

# Stability Testing according to GMP & FDA

**Vötsch**  
Industrietechnik



... you can be assured of that!  
We guarantee reliable state-of-the-art  
products for the pharmaceutical industry

# Environmental Simulation - the Basis for Quality ...

Founded in Berlin in 1929, Vötsch has been manufacturing at its present location in Balingen-Frommern since 1944. This is where we plan, design and construct the test systems and plants. These assure the quality and reliability of the final product in various industrial branches.

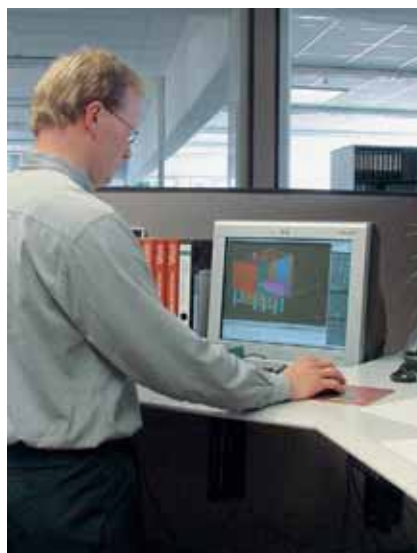
The accurate simulation of authentic environmental conditions speeds up the research into new materials and substances and improves the quality and reliability of these products.

Temperature and humidity, as well as the establishment of extreme stress parameters e.g. rapid temperature change, vibration, corrosive influences, air pollutants and light irradiation can be reproducibly realized in our equipment.

Our huge experience in all these areas has been well used for the development of our **Stability Test Productline**.

DKD (German Calibration Service) calibration of temperature and climatic test chambers, whether on site or in our accredited test laboratory, ensures the integrity of your test results. After all, customer satisfaction is our main priority.

Since 1995 Vötsch is a member of the Schunk Group. Combined know-how is the basis for trailblazing developments.



# ... and the Confidence for your Products



## The Application

### A Utopian dream!

- not for the systems of Vötsch Industrietechnik that guarantee reliability and reproducibility for stability and storage tests in the pharmaceutical industry, medicine, gene technology, biotechnology and food industry.

The International Conference on Harmonization, comprising councils representing the pharmaceutical industry, as well as scientists and authorities, defines the demands on functionality, performance and documentation for stability tests in the pharmaceutical industry in its **ICH guidelines**. Europe, Japan and the USA agreed to common stability tests.

The objective of these tests is to gather information in order to make recommendations regarding the stability of substances or pharmaceuticals. The ultimate goal is to verify the stability of chemical, microbiological and physical characteristics after exposure to temperature and humidity over a defined period.

The **ICH Guideline Q1A** stipulates the following climate conditions:

- **Long-term condition**  
at +25 °C / 60 % RH  
or 30 °C / 65 % RH
- **Accelerated condition**  
at +40 °C / 75 % RH
- **Intermediate condition**  
Temperature +30 °C / 65 % RH

The test with **intermediate conditions** is applied when the results of long-term and accelerated tests deviate.

The following test conditions were stipulated for substances or pharmaceuticals in semi-permeable packaging:

- **Long-term condition**  
Temperature +25 °C / 40 % RH
- **Accelerated condition**  
Temperature +40 °C /  $\leq$  25 % RH

The deviation is stipulated in temperature  $\pm 2$  K and  $\pm 5$  % for relative humidity during the entire test.

The ICH Guidelines not only stipulate the number of batches but also the sequence of the required analytic tests.



The **ICH Guideline Q1B** describes the methods for performing photostability tests with an irradiation dose of 1.2 mio lux hours and an integrated UV part of 200 Wh/m<sup>2</sup>.

# We guarantee ...

Exposure Equalisation



Homogeneous Airflow



Independent Monitoring Center



## Extensive product range

An extensive standard range of climatic chambers from 34 l to 2100 l for performing stability tests as well as our standard walk-in stability test chambers from 4 m<sup>3</sup> to 41 m<sup>3</sup> provide the ideal solution with regard to volume and construction **for all** who use this sophisticated application.

And if that's still not enough - we can adapt our stability test chambers to the actual space that is available.

**Special sizes, e.g. 200 m<sup>3</sup> are also possible.**

## Documentation

We can provide measurement values either from independent sensors or from the control loop sensors. Therefore, numerous recording possibilities are available for recording for temperature, humidity and/or light values:

- Analog line recorder (paper line recorder)
- Digital line recorder (line recorder with memory and display)
- Digital line recorder which complies with FDA 21 CFR Part 11 (line recorder with memory, display and the possibility of an electronic signature)
- Software package **SIMPATI\*** **Pharma complies with FDA 21 CFR Part 11** for connecting stability test systems to a PC.

Existing temperature or climate devices can be connected to independent recorders or computers using our software **SIMPATI\*** **Pharma** that complies with FDA 21 CFR Part 11 (using corresponding options).

## Qualification

For the approval of pharmaceuticals and providing evidence of stability tests, numerous steps must be taken to ensure that the stability test chambers function correctly, e.g. fluctuations in temperature and humidity remain within the stipulated range and this over extremely long periods of time.

These requirements are continuously confirmed by our extensive **Qualification Documentation**. **The entire system qualification comprises:**

<b>FAT</b>	Factory Acceptance Test
<b>DKD</b>	Calibration
<b>DQ</b>	Design Qualification
<b>IQ</b>	Installation Qualification
<b>OQ</b>	Operation Qualification
<b>PQ</b>	Performance Qualification

as well as all the necessary documents, such as circuit diagrams, component lists and certificates, e.g. ISO accreditation, EG conformity declarations or also maintenance recommendations.

Our trained technicians not only carry out **on-site qualification** on request, but utilize also the extensive measurement and calibration facilities of our accredited DKD laboratory.

Example of a terminal





## Calibration

In order to fulfil the requirements of the various QM systems, it is necessary that the calibration and monitoring of the test equipment can be traced back to standards that are approved both nationally and internationally. For this reason, Vötsch Industrietechnik GmbH conducts tests for measurable variables, e.g. temperature, dewpoint temperature and relative humidity in its own **DKD calibration laboratory which is accredited to ISO 17025.**

**International acceptance** of the DKD calibration certificate is underlined by the membership of the DKD in the ILAC (International Laboratory Accreditation Cooperation). All member countries of the ILAC must recognize DKD calibration certificates. Our trained calibration technicians perform calibration and spatial measurements of temperature and humidity both in our factory and on site.



## Training

Our skilled team of instructors advise you on all questions relating to stability testing, qualification, documentation as well as environmental simulation and heat technology.

We offer seminars and work-shops on all current topics relating to our product range and its application both in our **in-house training centre and on site** (e.g. FDA 21 CFR Part 11 in practice).

This team also qualifies and trains our service technicians in regular training-on-the-job for performing service, maintenance, calibration and qualification.

## Service and maintenance

In Germany, our Service Hotline is available 24 hours a day and we guarantee that a service technician will be on site within Germany on **weekdays within 24 hours** after receiving a failure notice.

If you have a maintenance contract with an **additional agreement**, we can serve you round the clock even at weekends.

As a specialist for refrigeration, climate and control technology, our technician is familiar with all the functions and components of your system.

Every technician can provide you with an optimum range of spare parts on site. Our extensive service network means that we are always on the spot when you need us.

Whether we assist you from the Service Centre or directly on site - **our customers are always given top priority.**

(DKD = German Calibration Service)

# Pharma Tests ...



## The Application

When testing the stability of drugs according to the guidelines ICH (International Conference on Harmonization) products must be stored under defined climatic conditions.

The test systems VP 600, VP 1300 and VP 2000 were specially developed for use in laboratories and supplement the spacious walk-in chambers that are used in production areas.

### Our solution for the laboratory:

- 600 l, 1300 l and 2000 l test space voluminas
- Storage areas of  
2.07 m<sup>2</sup> (600 l)  
4.14 m<sup>2</sup> (1300 l)  
6.21 m<sup>2</sup> (2000 l)  
with 6, 12 or 18 standard shelves (additional shelves as option)

The functionality of the cabinets satisfies the basic requirements of the official guidelines as well as the demand of special applications.

The chamber humidification is a patented system (**Sterile Steam System**) which is permanently monitored by an electronic module. The water evaporation is done at +140 °C. The parameters temperature and relative humidity are detected by a PT100 and a capacitive humidity sensor.

For monitoring and controlling, the test chamber is equipped with a powerful 32-bit control system **SIMPAC**\*

The touchpanel offers input and display of values and states.

## Standard

- Microprocessor monitoring and control unit **SIMPAC**\*
- Serial interface RS 232
- Humidity input and display in % rel. humidity
- Independent adjustable temperature limiter  $t_{min}/t_{max}$
- Calibration of 2 temperature and 2 humidity values with certificate
- Air-cooled refrigeration unit
- Patented vapour humidification (Sterile Steam System)
- Capacitive humidity sensor
- Entry port 50 mm Ø
- Interior stainless steel
- Water tank 19 l, manual and automatic water supply possible
- Door switch
- Single wing door, lockable
- Mobile on wheels
- Shelves 6, 12 or 18 pieces (depending on the volume)
- Door lock
- Password protected user panel

... tailored to your needs



## Important Options

- SIMPATI\* Pharma
- Networking (RS 485 interface)
- TCP/IP interface
- Registration of temperature and humidity
- Independent sensor for temperature and humidity
- Acoustic and optical warning signal
- Water-cooled refrigeration unit
- Glass door, heated
- Feet separately adjustable in height
- Additional shelves
- Additional entry ports
- Demineralization unit for connection to domestic water supply
- Qualification documentation
- Special voltages
- Analog outputs
- Line recorder

## Technical Data

Type			VP 600	VP 1300	VP 2000
Shelves 650 x 530 mm	piece		6 <sup>3)</sup>	12 <sup>3)</sup>	18 <sup>3)</sup>
Storage space standard	m <sup>2</sup>		2.07 <sup>3)</sup>	4.14 <sup>3)</sup>	6.21 <sup>3)</sup>
Temperature range	°C		+10 to +50		
Temperature deviation in time	K		±0.1 to ±0.3		
Temperature deviation in space	K		±0.5 to ±1.0		
Temperature gradient <sup>1)</sup>	K		1 to 2		
Humidity range	%		20 to 90		
Humidity deviation in time	%		±0.5 to ±1		
Calibrated values			+25 °C / 60 % RH and +40 °C / 75 % RH		
External dimensions	Width	mm	740	1460	2155
	Depth	mm	1050	1050	1050
on wheels (standard)	Height	mm	1975	1975	2067
	Height	mm	2030	2030	2112
Test space dimensions	Width	mm	620	1340	2034
	Depth	mm	685	685	685
	Height	mm	1300	1300	1300
Entry port	mm		1 pce. 50 mm diameter, on the right		
Electrical connection			1/N/PE AC 230 V ±10 %, 50 Hz		
Rated power	kW		2.3	2.7	3.5
Weight	kg		150	250	350
Noise level <sup>2)</sup>	dB(A)		52	52	52
Humidity water			demineralized water, pH-value 6-7 conductivity 5 to 20 Microsiemens/cm		

Performance values refer to +25 °C ambient temperature - <sup>1)</sup> In accordance with IEC 60068-3-5. <sup>2)</sup> Free field, 1 m distance from the front, as per DIN 45635, part 1, accuracy class 2. <sup>3)</sup> Additions possible

# Photostability Test Chamber VP 500-L ...



The Vötsch **photostability test chamber VP 500-L** has an ideal light, temperature and humidity distribution and is thus able to simulate reproducible light and climatic conditions.

The lighting equipment complies with the **ICH Guideline Q1B Option 2** and enables photostability tests to be performed in less than 100 hours.

All specimens are positioned at the same distance from the light source and **are evenly irradiated by a special light/UV filter system.**

This system can be equipped with appropriate light and UV sensors for recording irradiation values, e.g. the total number of lux hours as well as the total irradiation.



## Standard

- Microprocessor monitoring and control unit **SIMPAC\*** with touchpanel
- 2 shelves illuminated with UV-light and 2 shelves illuminated with white light
- Timers for light and UV-light
- Light and UV filters for ideal distribution
- Lockable door
- Water tank 19 l, with manual and automatic water supply possibility
- Patented vapour humidification (Sterile Steam System)
- Interface TCP/IP
- Password protected user panel

## Important Options

- UV and Lux-Sensors with automatic integration function
- Analog line recorder
- Digital line recorder
- Software **SIMPATI\*-Pharma FDA 21 CFR Part 11 conform**
- Qualification documentation
- DKD calibrations
- Mapping of light- and UV-distribution
- Spatial measurements for temperature and humidity
- Maintenance contracts

## Technical Data VP 500-L

Volumes:	Litre	gross approx. 700 net approx. 460
External dimensions	WxDxH mm	815 x 935 x 2070
Test space dimensions	WxDxH mm	595 x 600 x 1305
Temperature range	°C	+10 to +50
Humidity range	%	20 to 90
Temperature deviation in time	K	±0.1 to ±0.5
Temperature deviation in space	K	±0.5 to ±1.0
Temperature gradient <sup>1)</sup>	K	1 to 2
Humidity deviation in time	%	±1 to ±2
Illumination	lx	max. 25000
UV energy	W/m <sup>2</sup>	max. 3.7
Light distribution	%	approx. ±6
UV distribution	%	approx. ±10
Noise level <sup>2)</sup>	dB(A)	52
Electrical connection		1N/PE AC 230 V ±10 %, 50 Hz

Performance values refer to +25 °C ambient temperature - <sup>1)</sup> In accordance with IEC 60068-3-5.

<sup>2)</sup> Free field, 1 m distance from the front, as per DIN 45635, part 1, accuracy class 2.





# ... Stability Test Chambers VB Pharma



## The Series VB ...

**provides maximum storage area where minimum space is available.** The spacious shelf system of stainless steel provides you with the same storage conditions on all 15 or 30 shelves.

The airflow fiber and the sterile humidification system ensures excellent **ICH climate conditions.** The storage space is easy to clean.

An alarm system provides the necessary safety. Low energy consumption and a thick layer of thermal insulation ensure economical long-term operation.

For monitoring and controlling, the test chamber is equipped with a powerful 32-bit control system **MINCON/32.**

The terminal with LCD-display **MINCONTROL\*** offers input and display of values and states.

Documentation of temperature and humidity is obtainable via an interface and our optional software **SIMPATI Pharma** (in accordance with **FDA 21 CFR, Part 11**).

## Technical Data

Type		VB 1000 Pharma	VB 2100 Pharma
Volume	Litre	1010	2080
Storage space dimensions	Width mm	970	1990
	Depth mm	750	750
	Height mm	1400	1400
<b>Performance for climatic tests</b>			
Temperature range	°C	+ 5 to +45	
Temperature deviation in time	K	±0.1 to ±0.5	
Temperature deviation in space	K	±0.5 to ±2.0	
Temperature gradient <sup>1)</sup>	K	1 to 4	
Humidity range	%	25 to 95	
Humidity deviation in time	%	±1 to ±3	
Rack system		Stainless steel 1.4301	
Shelves max.	piece	15	30
Storage space max.	m <sup>2</sup>	9.6	19.2
Max. loading capacity	kg	75	150
Air flow		Horizontal with airflow fiber	
Humidification		Sterile vapour (Sterile Steam System)	
Control Terminal Interface		<b>MINCON/32</b> MINCONTROL RS 232	
External dimensions	Width mm	2020	3040
	Depth mm	975	975
	Height mm	1980	1980
Noise level <sup>2)</sup>	dB(A)	58	58
Rated power	kW	2.4	2.4
Electrical connection		1/N/PE AC 230 V ±10 % 50 Hz	
Option: Lockable door		on request	

Performance values refer to +25 °C ambient temperature - <sup>1)</sup> In accordance with IEC 60068-3-5. <sup>2)</sup> Free field, 1 m distance from the front, as per DIN 45635, part 1, accuracy class 2.

# Climatic Test Chambers for Stability Tests ...



## Equipment for Laboratories ...

Compact, quiet, yet powerful units are required to tackle special laboratory conditions that include limited space, even smaller specimens and the need to conduct tests directly at the workplace.

The VTL & VCL series of temperature and climatic test chambers are ideally suited to such applications. These systems have a volume of 34 l, 64 l and 100 l respectively and provide an optimum solution where space is limited.

More info in leaflet VIT-E 8/02.  
“Equipment for Laboratories”.

## Constant Climate ...

For even higher demands, we offer our climatic chambers of the VC 0 ... series. The desired climate is produced reliably and exactly to your requirements. Long-term tests in climatic chambers are the quickest way to optimize and secure your product quality. Stability tests as per the ICH guideline, constant climatic tests as per DIN 50014 and IEC 60068-2-3, ...-56, ...-67 and ...-78 can be easily performed.  
(More info in leaflet VIT-E 2/02)

For samples which can form an explosive atmosphere e.g. alcoholic liquids, we offer Ex-protected units classified to Atex-regulations. (leaflet VIT-E 9/04)

## Technical Data Series VTL & VCL and VC 0 ...

VTL & VCL	Series	VC 0 ...
34, 64 and 100 l	Test space volume in litre	190 to 1540
	<b>Performance for temperature tests</b>	
+10 / -40 / -70 to +180	Temperature range °C	-10 / -5 / 0 to +90
±0.3 to ±1	Temperature deviation in time K	±0.1 to ±0.5
±1.0 to ±2.0	Temperature deviation in space K	±0.5 to ±1.0
2 to 4	Temperature gradient <sup>1)</sup> K	1 to 2
+23 °C and +80 °C	Calibrated values	+4 °C and +90 °C
	<b>Performance for climatic tests</b>	
+10 to +95	Temperature range °C	+10 to +90
±0.1 to ±0.5	Temperature deviation in time K	±0.1 to ±0.3
±0.5 to ±1.5	Temperature deviation in space K	±0.5 to ±1.0
1 to 3	Temperature gradient <sup>1)</sup> K	1 to 2
10 to 98	Humidity range %	10 to 98
±1 to ±3	Humidity deviation in time %	±1 to ±3
+25 °C / 50 % RH and +80 °C / 50 % RH	Calibrated values on ICH-Guideline	+25 °C / 60 % RH and +40 °C / 75 % RH
56 (59 at -70 °C)	Noise level <sup>2)</sup> dB(A)	47
1/N/PE AC 230 V ± 10 %, 50 Hz	Electrical connection	1/N/PE AC 230 V ± 10 %, 50 Hz

Performance values refer to +25 °C ambient temperature - <sup>1)</sup> In accordance with IEC 60068-3-5.

<sup>2)</sup> Free field, 1 m distance from the front, as per DIN 45635, part 1, accuracy class 2.

# ... Walk-in Test Chambers



## Standard ...

The standard stability chambers from Vötsch Industrietechnik GmbH can be accredited and are specially designed to meet your requirements. Thanks to flexible design and construction techniques, our walk-in chambers can be integrated into existing structures.

**Virtually any size is possible.**

### Major features:

- PU-insulated walk-in chambers (CFC-free) with easy to clean metal coated panels on both sides
- Lockable door with emergency opening mechanism

- Temperature conditioning system comprising ceiling evaporator with integrated electric heater and air-cooled refrigeration unit
- Air-conditioning system with energy-saving ultrasonic humidifier and separate dehumidifier
- Microprocessor-controlled monitoring system according to GAMP 4 and FDA 21 CFR Part 11 with maintenance-free electronic temperature/humidity sensor
- Safety temperature limiter for electric heater and test chamber
- Test specimen protection  $t_{min}/t_{max}$

## Options

- Extended temperature and humidity ranges
- Temperature chamber version (without controlled humidity)
- Entry ports
- Additional observation window
- Shelves
- Explosion-proofed components
- Software package **SIMPATI**\* for recording and processing measured values
- Additional calibration points
- Spatial measurements
- Further options on request

## Technical Data

Standard volumes	m <sup>3</sup>	4, 10, 15, 25, 32, 41
Temperature range	°C	+20 to +45
Temperature deviation in time	K	±0.1 to ±0.5
Temperature deviation in space	K	±0.5 to ±1.0
Temperature gradient <sup>1)</sup>	K	1 to 2
Humidity range	%	20 to 80
Humidity deviation in time	%	±1 to ±3
Dew point range	°C	+9 to +41

Performance values refer to +25 °C ambient temperature

<sup>1)</sup> In accordance with IEC 60068-3-5.

**SIMPATI\* Pharma** our control and test management software enables you to make even better use of your systems. It not only simplifies the recording of data but also the archiving.

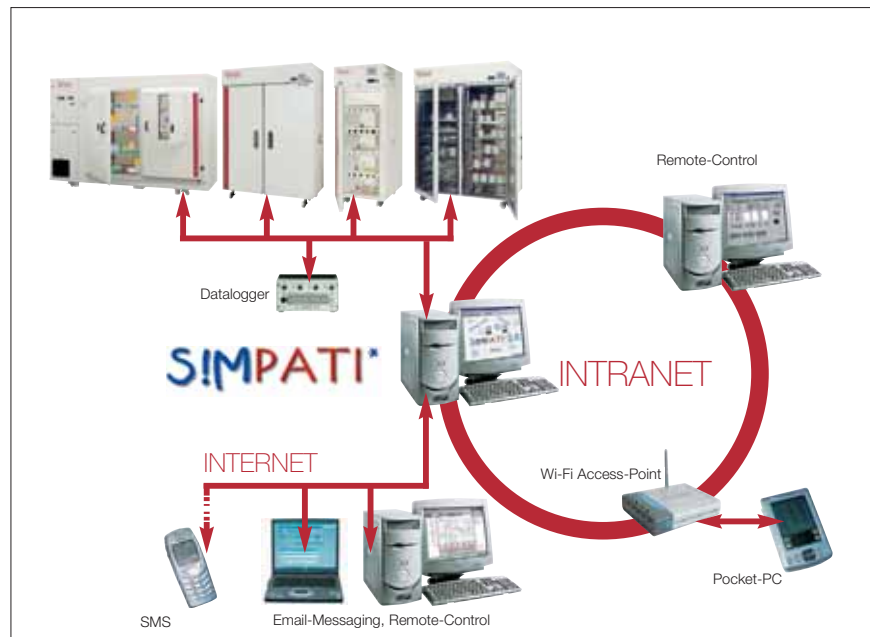
All warning and alarm messages are recorded and if necessary an alarm signal can be transmitted to the person responsible for the system.

Access rights can be specially defined for every user. The recording and storage of data is manipulation safe but can still be used for further processing, e.g. in Excel.

It goes without saying that the software **SIMPATI\* Pharma** complies with the **FDA Guideline 21 CFR Part 11**. We also provide qualification documentation with Audit Trail for our control and test management software **SIMPATI\* Pharma**.

Operation of our systems is simple and time-saving.

**SIMPATI\* Pharma** can be integrated in your PC network and enables operation at individual stations without requiring special software - simply by using your Internet browser.



### The most important functions and features:

- Barcode reader for managing batches
- Remote alarming
- Alarm output per email, SMS, telephone or alarm contact
- Recording of door openings and documentation of opening times
- Recording of alarms
- Recording of temperature and humidity curves
- Recording of light and UV intensity during photostability tests
- Mobile solutions for site-independent monitoring of devices, e.g. per PDA within the range of the installed WLAN
- **SIMPATI e-Sign** (electronic signature with biometric data)
- Data recording via a special system network or TCP/IP network
- Management of access rights
- Conformity with FDA Guideline 21 CFR Part 11
- Documentation of climatic chambers and rooms irrespective of manufacturer

In some case options and/or special constructions are required for these functions.

**We reserve the right of changes in construction resulting from technical progress. Some of the illustrated systems contain optional extras.**

# Vötsch

Industrietechnik

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