1,2-Dichloroethene		Dichloromethane (Methylen chloride)	
1,2-Dimethoxyethane		N,N-Dimethylacetamide	
N,N-Dimethylformamide		1,4-Dioxane	
2-Ethoxyethanol		Ethylene glycol	
Formamide		Hexane	
Methanol		2-Methoxyethanol	
Methylbutylketone		Methylcyclohexane	
N-Methylpyrrolidone		Nitromethane	
Pyridine		Sulfolane	
Tetralin		Toluene	
1,1,2-Trichloroethane		Xylene	
Tetrahydrofuran (USP)			

Class 3 Solvents

Are class 3 solvents:

- **used in the manufacture or purification of the Product**
- **likely to be produced during manufacture of the Product**
- **impurities of the starting materials used to manufacture the Product**

Yes [x] No [ ]

Acetic acid		Acetone	
Anisole		1-Butanol	
2-Butanol		Butyl acetate	
tert-Butylmethyl ether		Cumene	
Dimethylsulfoxide		Ethanol	
Ethyl acetate		Ethyl ether	
Ethyl formate		Formic acid	

Heptane		Isobutyl acetate	
Isopropyl acetate		Methyl acetate	
3-Methyl-1-butanol		Methylethyl ketone	
Methylisobutyl ketone		2-Methyl-1-propanol	
Pentane		1-Pentanol	
1-Propanol		2-Propanol	**x**
Propyl acetate		Tetrahydrofuran (ICH)	

Other Solvents

Are the following solvents [Solvents for which no adequate toxicological data was found]:

- **used in the manufacture or purification of the Product**
- **likely to be produced during manufacture of the Product**
- **impurities of the starting materials used to manufacture the Product**

Yes [ ] No [X]

1,1-Diethoxypropane		1,1-Dimethoxymethane	
2,2-Dimethoxypropane		Isooctane	
Isopropyl ether		Methylisopropyl ketone	
Methyltetrahydrofuran		Petroleum ether	
Trichloroacetic acid		Trifluoroacetic acid	

Comments

The above mentioned product is manufactured by fermentation of carbohydrates. During its production process the product does not get into contact with solvents from class 1 and 2 listed in appendix 1 of chapter 5.4 of the Ph. Eur. Supplement 2000.

Above mentioned product does only get into contact with isopropanol which is a class 3 solvent according to appendix 1 of chapter 5.4 of the Ph. Eur. Supplement 2000 or the USP General Chapter <467>. The maximum concentration of isopropanol is 0.05% or 500 ppm as given in the Jungbunzlauer specification.

Therefore, Jungbunzlauer xanthan gum food and pharmaceutical grade fully meets the requirements of the ICH guideline (CRMP/ICH/283/95).

Jungbunzlauer
Technical Service