PHARMACEUTICAL TECHNOLOGY

GMP SIZE REDUCTION SYSTEMS

HOSOKAWA MICRON

HOSOKAWA ALPINE

PROCESS TECHNOLOGIES FOR TOMORROW℠

OUR PORTFOLIO

OUR SERVICE RANGE

We develop versatile and efficient processing solutions for the size reduction/micronising of pharmaceutical products. With many years of experience, our team of engineers can offer you tried-and-tested, versatile concepts and standard solutions as well as special solutions tailored to your specific requirements.

Our customers process the following products (examples):

- Pharmaceutical substances of category OEB 1 - OEB 6 with resultant OEL values of between < 50 mg/m^3 and < 200 ng/m^3
- Excipients such as lactose, sugar, cellulose
- DPI (carriers and active substances)
- Parenterals
- Nanopharmaceuticals
- Hot-melt-extruded pharma polymers

FROM MILLIMETRE TO NANOMETRE – FROM MILLIGRAM TO TONNE: INNOVATIVE AND SPECIALISED SOLUTIONS

For us, innovative technologies are state of the art. Our Pharma Division leads the international market for powder processing equipment. We provide the entire range of size reduction technology, from deglomeration in the millimetre range right through to micronisation and nano-scale milling in the µm and nm range. We cater to R&D gram-scale requirements as well as to production batches that weigh several tonnes.

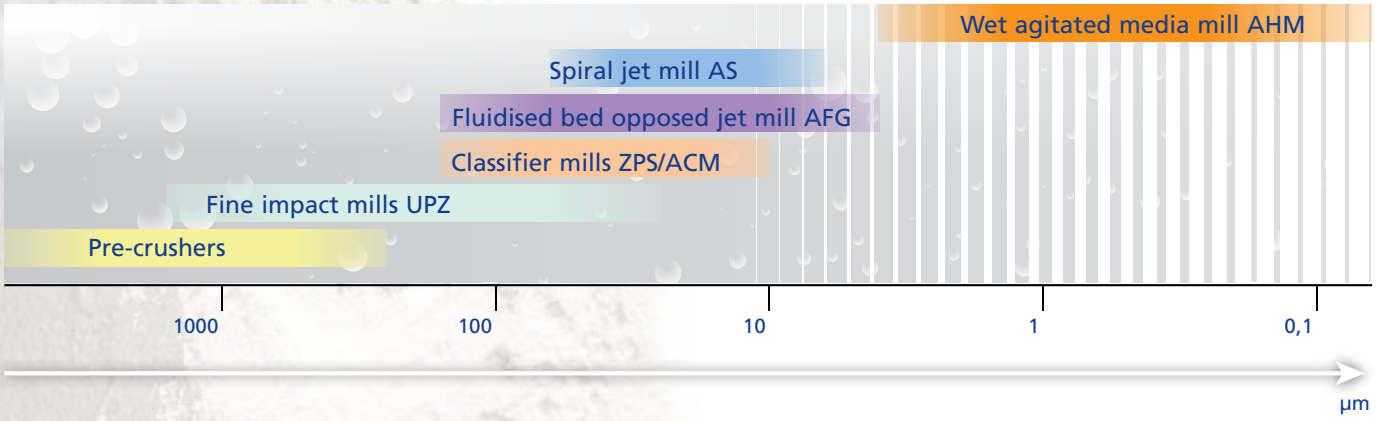
R&D – WHEN EVERY GRAM COUNTS

The course of future production methods is set as early as the R&D stage. Research laboratories need to work with technologies that are also available for later production processes. At this early stage, it is important that research labs have the right equipment at their disposal. We offer very small systems such as the Picoline machines for processing gram-scale batches. They are based on well-established production lines and provide customers with a high level of reliability, ensuring that the production method can easily be applied to the required production scale at a later date.

MULTI-MILL SYSTEMS

Multi-processing systems are a speciality of the Pharma Division. These systems comprise different mill types which share the same ancillary equipment. These systems are not only extremely versatile, but they also reduce capital expenditure and validation requirements to a minimum.

APPLICATION AREAS OF DIFFERENT MILL TYPES



CIP / SIP

Cleaning In Place and Sterilisation In Place are highly exacting processes which place stringent requirements on system design and engineering. Our Pharmaplex® bearing assembly allows sterilisation with saturated steam for high-speed, oil-free bearing concepts used in mills and metering equipment.

CONTAINMENT

Increasingly exacting occupational safety requirements and the use of highly active pharmaceutical substances compel manufacturers to reassess their system components. The integration of grinding technology into isolators proved to be highly challenging and often turned out to be too complex for isolator manufacturers. As the responsibility for the complete system should lie with only one single supplier, Hosokawa Alpine has been developing integrated containment milling systems for fifteen years. The benefits are obvious: our customers are supplied with complete solutions from one source that do not pose any integration problems.

PAT

Process safety and repeatability is ensured by monitoring and controlling all relevant parameters. We also integrate in-line laser diffraction systems made by different manufacturers into our systems. These allow monitoring and inspection of particle sizes.

TEST AND RENTAL EQUIPMENT

Our state-of-the-art test centre equipment is available for customer tests. However, many pharmaceutical chemicals are highly toxic and cannot be sent to us for safety- or customs-related reasons. In these cases, we offer our customers a wide range of rental equipment which allow tests on the customer's site.

PASSION FOR PHARMA MACHINE DESIGN

- Our systems comply with the most exacting international standards:
- Product- and process-contact parts are made of AISI 316L stainless steel
- Surface roughness standard Ra < 0.8 µm (depending on the project Ra < 0.4 µm or Ra < 0.25 µm with/without electropolishing)
- Seal and filter material suitable for use with food and drugs according to FDA 21CFR177.2600
- Particle- and oil-free, clear separation between drive and process thanks to pharmaceutical bearing concept
- Encapsulated, permanently lubricated bearings or use of USDA-H1 lubricant
- Fully CIP/SIP compatible machines thanks to patented Pharmaplex® bearing concept
- Mostly monobloc components with a low number of welding seams and seals
- Design free of dead spots
- Drainage and evacuation points for residual air removal in CIP/SIP-compatible systems
- Control according to GAMP 4/5 and 21 CFR Part 11

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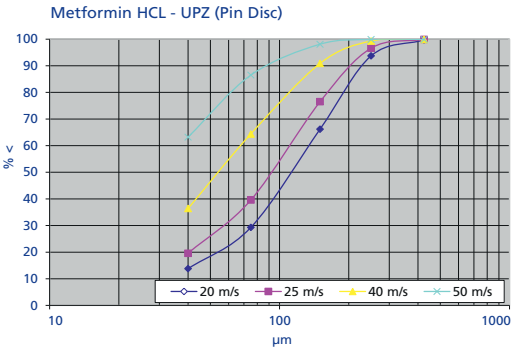
FINE IMPACT MILLS

UPZ – COARSE TO FINE

AREAS OF APPLICATION

Fine impact mills or universal mills are used for fine and ultrafine grinding. Depending on the product, these mills cover a fineness range of between appr. 30 µm and 1,500 µm. As this mill type can be used with different grinding elements, it is very versatile. Thanks to the rotor's ventilation effect, the product is conveyed and cooled at the same time. The end products are low in fines and have good flow properties.

Application example



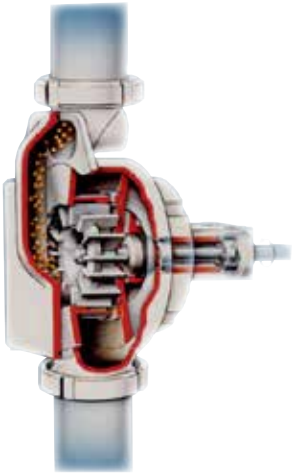
Features:

- Typical area of application: deglomeration/ milling for end-product fineness of between 30 µm and 1,500 µm
- Grinding of soft to medium-hard materials
- Highly versatile thanks to different grinding elements
- Cooling effect thanks to high air flow
- End products are low in fines

315 UPZ fine impact mill
Pressure-shock-proof design

PRINCIPLE OF OPERATION

UPZ mechanical impact mills are designed for dry grinding soft to medium-hard materials. The feed material is charged to the centre of the rotor equipped with grinding elements and is comminuted by impact against the rotor and stator elements. After passing through the grinding zone, the product enters the mill housing and is then discharged from the mill by gravitational force. The rotation generates an air flow from which the end product is extracted and charged to a filter. Different grinding elements can be employed, e.g. a pin disc or a plate beater unit with profiled grinding track or a sieve grate. The fineness is set by adjusting the rotor speed and the feed rate.



Pharma range

UPZ fine impact mill	Scale-up factor	Power (kW)	Max. air flow rate* (m³/h)	Speed** (1/min)
100	ca. 0.06	1	100	22,000
160	0.25	5.5	450	18,000
250	0.5	11	900	11,000
315	1	18.5	1,600	9,000
500	2	37	3,200	6,000

* Max. values, depending on grinding tools
** Max. speed, depending on grinding tools

For R&D application
picoplex HOSOKAWA ALPINE

PRACTICAL EXAMPLES

Product	End-product fineness	Through-put kg/h	Machine size
Acetylsalicylic acid	97% < 250	1.250	315 UPZ
Acetylsalicylic acid	99% < 250	500	315 UPZ
Ascorbic acid	97% < 27	15	100 UPZ
Clarithromycin	97% < 20	2	100 UPZ
Maltodextrin	99% < 100	55	100 UPZ
Sodium chloride	99,7% < 500	540	160 UPZ
Nifedipine	97% < 32.5	13	100 UPZ
Paracetamol	90% < 90	320	250 UPZ

Powder fineness in % < µm – measuring points of particle size distribution
All values are non-binding reference values only



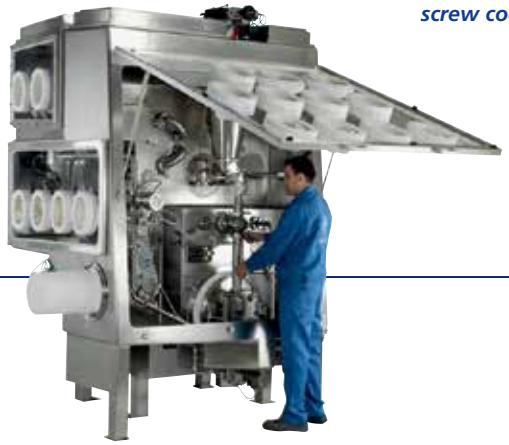

Versatility:

- Pin discs – for very high end-product fineness or for homogenisation
- Plate beater unit – cooling effect thanks to higher air flow
- Plate beater unit with sieve ring – particle size limitation with low fines content
- Plate beater unit with grinding track – comminution of hard material
- Combination of grinding track and sieve for better particle size control
- Grinding tracks available in different geometries for optimsation

THE VERSATILE UPZ

160 UPZ
sterile milling system incl. feeding screw PDD 35 in CIP/SIP-able design

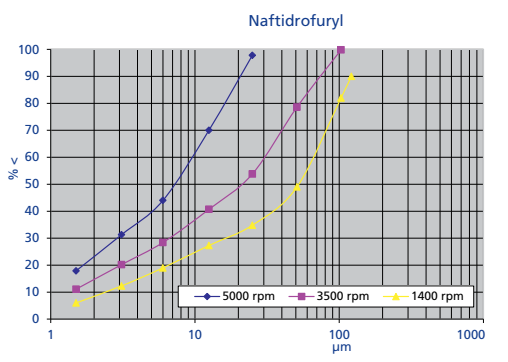
100 UPZ
isolator solution with integrated in-line particle analysis and PDD 25 screw feeder



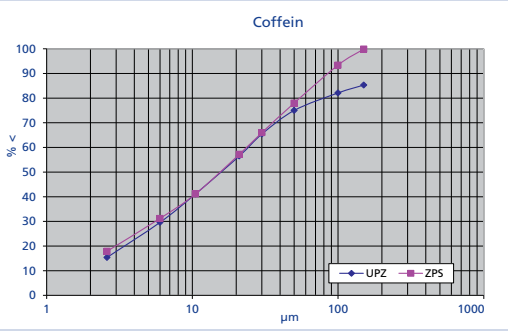
100 UPZ
cryogenic milling system with Alpine KF 40 screw cooler

CLASSIFIER MILLS

Application example



Classifier mill vs. fine impact mill



Features:

- Typical area of application in the pharmaceuticals industry is for particle sizes of between 10 µm and 150 µm
- Guaranteed top cut control thanks to integrated air classifier
- Steep particle size distribution
- Optimum setting of grinding parameters
- Cool grinding thanks to high air/gas flow

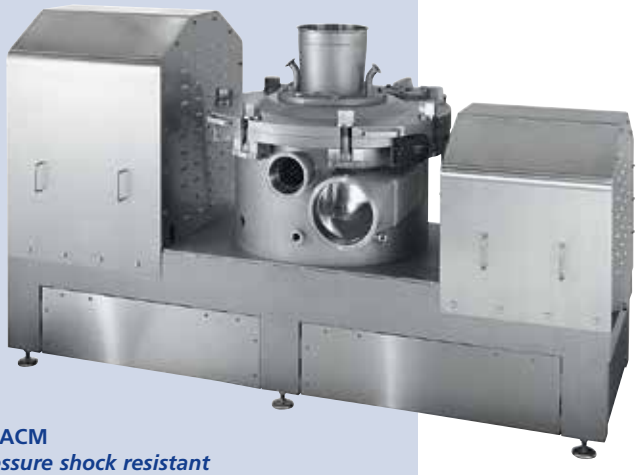
MIKRO ACM + ZIRKOPLEX ZPS – SHARP TOP CUT

AREAS OF APPLICATION

Classifier mills are used for the ultrafine grinding of soft material with an end-product fineness of appr. < 10 - 150 µm. They offer a range of advantages over fine impact mills. The integrated air classifier guarantees end products that are free of oversized particles with a steep particle size distribution and sharp top cut control. Grinding and separation parameters can be set independently for optimum results, which ensures reliable product quality for the different particle sizes or product properties required. The high air/gas flow cools the product.

DISTINCTION BETWEEN ACM + ZPS

During its corporate history, Hosokawa Alpine has developed two different types of classifier mills, and both have become established in their own right and have found their optimum area of application. The Mikro ACM with its straightforward design is used all over the world in practically all industries, also in the pharmaceuticals segment.



40 ACM
Pressure shock resistant
Execution Easy Clan

200 ZPS
Maschine for Integration
in Cleanroom wall

70 ZPS isolator solution with PDD 25 metering screw

Like the ACM, the pharma execution of the ACM is a twin-rotor classifier mill with a compact footprint that can be opened from the top for easy access, inspection and cleaning. Thanks to its lean design, the ACM is inexpensive and cost-efficient in maintenance. The increased air flow allows easy processing of heat-sensitive materials. In the pharmaceuticals industry, the ACM is typically used for the production of excipients and carrier materials, often in mono-product systems with continuous production or for large batch sizes.

The ZPS with its horizontal classifying wheel offers sharp top cut control even when processing challenging materials. The larger product chamber often allows the comminution of sticky and adhesive product. The classifier head of the ZPS is identical to that of Hosokawa Alpine's classifiers of the ATP range and is also used in simple air classifiers or in combination with AFG fluidised bed opposed jet mills. This approach allows the use of the ZPS in so-called multi-process systems. In this set-up, the ATP classifier head is the central component and the grinding units for ZPS, AFG and ATP can be interchanged very easily. The bearings for ZPS classifiers and mills are tried-and-tested air-purged systems which are available in a CIP/SIP-compatible design. Used by the pharmaceuticals industry, the machine sizes from 50 ZPS through to 200 ZPS are popular for very small API batches – also for high active pharmaceuticals in contained installations.

PRACTICAL EXAMPLES

Product	End-product fineness		Throughput kg/h	Machine size
Acemetacin	99% < 32;	50% < 8	190	200 ZPS
Amoxicillin	99% < 18;	50% < 6	9	50 ZPS
Bisphenol A	99% < 63		370	40 ACM
Flutrimazole	97% < 38;	50% < 4.4	5	50 ZPS
Lactose	97% < 25;	50% < 8	20 - 25	50 ZPS
Lactose	99% < 30		137	10 ACM
Naftidrofuryl	90% < 19,6;	50% < 7.4	45	100 ZPS
Sodium ascorbate	99% < 130;	50% < 19	140	100 ZPS
Nifedipine	97% < 45;	50% < 17.9	125	200 ZPS
Piroxicam	99% < 61		30	50 ZPS
Piroxicam	99,9% < 15		3,2	50 ZPS
Sorbitol	99% < 300		230	10 ACM
Theophylline	99% < 87		170	200 ZPS
Tartaric acid	95% < 100		100	10 ACM

Powder fineness in % < µm – measuring points of particle size distribution
All values are non-binding reference values on

For R&D application

picozirk HOSOKAWA ALPINE

Pharma range ZPS

ZPS classifier mill	ø grinding disc (mm) Power (kW)	ø classifier (mm) Power (kW)	Max. air flow rate [m³/h]	Scale-up factor
50	100/1.1	50/1.1	80	0,06
70	150/2,.	100/1.5	150	0.15
100	200/3	100/1.5	300	0.33
140	280/7.5	140/2.2	600	0.5
200	400/11	200/4	1.200	1

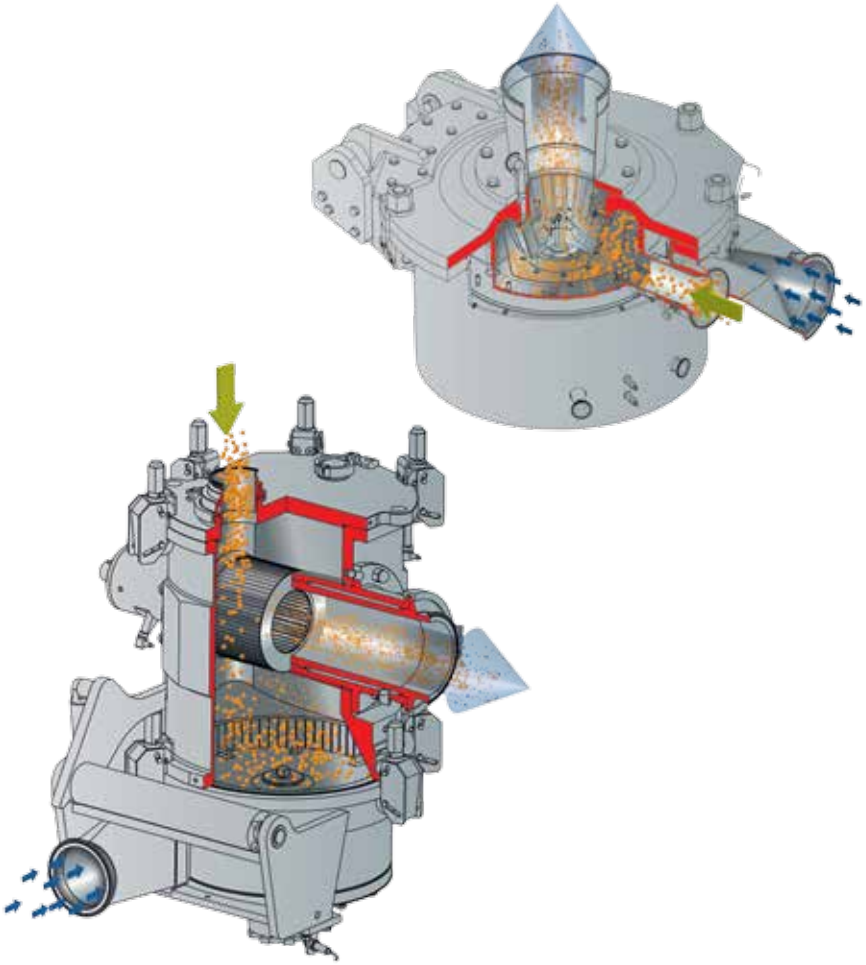
Pharma range ACM

ACM classifier mill	Power mill (kW)	Power classifier (kW)	Max. air flow rate ([m³/h])	Scale-up factor
2	3	0.55	330	0.2
5	5.5	1.1	510	0.5
10	7.5	2.2	900	1
15	11	3	1,350	1.35
20	15	4	1,800	1,.8
25	18.5	4	2,250	2.25
30	22	5.5	2,700	2.7
40	30	7.5	3,600	3.6

MIKRO ACM + ZIRKOPLEX ZPS – SHARP CLASSIFIER CUT POINT

PRINCIPLE OF OPERATION

The ZPS and the ACM are mechanical impact mills with an integrated classifier designed for the dry fine grinding of soft to medium-hard materials with a steep particle size distribution. Comminution is performed by a high-speed rotating disc with grinding elements. The feed material is charged to the grinding chamber and is accelerated by means of the grinding rotor. Comminution is the result of the particles impacting against the grinding elements of the rotor and against the grinding track. The grinding air flows through the grinding gap between the rotor and grinding track from below, passes through a deflector vane ring and then flows through the classifying wheel located in the mill head. The classifying effect of the classifying wheel means that fine particles are able to exit the mill entrained in the air and are collected in a filter. Coarse particles fall back onto the rotor and are comminuted further until the desired fineness is reached. The fineness is set by adjusting the speeds of the grinding rotor and the classifying wheel as well as the air flow rate.



THE VERSATILE ACM

40 ACM *classifier wheel*

200 ZPS *detail*

ACM 2 EC
in special Pharma design

THE VERSATILE ZPS

100 ZPS *detail*

200 ZPS *clean room installation*

70 ZPS Compact system installation
with PDD 25 metering screw and PH-ZS 150 pharma-design rotary airlock feeder

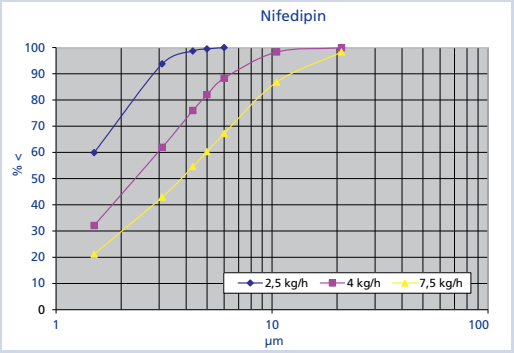
SPIRAL JET MILLS

AS - JUST FINE!

Spiral jet mills are used for the ultrafine comminution of dry pharmaceutical substances. Typically, particle sizes in the range of < 5 – 40 µm are achieved. The benefits of spiral jet mills are in their simple design without moving parts, which makes them easy to inspect and clean. As spiral jet mills do not generate heat during grinding, even heat-sensitive materials can be comminuted without problems. Spiral jet mills are not suitable are often not suitable for sticky products of for applications are prone to sedimentation or for applications that require a controlled, steep particle size distribution. For these cases, we recommend fluidised bed opposed jet mills. Smooth grinding of products with agglomerates in the batch to be processed require pre-crushing.

400 AS spiral jet mill

Practical examples



Features:

- Typical area of application:
  micronising in the range of < 5-40 µm
- Simple design – easy inspection and cleaning
- No moving parts
- No heat generation
- Pre-crushing to < appr. 2 mm is necessary
- Broad particle size distributionng

For R&D application
piconizer
HOSOKAWA ALPINE

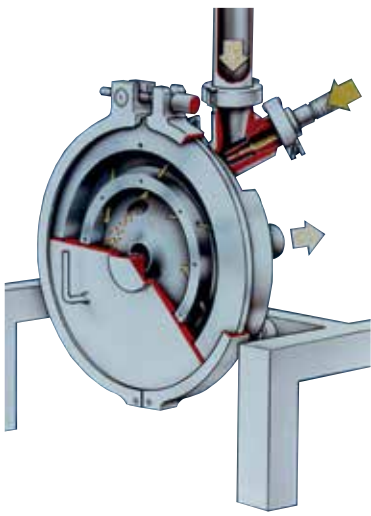
Pharma range

AS spiral jet mill range	Scale-up factor	Number of nozzles	Nominal air flow* (Nm^3/h)
50	ca. 0.075	4	18
100	0.25	4	45
140	0.4	6	110
200	1	6	200
315	2-2.5	18	420
400	3.5	18	1,200
500	4-6.3	45	1,900

* at grinding pressure of 6 bar g

PRINCIPLE OF OPERATION

The AS is a spiral jet mill designed for dry grinding soft to medium-hard materials. A number of air nozzles generate an air vortex that rotates at high speed. The feed material is fed to the grinding chamber via an injector assembly. Comminution is the result of inter-particle collision caused by the different velocity gradients in the air flow. The grinding air is extracted by means of a dip pipe located in the centre of the grinding chamber. Because of the free vortex, a classifying effect is generated, meaning that only fine particles can exit the mill through the dip pipe and be collected in a filter. Coarser particles remain in the grinding chamber until such time as they have reached the desired fineness. The mill settings can be adjusted by varying the grinding air flow rate, .air flow rate and the grinding gas pressure.



100 AS *detail*

315 AS *module with PDD 30 double metering screw*

Smallest AS for R&D processing of mini batches at maximum output (mg + g) with the Piconizer®

Isolator-integrated 100 AS

140 AS *sterile system*

PRACTICAL EXAMPLES

Product	End-product fineness	Throughput kg/h	Machine size
Celecoxib	90 % < 23 µm	33	200 AS
Dextromethorphan	97 % < 5 µm	0.5	50 AS
Lactose	97 % < 8.9 mm	16	200 AS
Lactose	99 % < 5 µm	1	100 AS
Nifedipine	90 % < 2.4 µm	32	500 AS
Nifedipine	97 % < 3.8 µm	2.7	100 AS
Omeprazole	97 % < 4.1 µm	0.8	100 AS
Progesterones	99 % < 14 µm	20	200 AS
Salbutamol	97 % < 5 .2 µm	4	100 AS
Vitamin B2	99 % < 50 µm	25	200 AS
Zaltoprofen	90 % < 9 mm	4	100 AS

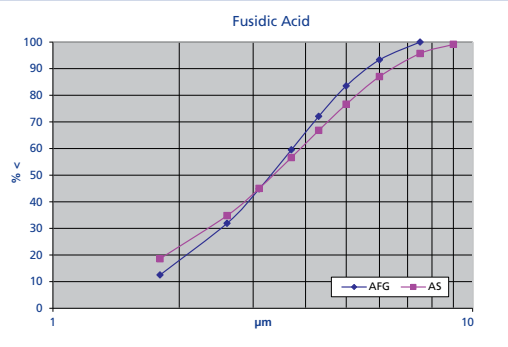
Powder fineness in % < µm – measuring points of particle size distribution
All values are non-binding reference values only

50 AS
Disposable mill concept

Plastic lining parts of the 100 AS

FLUIDISED BED OPPOSED JET MILLS

Practical examples



Features:

- Typical area of application: micronising in the range of < 4 µm – 150 µm
- Accurate fineness setting
- Sharp top cut control
- Steep particle size distribution
- No heat generation
- Suitable for products of sticky or adhesive nature
- No abrasion/wear

For R&D application
picojet
HOSOKAWA ALPINE

Pharma range

Fluidised bed opposed jet mill range (AFG)	Scale-up factor	Motor power classifier (kW)	Nominal flow rate* (m³/h)	Maximum classifier speed (1/min)
100	ca. 0.25	1	75	22,000
140	0.5	2.2	150	18,000
200	1	3	300	12,000
280	2	4	600	9,000
400	4	5.5	1,200	6,000

* at a grinding pressure of 6 bar g

AFG – ULTRAFINE AND SHARP

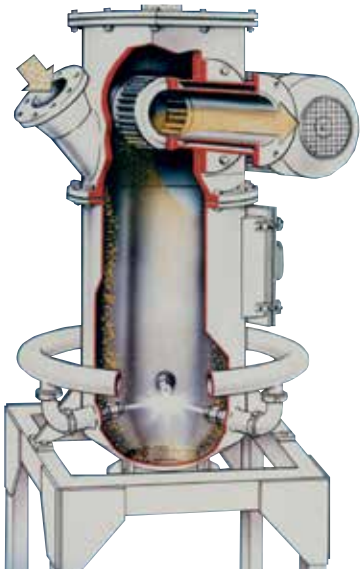
AREA OF APPLICATION

In addition to the tried-and-tested spiral jet mills for the production of ultrafine end products, fluidised bed opposed jet mills with their special housing geometry and the integrated classifier offer a significant technological benefit: the dynamic classifier ensures a high separation accuracy for an absolutely pure top cut which is free of oversized particles. Changes in the fineness setting can be achieved easily and reliably thanks to the frequency-controlled classifier drive. Compared to spiral jet mills, this approach allows a very broad setting range of between about 4 µm and 150 µm (d97). This type of mill is suitable for products that are prone to sedimentation.

PRINCIPLE OF OPERATION

The AFG is comprised of two components – the classifier head and the grinding chamber with integrated nozzles, the number of which depends on the mill size. The material particles entering the jets are accelerated and collide with each other in the focal point where the jets of air intersect. Comminution occurs due to inter-particle collision in the focal point and because of shear flows at the edges of the air jets. As a result, the risk of contamination due to abrasion is virtually non-existent. A high-performance Turboplex classifier discharges the end product from the internal grinding process to a separator system (cyclone or jet filter). The fineness can be set by adjusting the air flow rate, the grinding air pressure and the classifying wheel speed.

280 AFG *fluidised bed opposed jet mill*



100 AFG *Compact Pharma System*

100 AFG *Isolator integration*

200 AFG *Installation for pharma lactose*

140 AFG - *Installation in clean room wall*

PRACTICAL EXAMPLES

Product	End-product fineness	Throughput kg/h	Machine size
Acyclovir	97 % < 28	20	140 AFG
Carbamazepine	86 % < 8	2	100 AFG
Cholestyramin e	99 % < 7,5	0,3	100 AFG
Cilostazol	99 % < 10	4	100 AFG
Cimetidine	99 % < 32	11	100 AFG
Sodium chloride	99 % < 4	10	200 AFG
Lactose	95 % < 6	39	200 AFG
Lactose	98 % < 10	100	400 AFG
Metformin	99 % < 150	480	400 AFG
Nifedipine	98 % < 96	23	100 AFG
Omeprazole	98 % < 7,5	10	200 AFG
Oxytetracycline	99 % < 25	50	140 AFG
Pharma polymer	90 % < 50	2	100 AFG
Salbutamol sulphate	97 % < 9	4	100 AFG
Simvastatin	90 % < 10	3	100 AFG
Ticlopidine	99 % < 30	13	100 AFG
Vitamin B2	99 % < 5	12	200 AFG

Powder fineness in % < µm – measuring points of particle size distribution
All values are non-binding reference values only

MULTI-PROCESSING SYSTEM

MPS – UNBEATABLE VERSATILITY

AREA OF APPLICATION

In the wake of the steady flow of newly developed products with unpredictable grinding properties, mills have to offer maximum versatility. This is the objective of so-called multi-mill systems, which offer the perfect solution to changing requirements. Multi-mill systems are mobile, very versatile concepts where two or more different mill types are integrated into one ancillary installation, allowing a quick change-over between the required units.

Features:

- Different mill types share the same ancillary equipment
- Highly versatile for production of different products
- Fast change-over
- Reduced capital expenditure
- Reduced documentation and validation requirements

Multi-process modular system:

The following modules can be used alternately:

- AFG fluidised bed opposed jet mill
- ATP ultrafine classifier
- ZPS classifier mill
- AS spiral jet mill
- UPZ fine impact mill
- Pre-crusher

200 AFG 100 ZPS

PRINCIPLE OF OPERATION

The size of the installation is based on similar batch volumes, product throughputs, process gas flow rate, etc. The configuration allows different metering systems, fittings, drives, product filters, ventilators, etc. to be used. The benefits are obvious: in addition to a high level of versatility – retrofitting is also possible – capital expenditure, documentation and validation requirements are reduced to a minimum. Multi-mill system combinations can be used both on an R & D (Picoline®) and on a production scale.

Module 100 UPZ

Module 100 AFG

***Disconnect* 100 AFG Module**

Detail technical area

Multimill Isolator Integration
100 AFG / 100 UPZ / 100 AS /
Cone MillExchange of Mill Modules
within technical area of isolator

100 AFG | 50 ZPS Multi mill

MULTI-MILL – COMBINATION OPTIONS

For R&D application
picoline HOSOKAWA ALPINE
The ultimate multi-mill

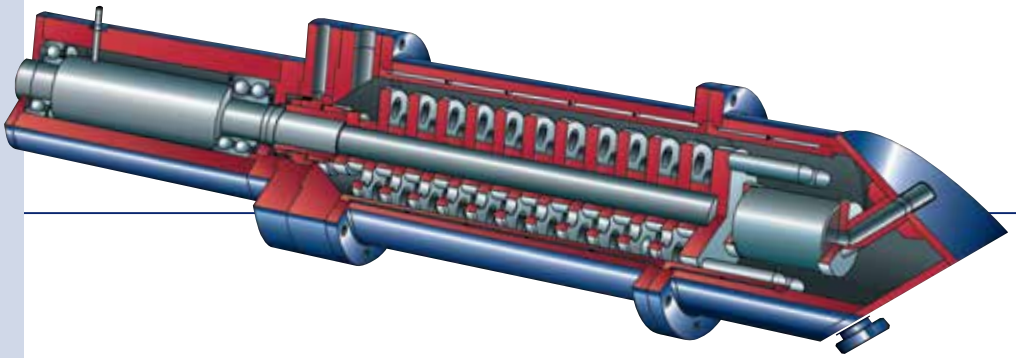
Combination options	AFG	ATP	ZPS	AS	UPZ
1	100	50	50	100	100
2	140	70	70	140	---
3	200	100	100	200	160
4	280	140	140	315	250

PHARMA-DESIGN
AGITATED MEDIA MILLS

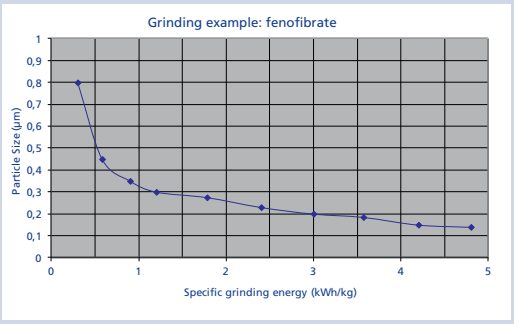
AHM – WET GRINDING AT ITS FINEST

WET GRINDING DOWN TO NANOSCALE SIZE

The amount of poorly soluble pharmaceuticals among NCEs is on the increase. New drug delivery methods are required to help increase the bioavailability of these substances. The ultrafine grinding of particles down to nano-scale size with the help of agitated media mills is one way of improving their bioavailability. This approach opens up a range of additional benefits: accurate dispensing, minimised volumes and fast effectiveness. The minimal volume of nanosuspensions in syringes improves the injectability of the drug and minimises sedimentation problems.

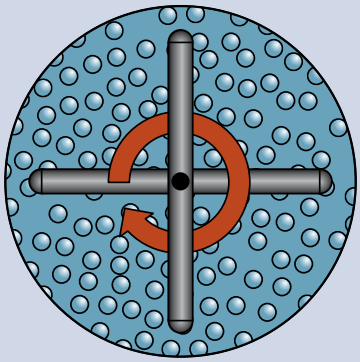


Practical examples



Typical features:

- Grinding of insoluble APIs in the submicron and nanoscale range
- Versatile, exchangeable wear protection elements (ceramics, plastic) possible
- Easy to clean, GMP design
- Double-action mechanical seal
- Sterile equipment option



For R&D application
picoliq HOSOKAWA ALPINE

Pharma range

AHM	Grinding chamber (l)	Motor power (kW)
90	0.25 - 1.1	2.2
132	5	7.5
200	17	22

PRINCIPLE OF OPERATION

The AHM is an agitated media mill designed for the continuous or batch-operated wet ultrafine grinding of particles in solution. The grinding chamber of the mill is usually filled with ceramic grinding beads which are set into motion by a rotating agitator. The feed product is suspended in a fluid and is conveyed through the grinding chamber by means of a pump. Comminution is a result of the friction caused when the feed particles impact against the agitated grinding beads. In continuous operation, the suspension exits the mill after passing through the grinding zone, while a screening element retains the grinding beads in the mill. The fineness level is set by adjusting the rotor speed, the filling ratio of grinding beads in the mill and the suspension flow rate, as well as by selection of the grinding bead size.

Mill equipment in various construction materials

90 AHM

50 AHM
Pico*liq*

200 AHM
In pharma-design

90 AHM
Complete installation

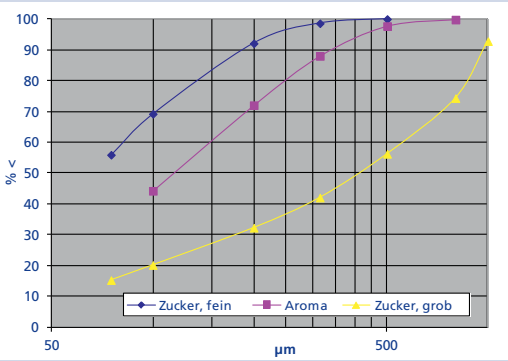
PRACTICAL EXAMPLES

Product	Required fineness	End-product fineness	Specific grinding energy kWh/kg	Machine size
Fenofibrate	d_{97} = 120 µm	d_{90} = 0.504 µm	2.5	200 AHM
Pharma product	d_{97} = 29.9 µm	d_{97} = 0.29 µm	0.82	90 AHM
Cyclosporine	d_{97} = 350 µm	d_{97} = 1.5µm	0.12	50 AHM (Pico*liq*)

DEGLOMERATION

SOME LIKE IT COARSE

Pre-crushers: practical examples



Typical examples:

- Disintegration of agglomerates and lumps of up to <500 µm
- Processing of soft and medium-hard products
- Easy cleaning/dismantling
- Cantilevered bearing
- Purged pharma bearing
- CIP/SIP design

Pharma range

HA hammer mill	Rotor diameter (mm)	Number of beaters	Power* (kW)	Max rotor speed* (1/min)
20/10	200	14	2.2	6,000

DB pre-crushing range	Sieve grate gap* (mm)	Power (kW)	Breaker speed (1/min)
500	18/12	4	200

* = depending on the application

PHARMA-DESIGN HA 20/10 HAMMER MILL

Pharma-design laboratory hammer mill for the size reduction and disintegration of agglomerates and lumps producing an end-product fineness of < 500 µm with minimum fines. Depending on the project, the mill can be delivered integrated into an isolator.

For R&D application
picocrush HOSOKAWA ALPINE

Ha 20/10
Complete installation

PRE-CRUSHERS: PRACTICAL EXAMPLES

Product	End-product fineness	Throughput kg/h	Machine size
Alkaloid	97 % < 1.000 µm	70	Ha 20/10
Hormone	50 % < 100 µm	40	Ha 20/10
NaCl (table salt) Hand-sized lumps	< 10 mm; 90 % < 1 mm	15.000	500 DB
Citric acid Large lumps	< 30 mm	18.000	500 DB
Celiprolol Lumps of about 100 mm	< 10 mm	2.600	500 DB

Powder fineness in % < µm – measuring points of particle size distribution
All values are non-binding reference values only

20/12 RO *detail*

DB 500 PRE-CRUSHER

Crusher for soft, slightly crumbly materials and lumps. Ideal for disintegrating and aerating agglomerates and for processing lumps. Typical areas of application include the size reduction of agglomerated excipients and additives after transport or storage. Easy and compact installation. Available with sieve grate gaps of 12 mm and 18 mm.

DB 500

PHARMA-DESIGN ROTOPLEX RO 20/12 GRANULATOR

Pharma-design granulator for pre-cutting pharmaceutical and chemical products. The granulator has a twin-knife rotor and a three-knife stator. A range of different screen inserts allows definition of the maximum top cut.

20/12 RO
Complete installation

36/60 RO

Pharma range

Rotor diameter	Rotor length (mm)	Rotorlänge (mm)	Power * (kW)	Maximum rotor speed (1/min)
20/12	200	120	2.6/4.6	6,750/ 1,500
36/60	360	600	22	

* = depending on the application

Typical features:

- Size reduction of materials suitable for cutting such as medicinal herbs, fibres, and polymers to end-product fineness < 1 – 2 mm
- Pharma/GMP-qualified design
- Easy cleaning
- High output
- Compact footprint

PRACTICAL EXAMPLES ROTOPLEX

Product	End-product fineness	Throughput kg/h	Machine size
Medicinal herbs, stalks	< 8 mm	60	Ro 20/12
Medicinal herbs, flowers	< 1.5 mm	12	Ro 20/12
Pharma polymer	97 % < 2 mm	100	Ro 36/60
Pharma Polymer	96 % < 3.15 mm	700	Ro 36/60
Collagen	97 % < 4 mm	70	Ro 20/12
Granulated pharma products	16 % < 250 µm; 97 % < 2 mm	180	Ro 36/60

Powder fineness in % < µm – measuring points of particle size distribution
All values are non-binding reference values only

METERING SYSTEMS – IT ALL DEPENDS ON THE DOSAGE

PDD PHARMA DOUBLE FEED METERING SCREW

Typical features:

- GMP-qualified design
- Modular configuration
- Clear division between product-contact zone and drive
- Easy to dismantle, i.e. easy to clean the product-contact zone
- Product-contact components can be autoclaved when pre-assembled
- Optional volumetric or gravimetric metering
- Special design for isolator integration available

Feed screw range

Feed screw	Screw diameter (mm)	Feed rate (l/h)	Power (kW)
PMD 65	12	0.25-6	0.02
PDD 25	25	2-40	0.1
PDD 30	30	6-250	0.18
PDD 35	35	60-600	0.55

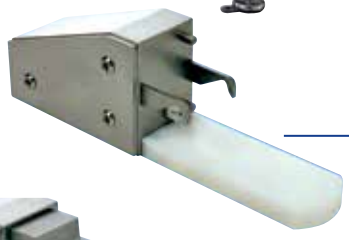
Filling station with **PDD 35 (SIP)** *for isolator installation*

Hosokawa Alpine develops its own system components to suit the special requirements of pharmaceutical applications and guarantee the compliance with GMP.

The ALPINE PDD double feed metering screw is a twin screw in continuous operation for the accurate metering of dry substances. The complete screw comprises the following modules:

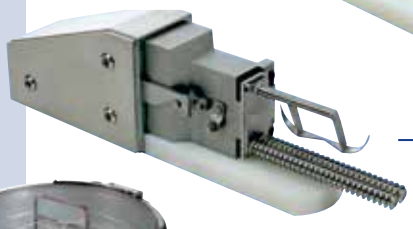
Options:

- different agitator and screw geometries available
- volumetric and gravimetric design
- containment solution for isolator integration
- CIP/SIP design



Module 1 – drive unit

Screw drive with DC motor, fully integrated into a stainless-steel housing.

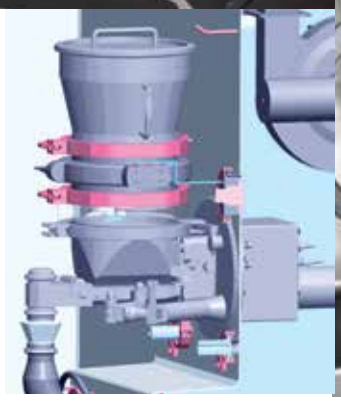


Module 2 – bearing unit

Screw bearing in closed monobloc housing with bayonet catch and lip sealing.

Module 3 – product container

Screw housing in monobloc design with integrated mixer.



PHARMA MICRO DOSING SCREW PMD

We offer metering solutions especially for pharmaceutical applications. Minimum metering rates and residue-free dosage of very small batch sizes is a major challenge.

The ALPINE PMD micro dosing screw is a volulmetric feeder in continuous operation for the accurate metering of minute volumes and is suitable even for substances with poor flow properties. The special design reduces product residues to a minimum.

PHARMA – PDR METERING CHANNEL

The ALPINE PDR is a volumetric vibration feeder in continuous in continuous operation for the accurate metering of free-flowing products.

RANGE OF VIBRATION FEEDERS

PDR 40-18	Open vibration chute - for lab applications
PDR 32	Closed vibration pipe Ø 32 mm
PDR 100	Closed vibration pipe Ø 100 mm

PMD
Micro Dosing Screw

PDR
feed chute

PDR 32
Vibration pipe

PDR 100
Vibration pipe

MORE THAN JUST ACCESSORIES

ZS 200
Installation in clean room wall

ZS 150/200 ROTARY VALVES

ALPINE ZS 150/200 rotary valves are used as rotary feeders, discharge devices, barriers for pressure-shock-proof installations and air/gaslocks. They are specially designed for compliance with cGMP requirements and are therefore characterised by their ease of dismantling and cleaning. They also allow force purging of bearings and housing covers.

Features:

- cGMP-qualified design
- Modular configuration
- Clear division between product-contact areas and drives
- Easy disassembly, i.e. easy cleaning of all product-contact areas
- Product-contact components can be autoclaved when pre-assembled
- 10 bar pressure-shock-proof and flameproof designse

Options:

- Gas-purged bearing and housing cover
- Alternative rotor chamber sizes

RANGE OF ROTARY VALVES

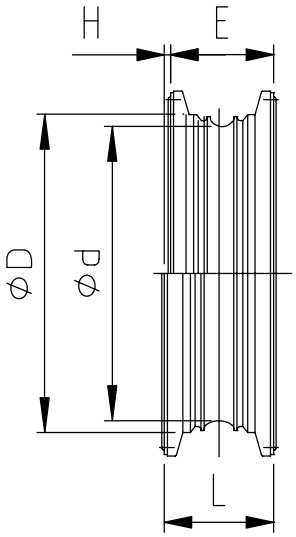
	Rotor Diameter (mm)	In-/Outlet Diameter (mm)	Max. Rotorspeed (1/min)	Capacity** (l/h)	Drive Power (kW)
ZS 150	150	DN 100	23	370	0,25
ZS 200	200	DN 150	23	690	0,37

* Clamp DIN 32676
** at max. speed

DN 50 EzConnect

ALPINE EZCONNECT COMPENSATORS
DN 50 – DN 300

Hosokawa Alpine's compensators are made from a single piece of silicone and a hygienic tri-clamp connection as an additional part.



OTHER FEATURES:

- Suitable for operating temperatures of between -20°C and +140°C
- Explosion protection: suitable for use up to zone 20
- Suitable for operating pressures of between -0.25 bar to +0.5 bar
- Simple, hygienic tri-clamp connection
- Clamp connections made from stainless steel AISI 316 L
- The compensator is made either of EPDM or silicone and complies with FDA directive 21 CFR § 177.2600
- The support rings are a principal part of the compensator
- (no loose parts, very easy assembly)

Size D	Standard	Total length L [mm]	Installation length E [mm]	max. compensation distance H [mm]	Diameter d [mm]
DN 250	DIN 32676	80	75	-10	244
DN 200	DIN 32676	70	65	-8	194
DN 150	DIN 32676	70	65	-8	144
DN 100	DIN 32676	70	65	-8	94
DN 80	DIN 32676	70	65	-6	75
DN 65	DIN 32676	70	65	-6	60
DN 50	DIN 32676	70	65	-5	45
10''TC	BS4825	73	70	-10	244
12''TC	BS4825	73	70	-10	292
DN 250	ISO 2852	80	75	-10	260
DN 300	ISO 2852	80	75	-10	309

PROCESS AUTOMATION

Hosokawa Alpine offers optimal process solutions. Process technology and automation engineering are tailored to customer requirements and come from one single source.

System automation has significant advantages:

- Overview of the complete system condition at all times
- Menu navigation for the operating modes
- Process operation
- Cleaning operation
- Maintenance
- Process data memory
- Trend visualisation
- Alarm archiving
- Password administration
- Recipe management
- Configured in compliance with GAMP 4/5 and 21 CFR Part 11

TRUST, BUT VERIFY

PROCESS AUTOMATION

Autmation by Hosokawa Alpine is process technological expertise translated into software and hardware. A team of experienced electrical engineers develops the basic principles of our automation technology and ensures the perfect interaction of all module interfaces and end-to-end documentation of all modules.

PROCESS VISUALISATION

The process sequences and process parameters are represented graphically on-screen. The system flowchart forms the basis of process display; it is formatted, animated and supplied with the required process parameters. It is important that the flowchart is easy to read and that process sequences are easy to follow. Colour-coding is used to highlight important information, while less important information is displayed in the background. The process is also operated on-screen. The user interface has a simple, logical design, user navigation of the menu structure is highly intuitive. This prevents operating errors and avoids additional training requirements.

EXPERTISE IN PROCESS ENGINEERING

Process engineers and electrical engineers cooperate in developing the best solution for each customer. Modular automation components are individually combined, depending on the process and the customer's automation requirements. Customers benefit from our process technology expertise.

VALIDATION

COUNT ON US!

Upon receipt of the URS, the characteristic process data such as the end-product fineness and throughput rate, etc. are determined, and the system-specific parameters such as construction materials and surface qualities, etc. are defined. The resultant system configuration is checked during the subsequent qualification phase for compliance with the URS.

The User Requirement Specification (URS) provides us with the customer's main system specifications, i.e. the grinding system requirements.

PROCESS IMPLEMENTATION
ALPINE TESTING CENTRE
ALPINE RENTAL EQUIPMENT

Alpine's testing centre offers unique facilities for carrying out customer trials aimed at finding the best possible system design and at determining the technical warranty parameters. If occupational safety restrictions prohibit the processing of materials at the testing centre, we can offer a range of rental systems which can be installed and operated at the customer's site. This way, customers can gather their own experience with the machines and compile their optimum URS.

DESIGN STUDY

Based on our experience and in close cooperation with our customers, we develop a system concept which is tailored to the customer's requirements and which illustrates ergonomic aspects.

MOCK UP

This service is available if required, e.g. for complex projects involving isolators, we create a 1:1 wooden model that allows simulation of all important process steps with original components wherever possible.

DETAILED DESIGN

Following acceptance of the layout, manufacturing drawings are prepared and, if required, special solutions are developed.

MANUFACTURE / ASSEMBLY

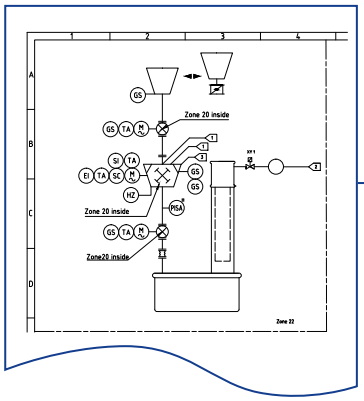
Manufacture, assembly, wiring and connection to the control unit are carried out on Alpine's premises, which ensures the perfect interaction of all interfaces.

FAT / SAT

The executed quality of the system is inspected by means of factory and site acceptance tests (FAT/SAT). Compact systems are completely assembled on Alpine's premises and subjected to a FAT, which reduces the effort for the SAT to a minimum

COMMISSIONING / TRAINING

Alpine supports its customers during system commissioning and provides training for the operating personnel.



HOSOKAWA ALPINE

Hosokawa Alpine has been in business for more than 100 years, and we have been setting the standards, regardless of the segment, be it blown film production or powder and particle processing. The challenges of market leadership and our experience inspire us to aim for a constant refinement of our technologies.

1. POWDER AND PARTICLE PROCESSING

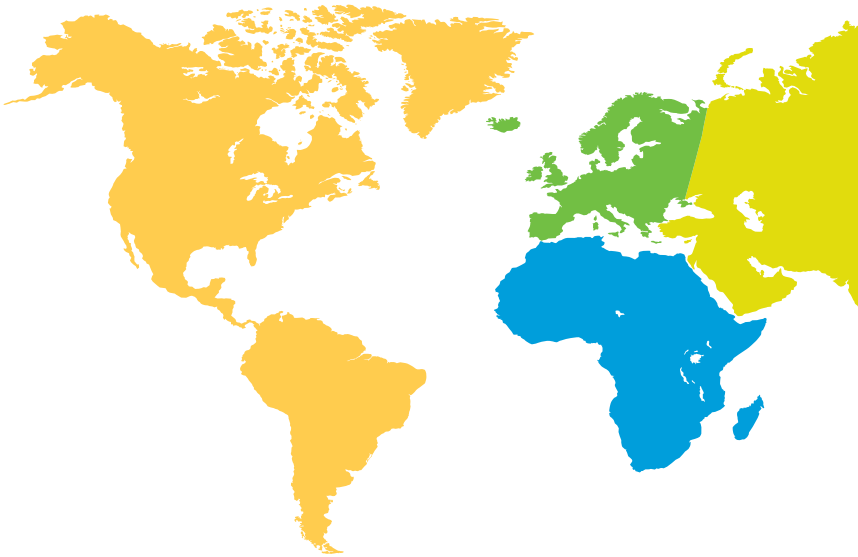
Hosokawa is the world's largest supplier of processing systems for the powder and particle processing segment. Renowned names such as Alpine, Bepex, Stott, Vitalair, Rietz, Mikro, Micron and Vrieco-Nauta are all part of the group's product range. Regardless of the size, be it production-scale system, pilot system or laboratory equipment, Hosokawa's products and technologies are used at numerous production stages, e.g. for size-reduction, mixing, drying, agglomeration, classification, weighing and metering.

2. BLOWN FILM LINES

Hosokawa Alpine is one of the world's foremost suppliers of blown film lines. Alpine supplies complete systems for blown film production and processing from a single source, from granule feeding systems to film winders, from single-layer die heads to 7-layer lines, from simple speed regulators to state-of-the-art process control systems. Thanks to Alpine's film orientation lines, the company can now offer complete systems for film conditioning.

3. CONFECTIONERY & BAKERY TECHNOLOGY

Benefiting from the vast expertise of companies such as Bepex, Kreuter and Ter Braak, Hosokawa Confectionery and Bakery is the ideal partner for the confectionery industry. A complete range of machines and production systems is available or can be tailored for the requirements of every stage of the production chain, from preparation of the raw materials and confectionery pastes to the end product.



DIVISIONAL STRUCTURE

The name Alpine stands for expertise in all areas of size-reduction technology. After many years of close cooperation between our engineers and our customers' R&D departments, we have become the world's leading specialist for powder and particle processing. In order to ensure that customers from different industrial segments receive professional assistance and consultancy, our particle processing division is divided into five subdivisions:

PHARMA & LAB

Producing powdery substances for the pharmaceuticals industry requires the skills and experience of experts. Hosokawa Alpine complies with international pharmaceutical standards and supplies a wide range of products and services, including laboratory applications and special processes. Whatever size reduction method is required, we are the specialists.

CHEMICALS

The range of chemical products is as diverse as the different demands on pigment or powder properties. We provide process engineering solutions for the chemicals industry from a single source. We also offer competent consultancy on basic chemical products and auxiliaries, toners, paints, pigments, herbicides and fertilisers.

MINERALS & METALS

We provide complete dry and wet processing systems with state-of-the-art mills and classifiers for processing mineral raw materials. Our machines and systems for processing fillers, ceramic raw materials, metallic compounds and alloys meet the exacting requirements of our customers.

RECYCLING & GRANULATORS

We design, engineer and deliver complete granulator systems which include all required system components. Be it for injection-moulded parts, sprues, film webs and edge trimming, our granulators are designed for the most challenging tasks.

FOOD

The food division develops special food processing techniques and supplies complete production lines for sugar, cocoa, lactose, proteins and spices.

SERVICE

Our service division provides support throughout the entire life-cycle of Hosokawa Alpine systems or machines. Our comprehensive service package includes spare parts supply, servicing, inspection, maintenance, repair, general overhauls, system upgrades and training. A recent addition to our service range is the supply of pre-owned Alpine machinery.

Hosokawa Alpine is at your service – no matter where you are and what your processing challenge is. Our service range includes project management, installation, commissioning, training, maintenance and system optimisation.

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HOSOKAWA ALPINE Aktiengesellschaft

Hosokawa Alpine is a member of the Hosokawa Micron Group, a high-performance manufacturer of systems for powder and particle processing, systems for the confectionery industry as well as plastics processing machines and systems. The group is known and reputed the world over for its power of innovation, constant product care and market-oriented R&D. The most important group resources are R&D, engineering and manufacturing as well as customer service in all global markets.

Pharma 04.13/1(EN)