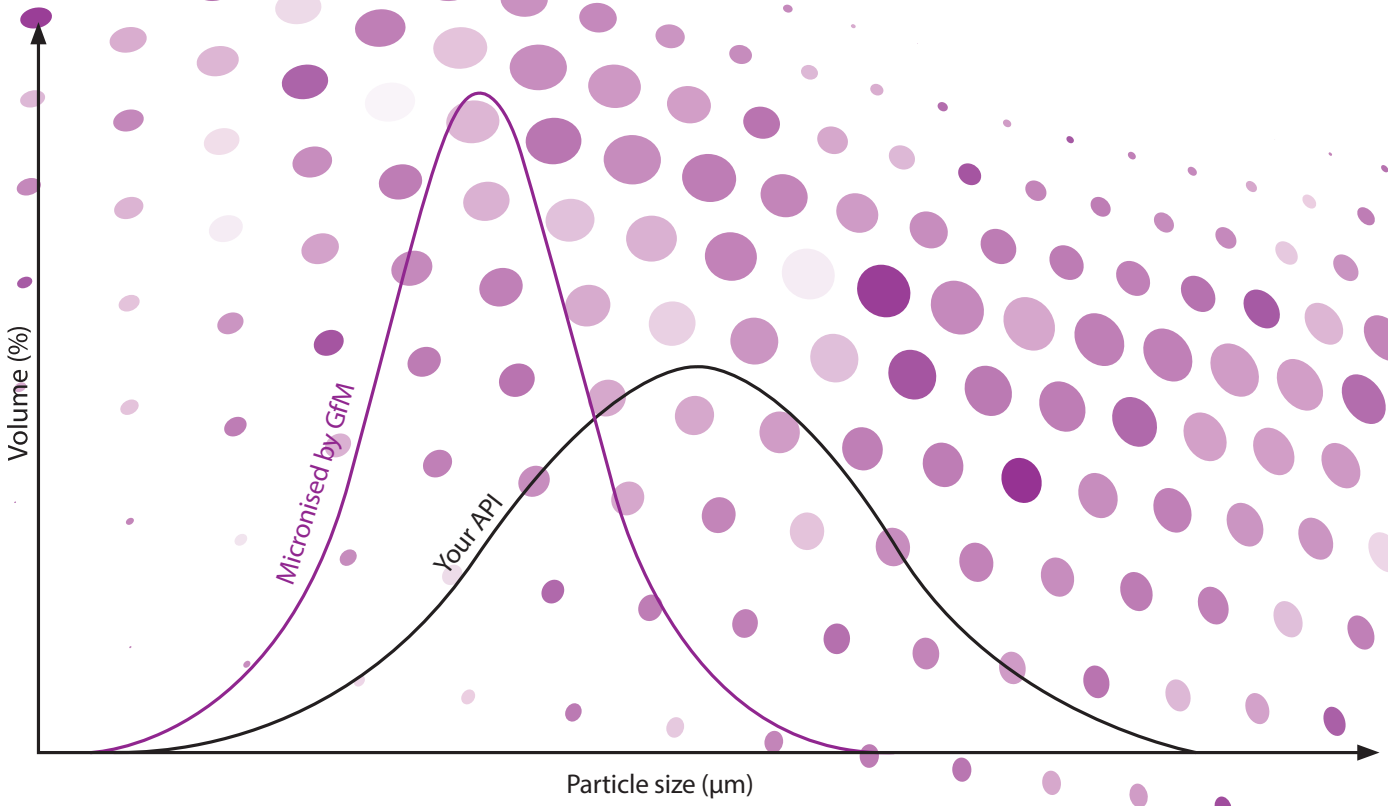
GfM

YOUR MICRONISATION AND MILLING PARTNER IN THE PHARMACEUTICAL INDUSTRY

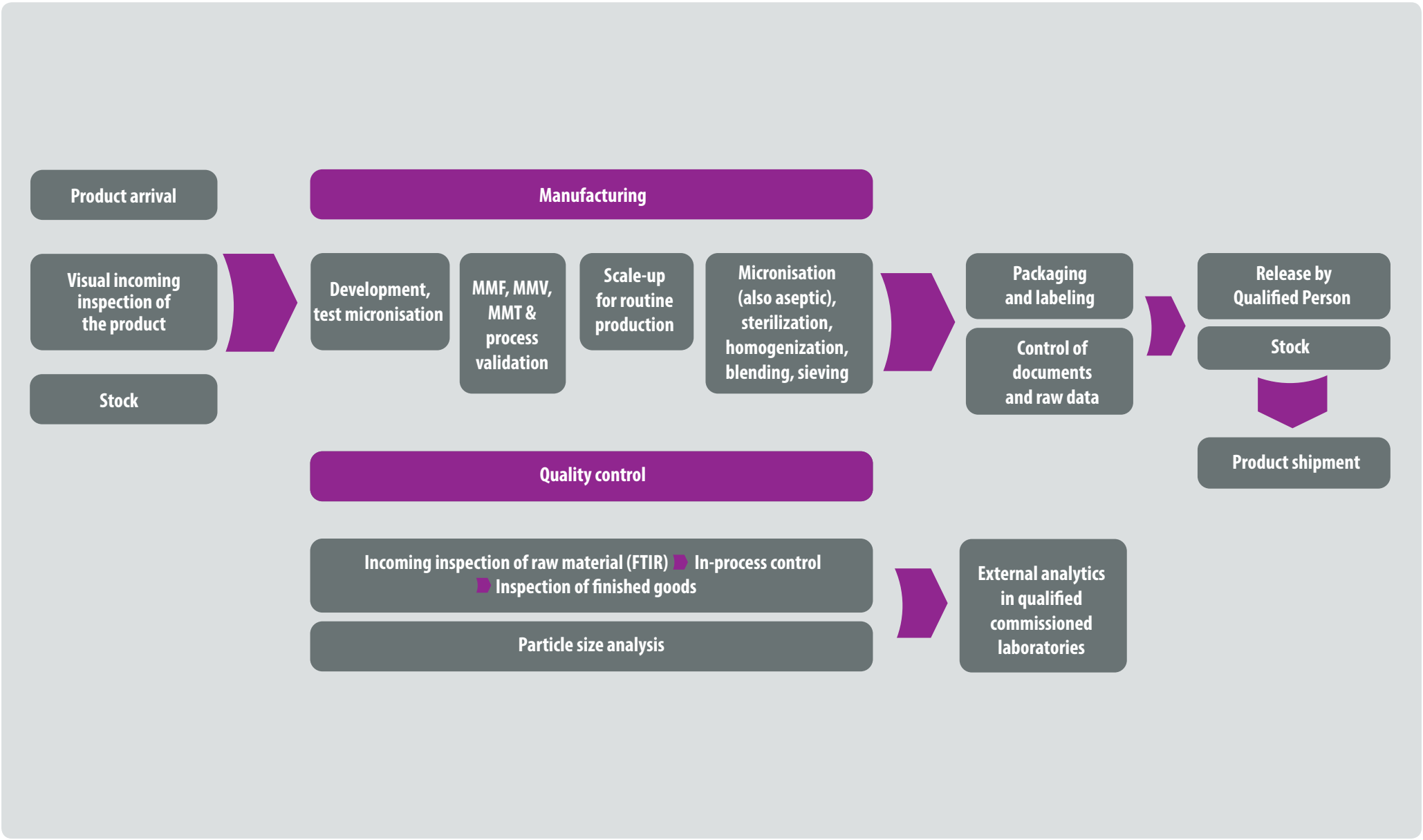


We take quality personally

We are a family business in the second generation.

- *Founding year: 1985*
- *Owner-managed company*
- *More than 30 years of experience*
- *Micronisation and refining of your pharmaceutical products*
- *Processing of quantities from a few grams to tones*
- *Highest quality and safety standards*
- *Certified quality: cGMP, FDA, PMDA, manufacturing authorization*
- *Trained employees*
- *Global customers*

Order processing at GfM



Our performance – our service

- *Development*
- *Micronisation*
- *Micronisation under aseptic conditions*
- *Milling*
- *Cryogenic Mill*
- *Homogenization / Blending*
- *Sterilization*
- *Fractionated sieving*
- *Process validation*

- *Determination of particle size distribution via laser diffraction*
  - *Mastersizer (wet and dry dispersion)*
  - *Microscopic particle size distribution*
  - *Sieve analyses (air jet sieve)*
- *Identity verification (FTIR)*
- *Development, validation and transfer of measuring methods*
- *Cleaning validation and cleaning controls (HPLC)*
- *Chemical and microbiological purity determination of raw materials and finished goods according to Ph. Eur.*

We see the most unusual requests as a personal challenge.

Micronisation

Micronisation:

Micronisation is the process of reducing the average diameter of a solid material's particles. Traditional techniques for micronisation focus on mechanical means, such as milling and grinding. Modern techniques make use of the properties of supercritical fluids and manipulate the principles of solubility.
The term micronisation usually refers to the reduction of average particle diameters to the micrometer range, but can also describe further reduction to the nanometer scale. Common applications include the production of active chemical ingredients, foodstuff ingredients, and pharmaceuticals.
These chemicals need to be micronised to increase efficacy.

Pharmaceuticals, chemical ingredients and foodstuff ingredients are the main industries in which micronisation is utilized. Particles with reduced diameters have higher dissolution rates, which increases efficacy. Progesterone, for example can be micronised by making very tiny crystals of the progesterone in order to improve bioavailability. It is available for use as infertility treatment, treat progesterone deficiency treatment, including dysfunctional uterine bleeding in premenopausal women.

Micronisation under cGMP conditions:

GfM is committed, as one of the largest contract manufacturing for micronisation, a broad range of product groups.
We provide a risk based product group concept in accordance to cGMP guidelines.
For this service we use our air jet mills (e.g., fluidized bed opposed jet mill AFG and spiral jet mills) and mechanical mills (e.g., fine impact mill and pin mill) to perform micronisation with more than 30 mills in total. From the first trial during development, with just a few grams up to routine micronisation with a few kg up to tones.

Micronisation under Aseptic conditions:

The aseptic micronisation is an important process step in the manufacture of sterile pharmaceuticals which cannot be sterilized in their final container. The micronisation will be done under aseptic conditions and is the highest quality in this business. Common technology for micronisation are supplemented with demand for aseptic micronisation process.
We perform monitoring during the whole production process, including the sampling and packaging. Aseptic micronisation gives prominence to GfM.

Picoline

This new series features two individual machines, specifically designed for the production of very small batches between 1 gram and more.
Picoline series comprises process engineering with spiral jet mill and fluid bed opposed mill. This new mill gives us the opportunity to have the best start during development and an extremely high reduction to the loss of small quantities.
It is even a good opportunity to give an idea which technology can be work for requirements of your product.

Spiral Jet Mill - AS33

Fluidised Bed Opposed Jet Mill AFG 40

Fluidised Bed Opposed Jet Mill AFG

AFG 100, 200 & ZPS 100

In jet milling, comminution is exclusively the result of interparticle collision in the gas jets. And because there are no machine components in the grinding zone, neither machine wear nor product contamination occurs. This is why jet milling is often used when contamination-free products are required. Jet milling is suitable for any material hardness value: from Mohs hardness 1(talc) to Mohs hardness 10 (diamonds).
Fluidised bed opposed jet mill for manufacturing powders with a narrow particle size distribution and sharp top size limitation in the range < 5 µm to 200 µm.

- Grinding nozzles arranged around the periphery of the grinding chamber.
- Classifying wheel(s) arranged horizontally in the classifier top section.
- By room temperature and contamination-free grinding.
- Cleaning is been made easy by the hinge-back and removable classifier top section and the inspection deck in the mill housing.

Spiral Jet Mill

A jet mill grinds materials by using a high speed jet of compressed air or nitrogen to break up particles by each other. Jet milling is used for decrease particles below a certain size and, on the other hand to narrow particle size distribution in order to standardize your product.
Leaving particles of the mill can be separated from the gas stream by cyclonic separation. A jet mill consists of a short cylinder, meaning the cylinder's height is less than its diameter. Compressed gas is forced into the mill through nozzles tangent to the cylinder wall, creating a vortex. The gas leaves the mill through a tube along the axis of the cylinder. Solid particles in the mill are subjected to two competing forces:

1. Centrifugal force, created by the particles traveling in circles.

2. Centripetal force created by the drag from the gas as it flows from the nozzles along the wall to the outlet in the center of the mill. In this case the drag on small particles is less than on large ones.
We can offer the micronisation from 1 gram with the AS33 up to higher quantities with the AS50, AS100, AS200, AS315 and AS500.

Cryogenic Impac Mill

The Cryogenic Mill 100 UPZ is a Fine Impac Mill where the material feed through liquid nitrogen to cool down up to -190°C.
To this reason is it possible to mill products, which are very elastic. You can even mill products who are affected by heat. This mill opens new possibilities for our customer and allows to walk on new paths.

Manufacturing

Product sterilization

We employ dry heat sterilization to produce active ingredients and excipients free of germs capable for further aseptic processing like micronisation, sampling and packaging.

Blending and homogenization of products

We can produce homogeneous blends according to your specifications both before and after the micronisation processes. Modern container blenders mean that even larger quantities are possible at any time and small quantities with an adequate free tumble blender.

Product-related sieving processes

We use specific sieving processes to fractionate your product into the grain sizes you specify. Modern technology allows sieving of even very fine material. With modern ultrasonic Sieves we are able to classify your product to very low particle size. In addition, we can offer protective screening of your products before further processing in our plant.

Process validation

cGMP-conform micronisation means having a valid process for the measurement of particle size and of the micronisation. We are pleased to offer this service by means of the validation of your product.
Our service, in which all documentation for validation is closely coordinated with the customer and completed with a wealth of expertise, results in a standard which really pays off. Whether for method-, process- and cleaning validation, we are the right partner for your product.

Laboratory

Particle size analysis

Laser diffraction with the Mastersizer

The Mastersizer offers you the possibility of dry dispersion as well as wet dispersion in an aqueous medium, oil or organic solvents for particle size analysis. We perform method transfer, development and validation for the Mastersizer as a service for you in our in-house laboratory and can even apply methods you already use in your company for particle size analysis following coordination.

Air jet sieving

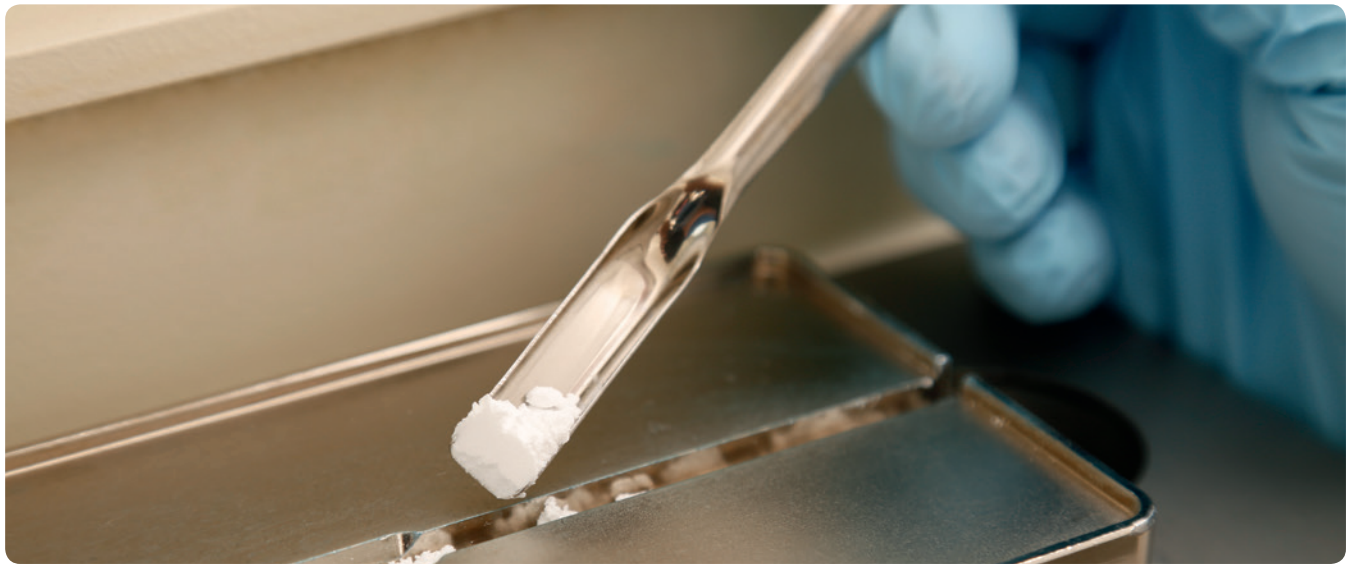
We determine the particle size distribution of your products for all standard sieve sizes with our Hosokawa Alpine air jet sieve. The software we use is FDA-compliant.

Sieve analyses

In addition to air jet sieving, we offer sieve analysis with our vibrating sieves. With this method, we determine the particle size distribution of your product in one step with different mesh sizes.

Microscopic analyses

For determining particle size distribution we offer the possibility of microscopic image analysis, with digital software guaranteeing a measurement in accordance with cGMP. Microscopic analysis is also been much used for the characterization of crystals.



Monitoring

Microbiological controls

Microbiological monitoring of individual production areas includes surface contact tests (squeeze test), measurement of airborne germs as well as control of process air. Our production employees and production facilities are regularly checked by contact tests. In addition, measurements are carried out to determine the air particle count in the chambers and the process air.

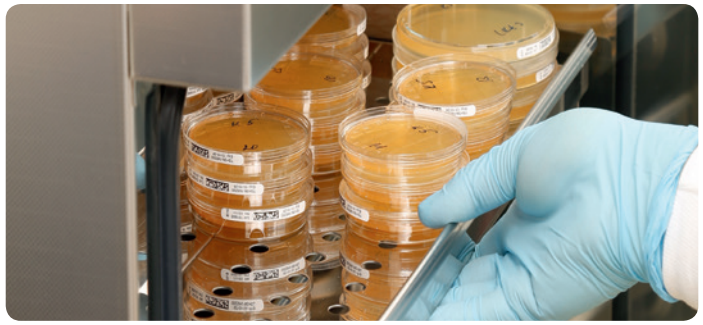
Trend analysis are employed to ensure long-term compliance with the standard.

Monitoring of environment parameters in sterile area are generally carried out alongside production and process validations.

Cleaning controls

Our internal, independent laboratory performs cleaning inspections employing HPLC analysis or TOC in order to monitor the success of our cleaning procedure.

On request, our experienced specialist staff can also conduct product-related cleaning validation procedures for you.



Certified quality

GMP certificate (current Good Manufacturing Practice)

cGMP describes guidelines for "good manufacturing practice". The focus here is on the quality assurance of the production processes and production environment for the processing of pharmaceuticals and active agents.

Quality management system (QM system)

Activities at GfM are under control of our QM System which is driven by good manufacturing practice (GMP). All in-house divisions concerned with the creation, maintenance and implementation of the QM system are permanently subject to the requirements of the EU GMP guideline.

Qualified Person

Our Qualified Person checks every batch and the release is carried out in accordance to EU GMP guideline.

FDA authorization (Food and Drug Administration)

To comply with the periodic checks conducted by the Food and Drug Administration of the United States, our company has an additional production qualification for the U.S. market.

Accreditation in Japan

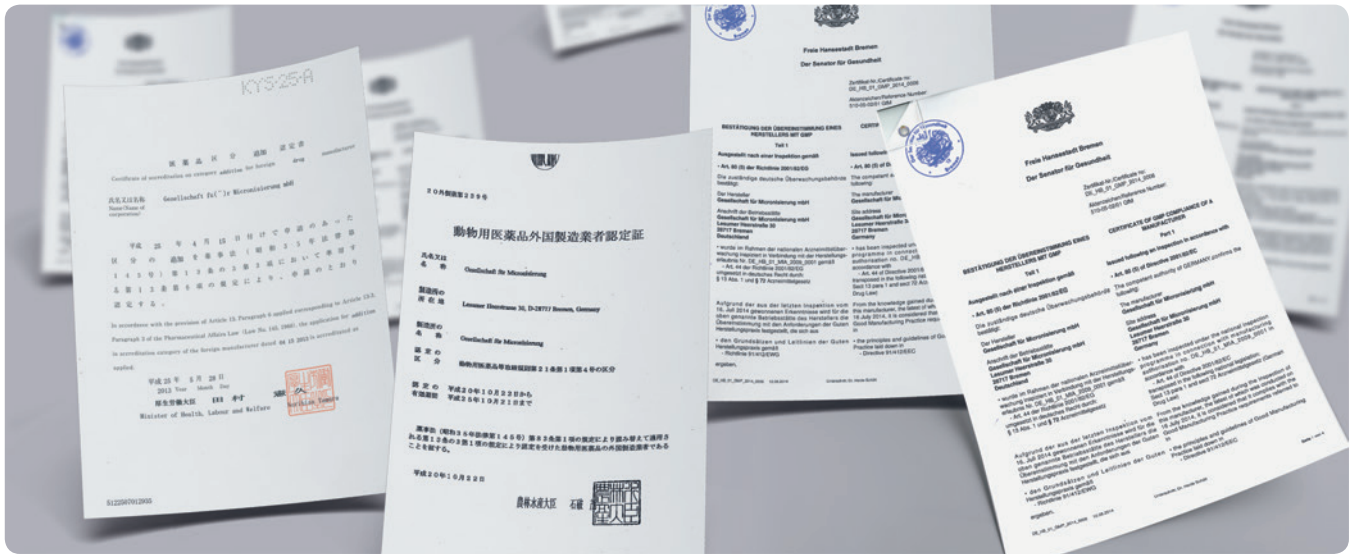
We are accredited in Japan as a certified manufacturer. In cooperation with our Japanese business agent, we will be happy to assist you to obtain accreditation for your products for the Japanese market as well.

Manufacturing authorization

Our company has a manufacturing authorization in compliance with §13 AMG (German Medicinal Products Act).

As such, our cGMP conformity is regularly confirmed by the responsible authorities.

All certificates and information can be found at www.gfm-bremen.de



Safety for products, environment and employees

Hygiene of implementation of the cGMP guidelines

Our success is based on the consistent implementation of cGMP guidelines regularly confirmed by the state authorities of Bremen. The central key factor behind our business success is product quality. The main building blocks for this are the continuous implementation of hygiene plans as well as product group-specific storage and manufacturing (dedicated equipment) of the active ingredients and excipients.

Environmental protection

Environmental protection is an important part of GfM's corporate philosophy. The prevention of environmental contamination and its consequences plays a major role.

Compliance with cGMP guidelines ensures comprehensive protection.

Safety of employees

As our service range includes the processing of potent pharmaceutical products, we guarantee a high degree of safety for our employees. This is possible, among other things, thanks to managing of potential endangering to processes and employees. Regular in-house training complemented with external advanced training ensure that our safety measures are always up-to-date.

Our highly qualified personnel are always available to offer our customers and contacts help and support.

Why not get in touch with us –
we are looking forward to hearing from you.

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