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**OECD guidelines and GLP compliance for
inhalation toxicological studies**



Organisation for Economic Co-operation and Development



The [*OECD Guidelines for the Testing of Chemicals*](#) are a unique tool for assessing the potential effects of chemicals on human health and the environment. Accepted internationally as standard methods for safety testing, the Guidelines are used by professionals in industry, academia and government involved in the testing and assessment of chemicals (industrial chemicals, pesticides, personal care products, etc.).



Contract Research



Pharmaceutical



Toxicological



Occupational



Agricultural

OECD Guidelines – Inhalation Toxicity



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Test No. 412: Subacute Inhalation Toxicity: 28-Day Study

This revised Test Guideline 412 (TG 412) has been designed to fully characterize test article toxicity by the inhalation route following repeated exposure for a limited period of time (28 days), and to provide data for quantitative inhalation risk assessments. It was updated in 2017 to enable the testing and characterisation of effects of nanomaterials tested. Groups of at least 5 male and 5 female rodents are exposed 6 hours per day for 28 days to a) the test chemical at three or more concentration levels, b) filtered air (negative control), and/or c) the vehicle (vehicle control). Animals are generally exposed [More](#)

Published on June 27, 2018 Also available in: [French](#)

In series: [OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects](#) (view more titles)

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Test No. 413: Subchronic Inhalation Toxicity: 90-day Study

This revised Test Guideline 413 (TG 413) has been designed to fully characterize test article toxicity by the inhalation route following repeated exposure for a period of 90 days, and to provide data for quantitative inhalation risk assessments. It

Test No. 403: Acute Inhalation Toxicity

This method provides information on health hazard likely to arise from short-term exposure to a test article (gas, vapour or aerosol/particulate test article) by inhalation. The revised Test Guideline describes two studies: a traditional LC50 protocol

Test No. 436: Acute Inhalation Toxicity – Acute Toxic Class Method

The method described by this Test Guideline provides information that allows hazard assessment for short-term exposure to a test article by inhalation, and allows the substance to be classified according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). The test method is based on a stepwise procedure, each step using 3 animals of each sex (the preferred species is rat). Animals are exposed in inhalation chambers to a pre-defined [More](#)

Published on September 08, 2009 Also available in: [French](#)

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OECD – 403 Acute Inhalation Toxicity

- ***PRINCIPLE OF THE TEST***

to obtain sufficient information on the acute toxicity of a test article to enable its classification and to provide lethality data (e.g. LC 50, LC 01 and slope)

- ***DESCRIPTION OF THE METHOD***

- Selection of animal species
- Preparation of animals
- Animal husbandry
- Inhalation chambers

- ***EXPOSURE CONDITIONS***

- Administration of concentrations
- Particle-size distribution
- Test article preparation in a vehicle
- Control animals

- ***MONITORING OF EXPOSURE CONDITIONS***

- Chamber airflow
- Chamber temperature and relative humidity
- Test article: Nominal concentration
- Test article: Actual concentration
- Test article: Particle size distribution

OECD – 403 Acute Inhalation Toxicity

- **PRINCIPLE OF THE TEST**

to obtain sufficient information on the acute toxicity of a test article to enable its classification and to provide lethality data (e.g. LC 50, LC 01 and slope)

- **DESCRIPTION OF THE METHOD**

- Selection of animal species
- Preparation of animals
- Animal husbandry
- Inhalation chambers

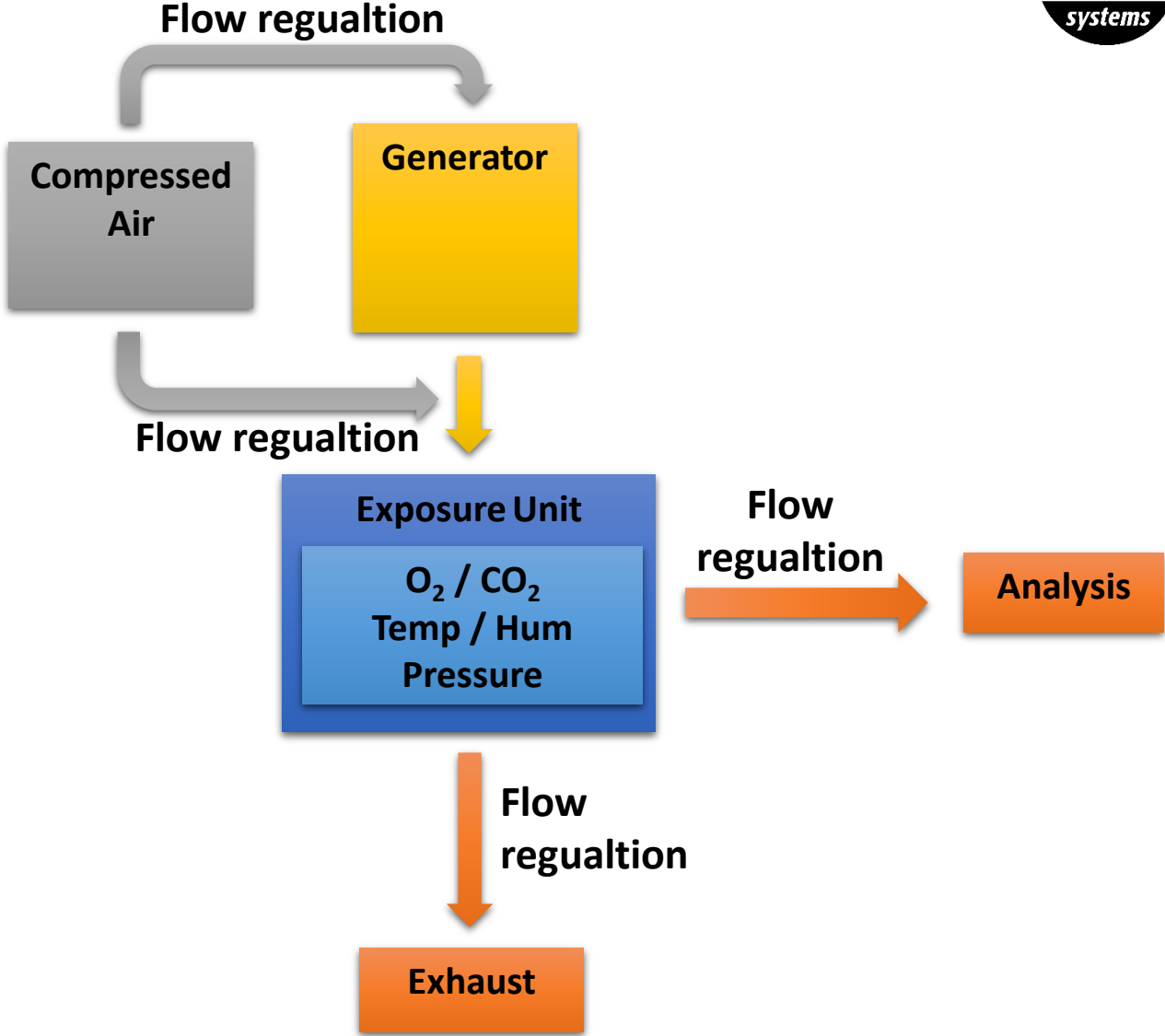
- **EXPOSURE CONDITIONS**

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- Control animals

- **MONITORING OF EXPOSURE CONDITIONS**

- Chamber airflow
- Chamber temperature and relative humidity
- Test article: Nominal concentration
- Test article: Actual concentration
- Test article: Particle size distribution

Inhalation System *Overview*



Inhalation System *Generators*



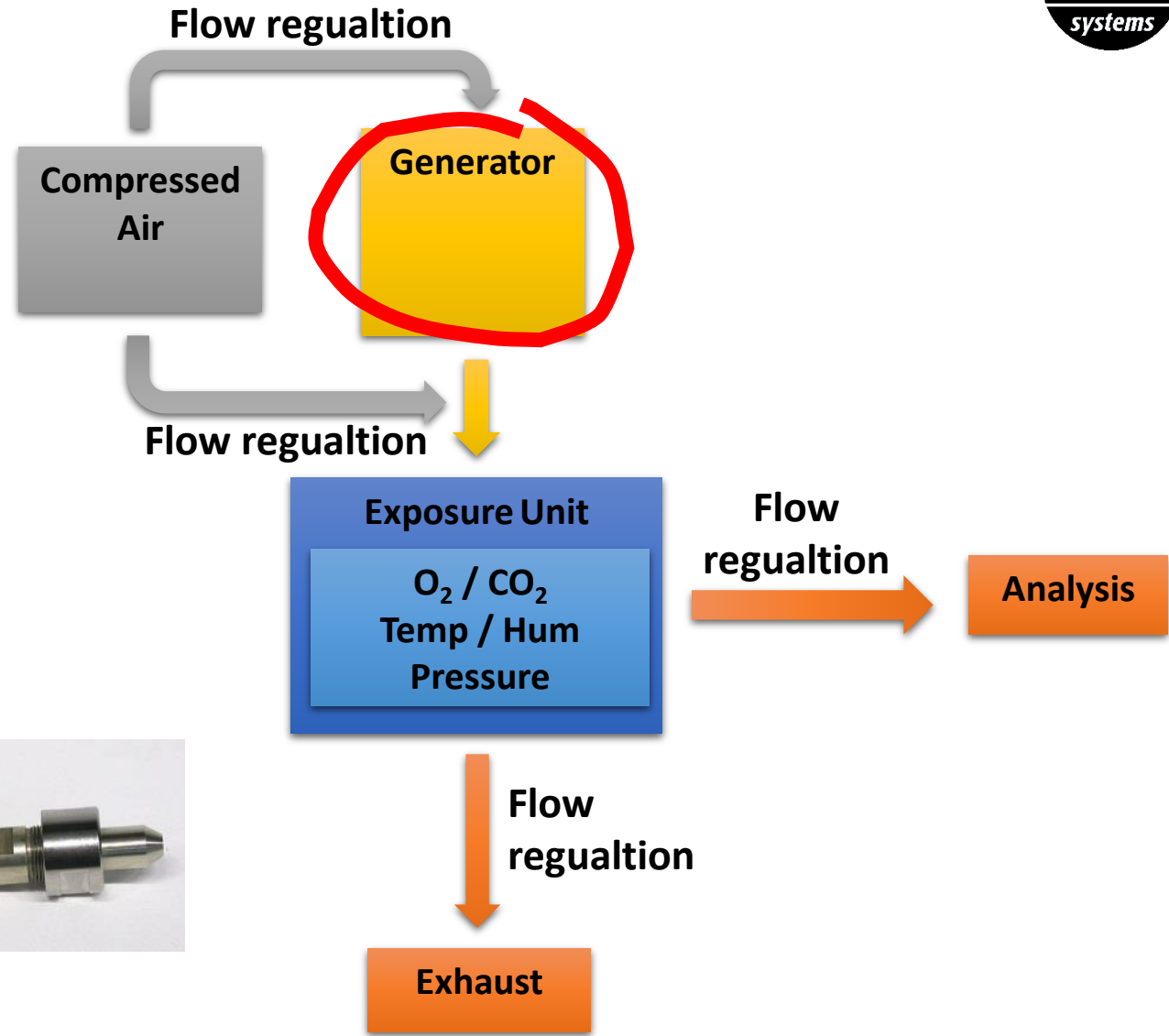
6 Jet Collision Nebulizer



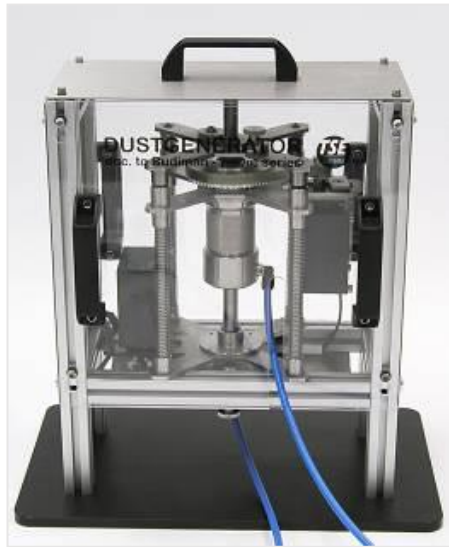
MDI Activating System



Ultrasonic Aerosol Generator



Dust Generator acc. to Bundschuh

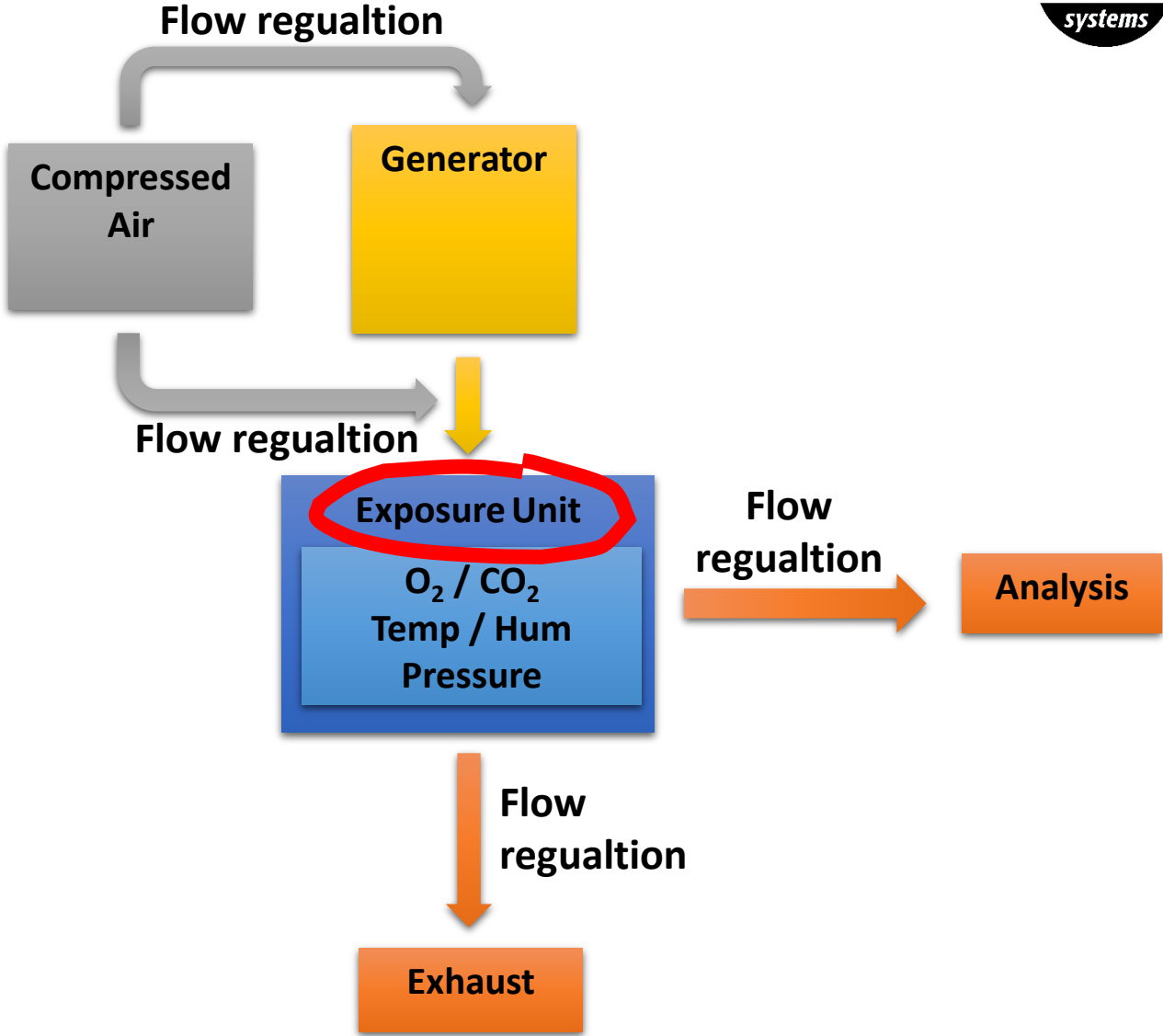


Dust Generator acc. to Budiman

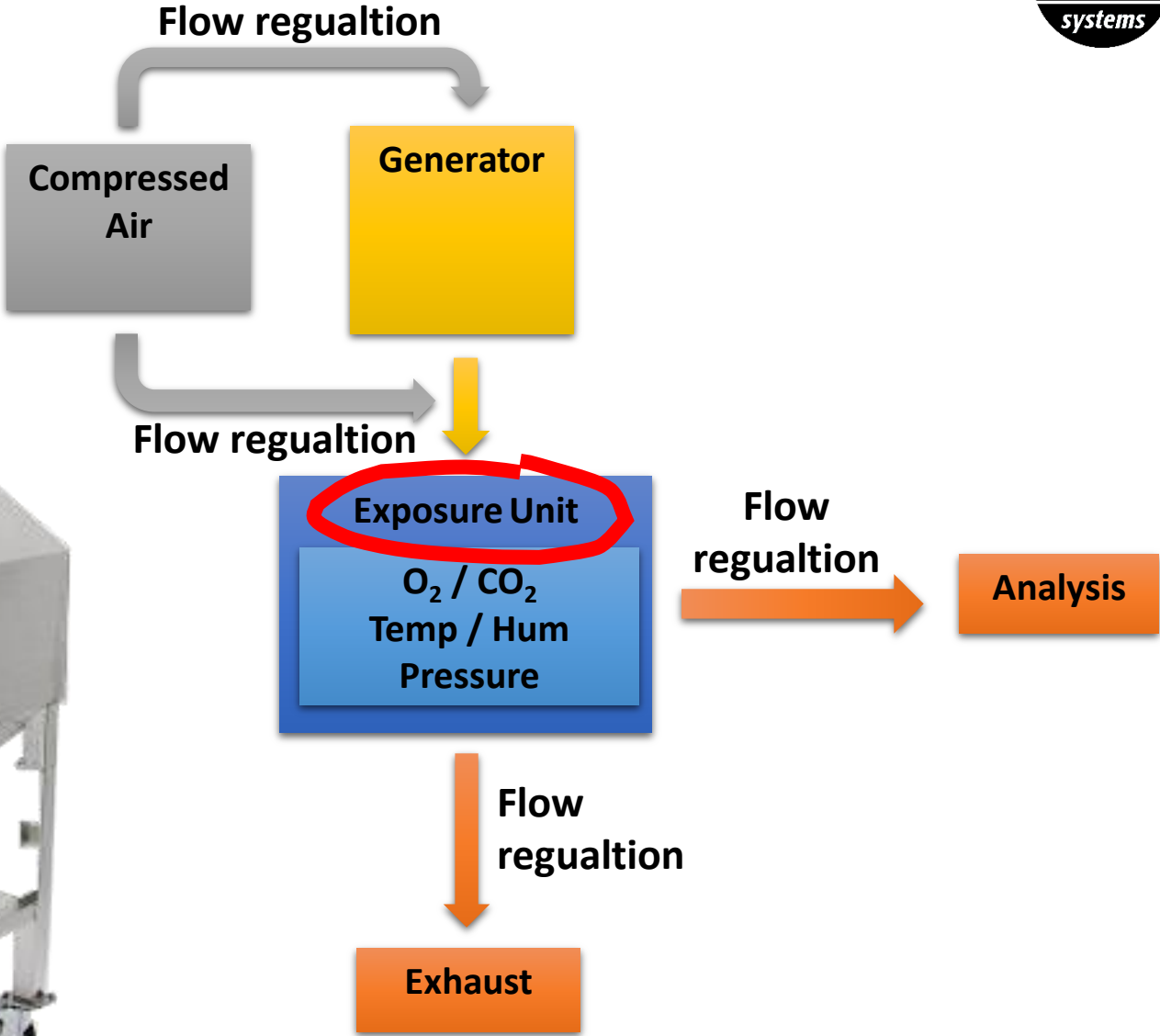


Aerosol Nozzle

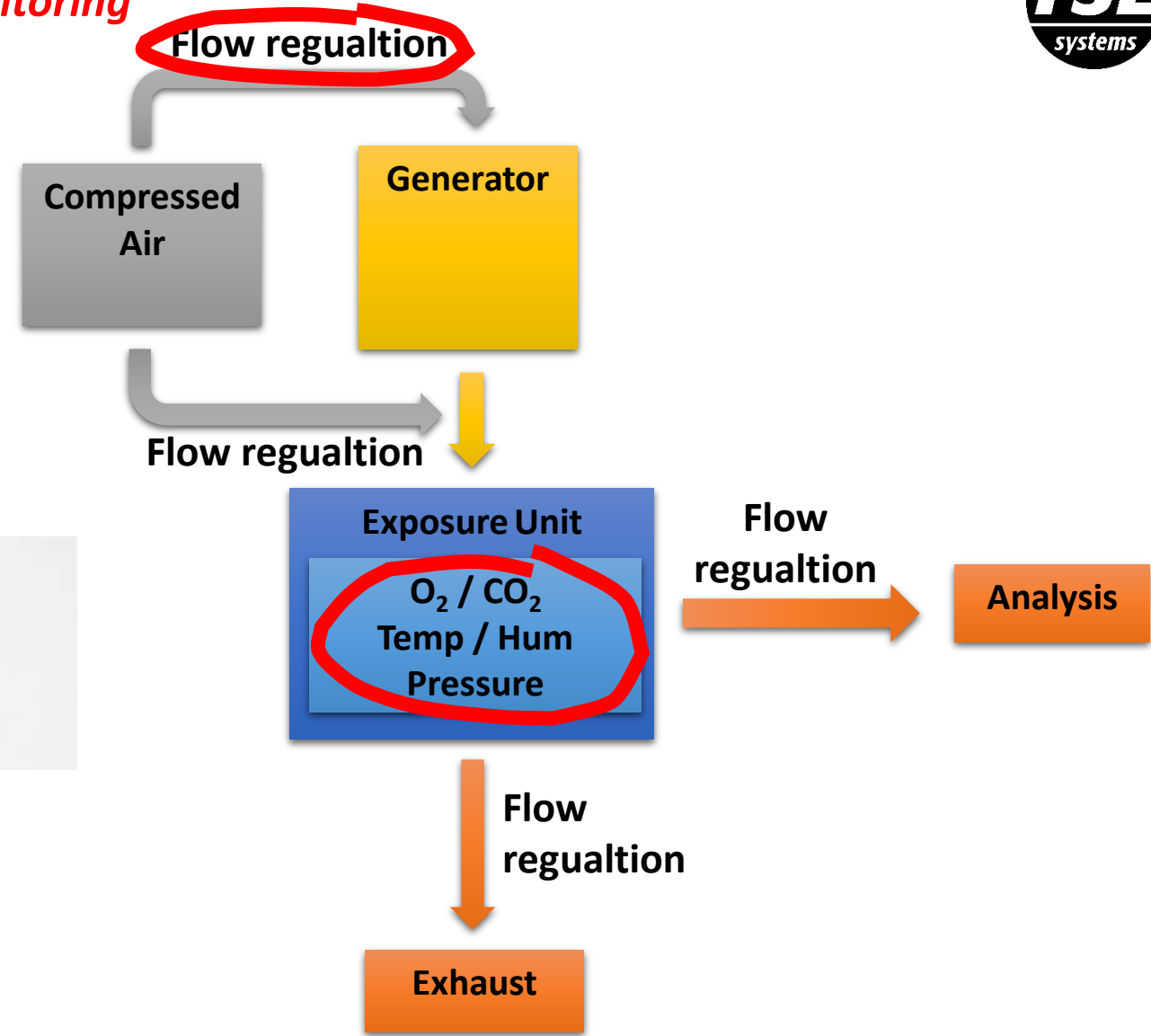
Inhalation System *Exposure Units*



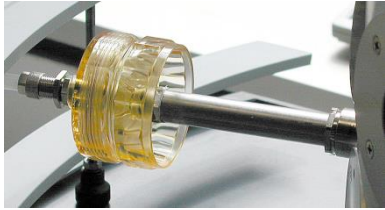
Inhalation System *Exposure Units*



Inhalation System *Regulating/Monitoring*



Inhalation System *Concentration (Analysis)*



Analysis Filter Sampling



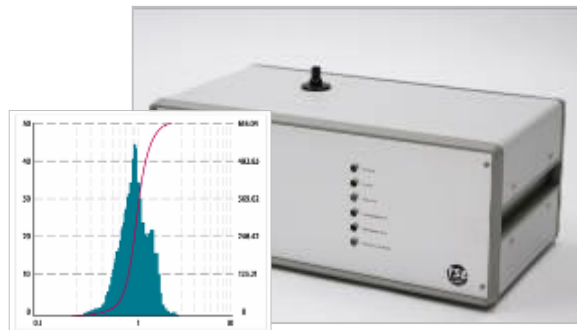
Cascade Impactors



Concentration Measuring Unit

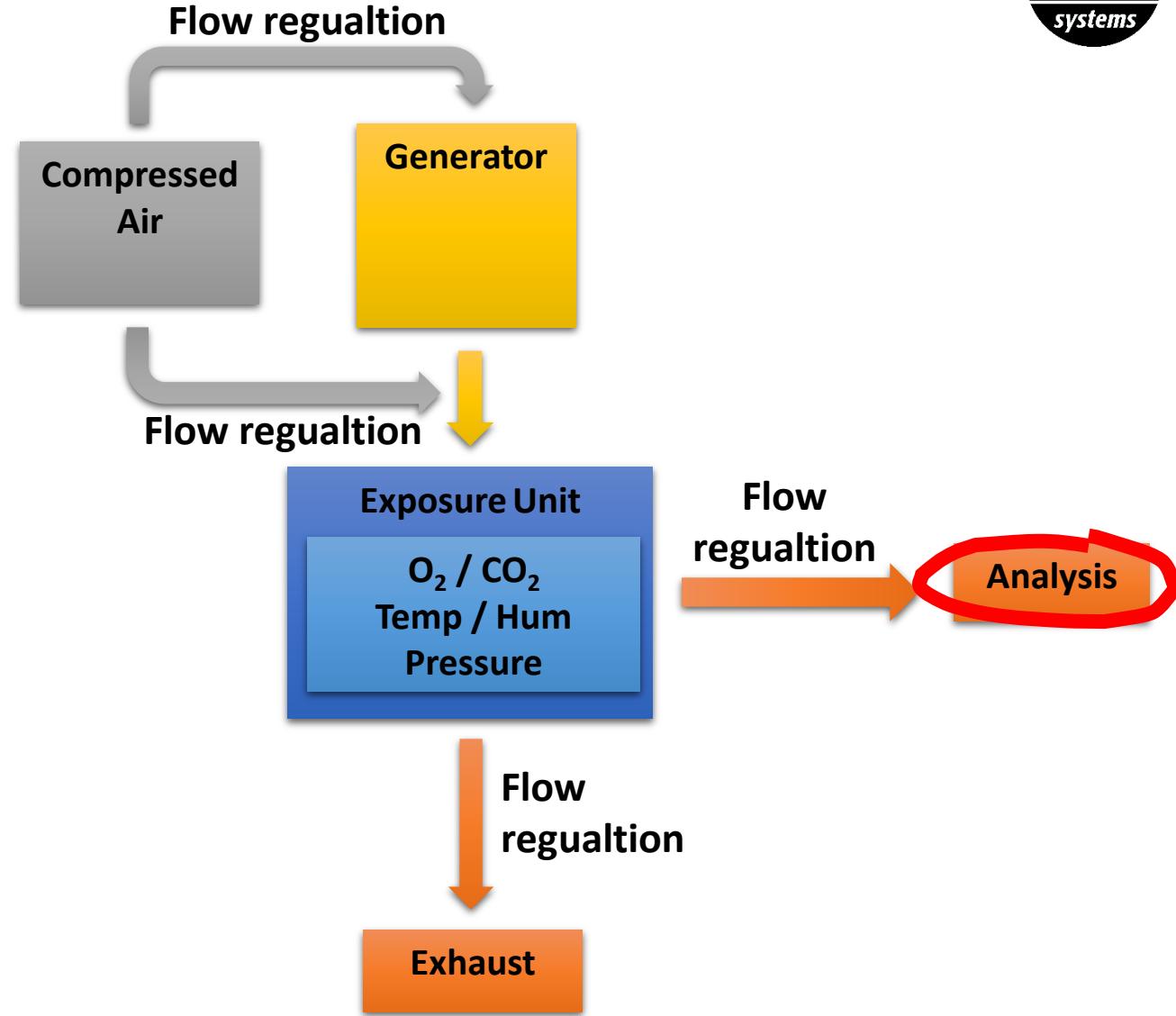


Midget Impingers

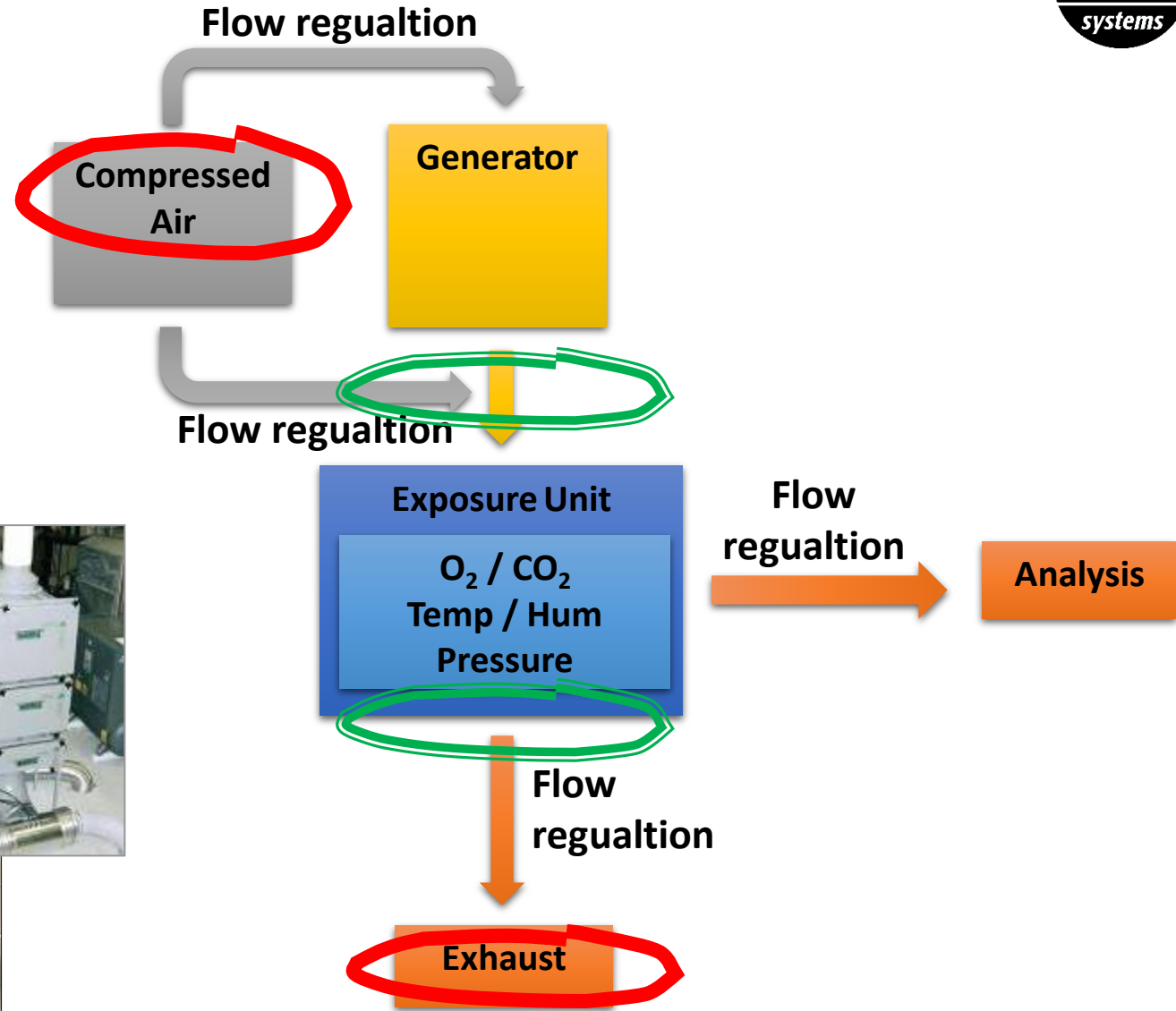


SpectroPan

(Particle Size Distribution Analyzer)



Inhalation System *Additional Components*



OECD – 403 Acute Inhalation Toxicity



- ***PROCEDURE***
 - Traditional Protocol
 - Concentration Time Protocol

- ***OBSERVATIONS***
 - Body weights
 - Pathology

- ***DATA AND REPORTING***
 - Data
 - Test report
 - Test animals and husbandry
 - Test article
 - Vehicle
 - Inhalation chamber
 - Exposure data
 - Test conditions
 - Results
 - Discussion and interpretation of results

OECD – 403 Acute Inhalation Toxicity

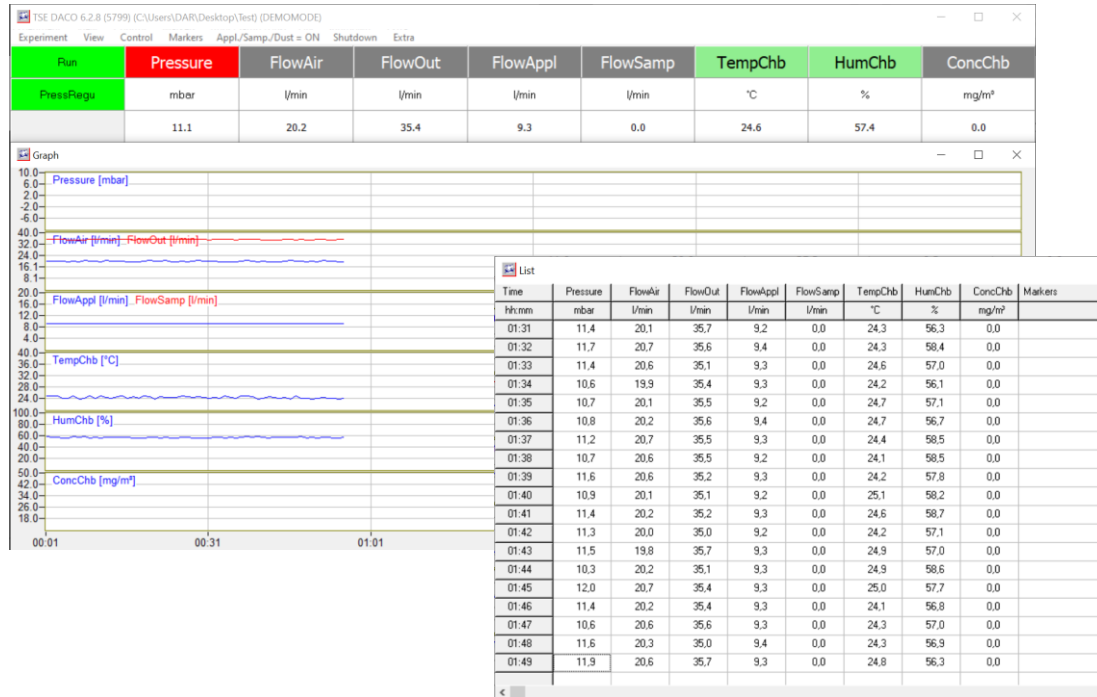
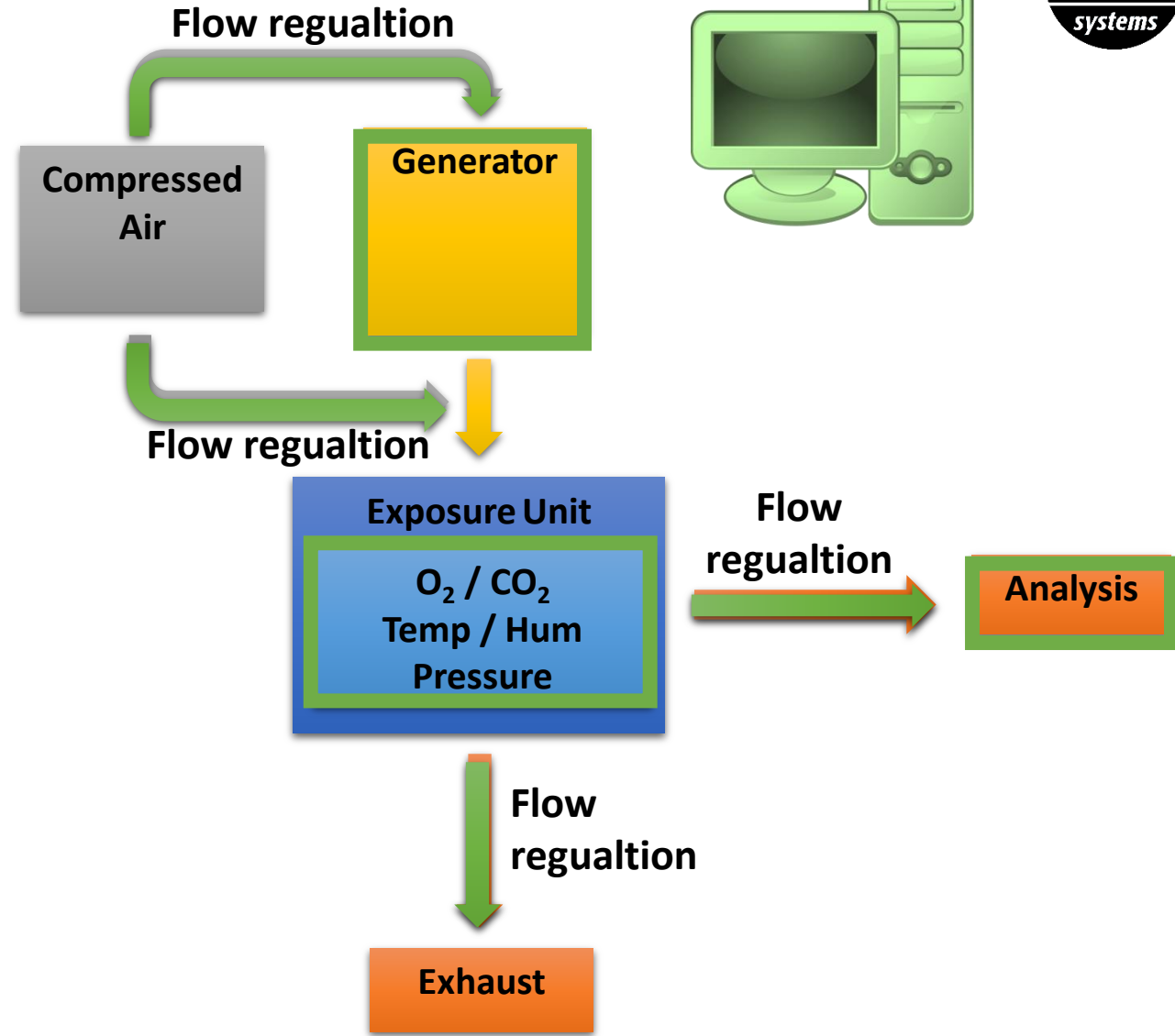
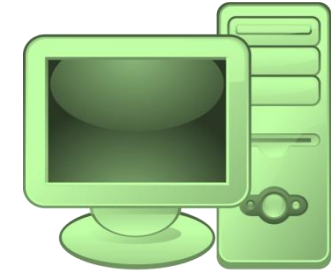


- **PROCEDURE**
 - Traditional Protocol
 - Concentration Time Protocol

- **OBSERVATIONS**
 - Body weights
 - Pathology

- **DATA AND REPORTING**
 - Data
 - Test report
 - Test animals and husbandry
 - Test article
 - Vehicle
 - Inhalation chamber
 - Exposure data
 - Test conditions
 - Results
 - Discussion and interpretation of results

Inhalation System *Software*



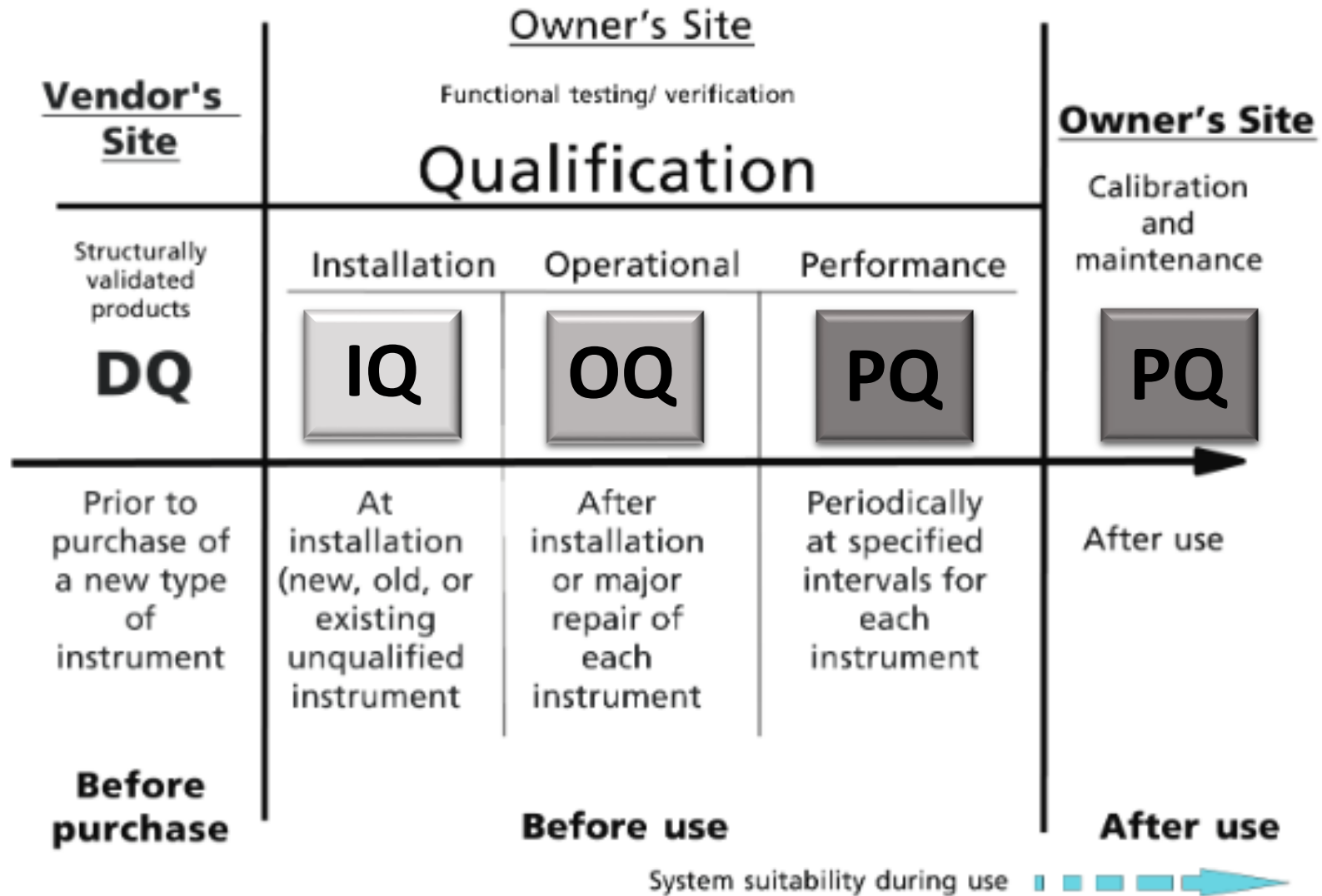
Good Laboratory Practice GLP



GLP is a quality regulation, which looks at the big picture. The organisational process and the conditions under which non-clinical studies are planned, performed, monitored, recorded, archived and reported.

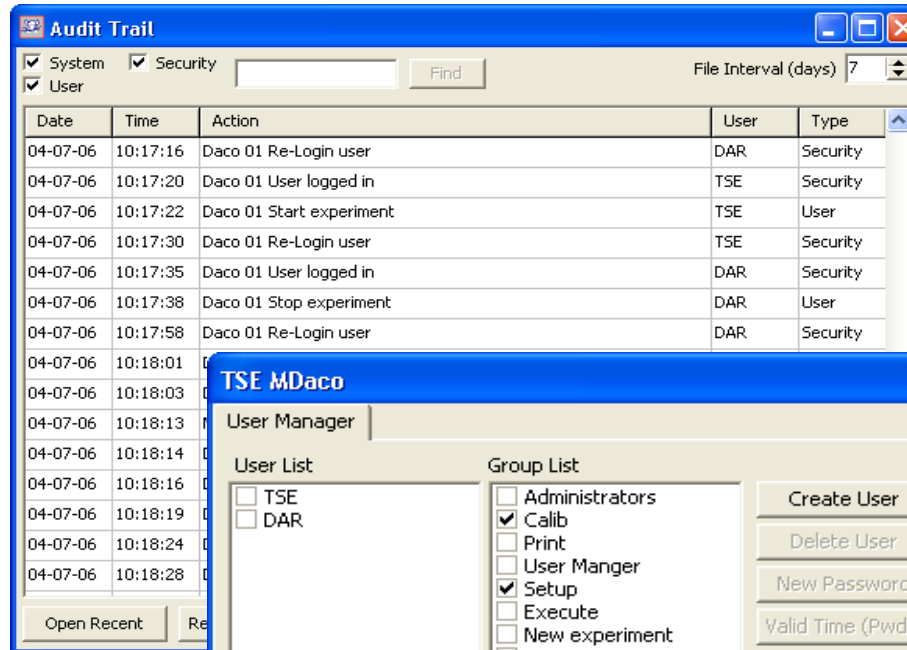


Good Laboratory Practice GLP

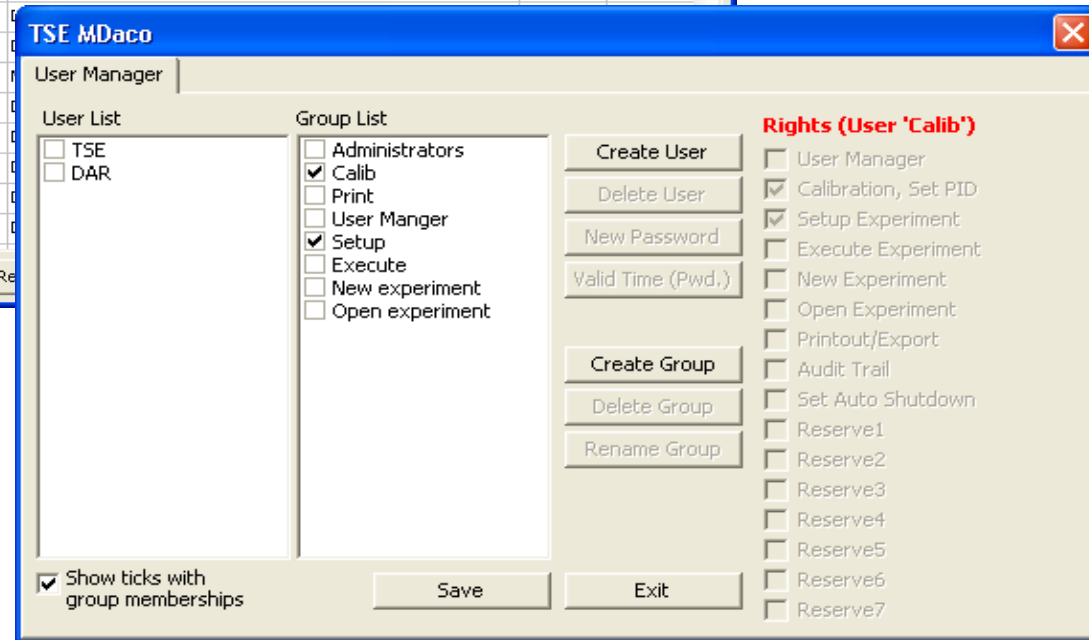


Inhalation Software GLP Version (DACO GLP)

- **User Manager**
 - Security requirements
 - Rights per user
- **Audit Trail**
 - System Changes
 - User Manipulation
 - Security Information
 - Date and time stamped
- **Locked data files**
 - Fraud resistant
 - Electronic Signature
- **User (identification)**
 - User responsibility
- **Warning windows**



Date	Time	Action	User	Type
04-07-06	10:17:16	Daco 01 Re-Login user	DAR	Security
04-07-06	10:17:20	Daco 01 User logged in	TSE	Security
04-07-06	10:17:22	Daco 01 Start experiment	TSE	User
04-07-06	10:17:30	Daco 01 Re-Login user	TSE	Security
04-07-06	10:17:35	Daco 01 User logged in	DAR	Security
04-07-06	10:17:38	Daco 01 Stop experiment	DAR	User
04-07-06	10:17:58	Daco 01 Re-Login user	DAR	Security
04-07-06	10:18:01			
04-07-06	10:18:03			
04-07-06	10:18:13			
04-07-06	10:18:14			
04-07-06	10:18:16			
04-07-06	10:18:19			
04-07-06	10:18:24			
04-07-06	10:18:28			



TSE MDaco

User Manager

User List

- TSE
- DAR

Group List

- Administrators
- Calib
- Print
- User Manger
- Setup
- Execute
- New experiment
- Open experiment

Buttons: Create User, Delete User, New Password, Valid Time (Pwd.), Create Group, Delete Group, Rename Group

Rights (User 'Calib')

- User Manager
- Calibration, Set PID
- Setup Experiment
- Execute Experiment
- New Experiment
- Open Experiment
- Printout/Export
- Audit Trail
- Set Auto Shutdown
- Reserve1
- Reserve2
- Reserve3
- Reserve4
- Reserve5
- Reserve6
- Reserve7

Show ticks with group memberships

Buttons: Save, Exit

IQ

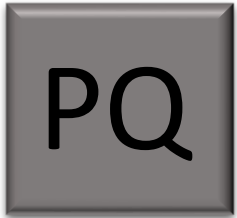
Installation Qualification verifies that an instrument or unit of equipment being qualified (as well as its sub-systems and any ancillary systems) have been installed and configured according to the manufacturer's specifications or installation checklist.

OQ

Operational Qualification is there to determine that equipment performance is consistent with the user requirement specification within the manufacturer-specified operating ranges.

PQ

Performance Qualification In this phase, the qualification and validation team verifies and documents that the equipment is working with reproducible results within a specific working range in simulated real-world conditions.



Document Version: Installation Qualification V
Version Date: 2013-02-20

7. Hardware Connection

The components delivered from TSE are function and integrated into the system. The positioning of the various components is described in Appendix A to identify the relevant positions. If required, the relevant Operating Instructions for the installation and operational procedure should be confirmed that each component is tested then the tests made by each section. In the event of an expansion, it should be confirmed that each component is tested then the tests made by each section. In the event of an expansion, it should be confirmed that each component is tested then the tests made by each section.

7.1 Rodent System 1

No.	Component
1	Head / Nose-Only Exposure Unit 30 Ports for Critical Applications
2	Inhalation Control Unit
3	PC
4	Electronic Mass Flow Controller FlowAppl 20
5	Electronic Mass Flow Controller FlowAir 40 Y
6	Electronic Mass Flow Controller FlowOut 60
7	Electronic Mass Flow Controller FlowSample
8	Differential Pressure Measuring Unit - 12.5 to + 12.5 mbar
9	Differential Pressure Measuring Unit 0 to + 25 mbar
10	Temperature and Humidity Measuring Device

Document Version: Operational Qualification V
Version Date: 2013-02-20

4.3 Air Tight Test

4.3.1 Air Tight Test for the Enclosure

Objective(s): Demonstrate that the enclosure is air tight.

Test Acceptance Criteria:

- Internal enclosure temperature
- Internal pressure
- Atmospheric pressure
- Temperature variation

Temperature of Enclosure [°C] + 273.15	Atmospheric Pressure [Pa]	Time	Enclosure Negative Pressure [°C] (for Record only)	Correction of the Final Reading 2 Pa	Enclosure Pressure = Final Reading 2 Pa	Correction of Pre-Initial Reading 1 Pa	Enclosure Leak Initial Absolute	Hourly Leak Rate Reading obtained at Time, in hours

Document Version: DACO Validation V.15
Version Date: 2012-01-22

13.2.5 User Manager - Access Rights

Objective(s): Demonstrate that the system can limit access rights for each user.

Test Acceptance Criteria: Each user can only access those areas to which they have the rights.

Prerequisite(s): A successful login has been made with the following administrator user name and password:

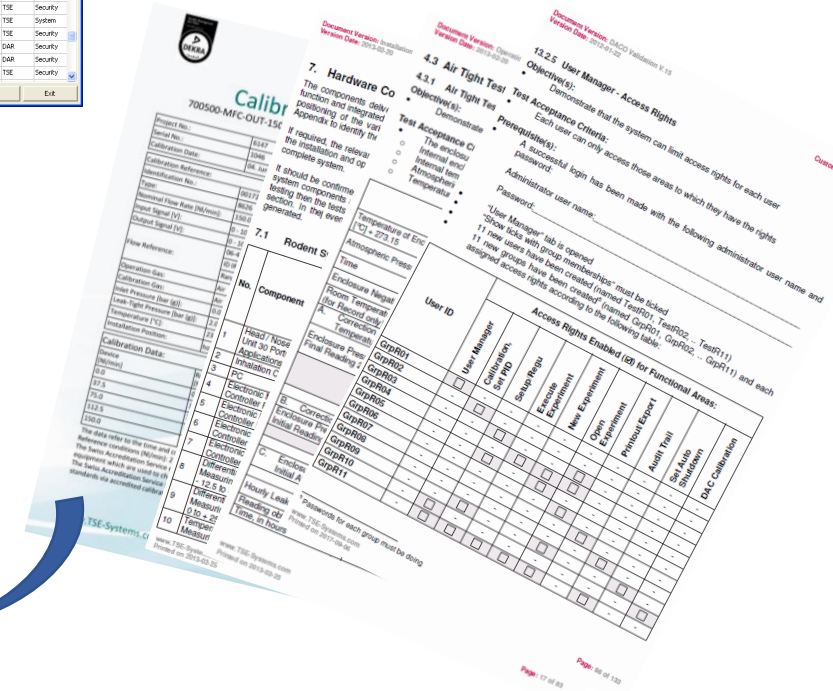
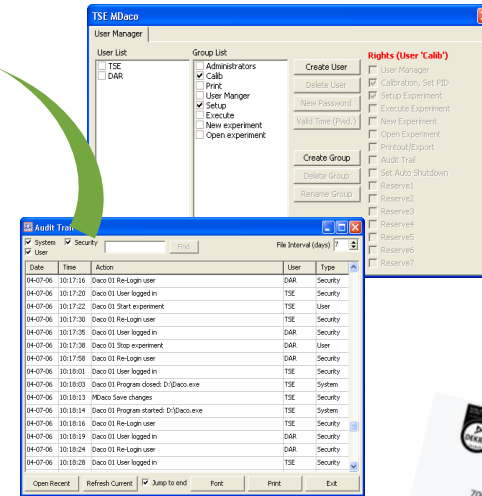
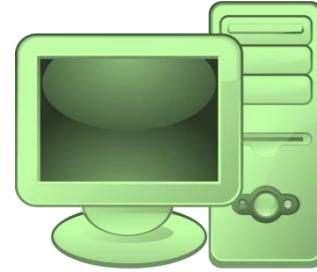
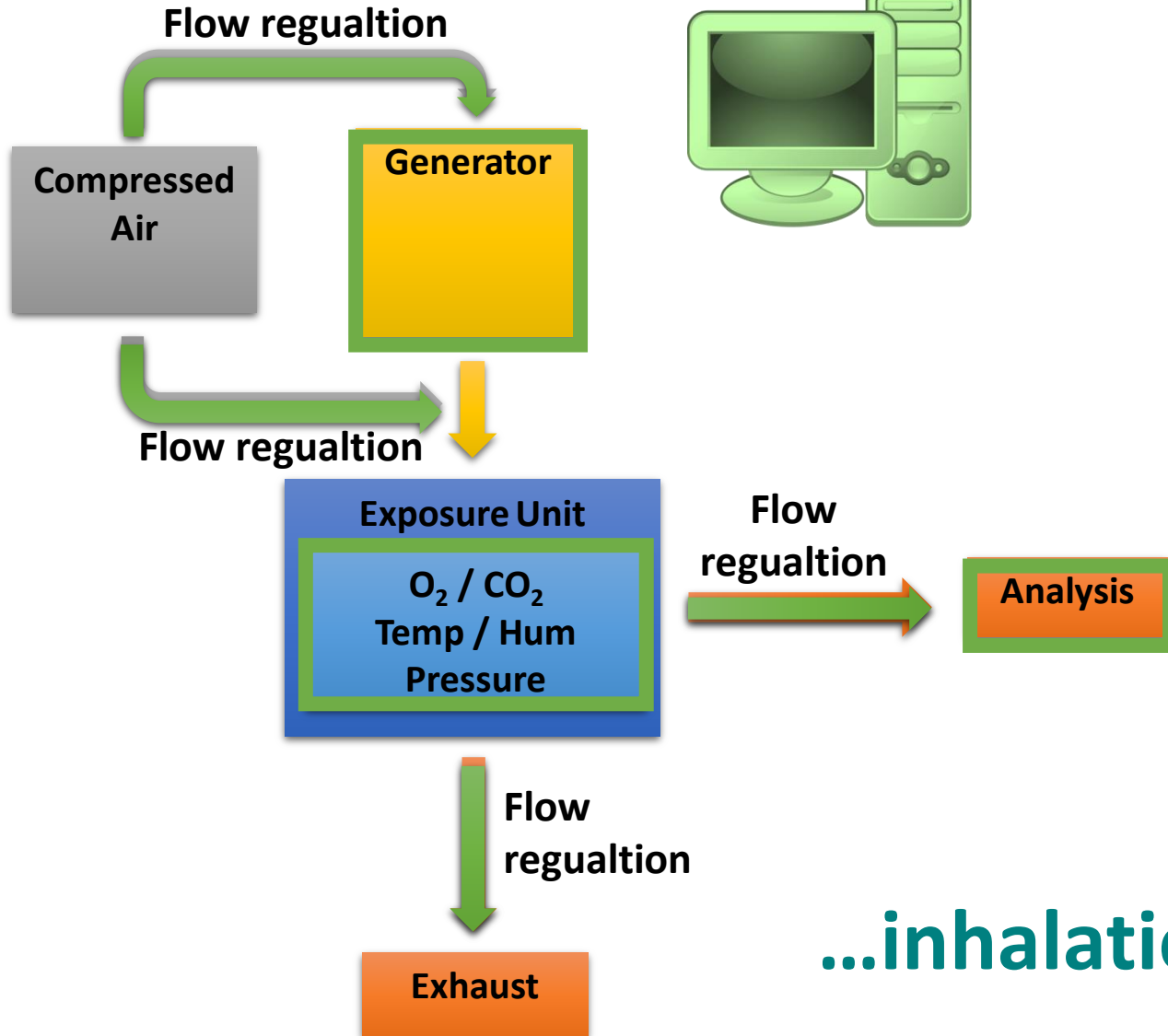
Administrator user name: _____
Password: _____

"User Manager" tab is opened
"Show ticks with group memberships" must be ticked
11 new users have been created (named GrpR01, TestR02, .. TestR11)
11 new groups have been created⁵ (named GrpR01, GrpR02, .. GrpR11) and each assigned access rights according to the following table:

User ID	Access Rights Enabled (E) for Functional Areas:									
	User Manager	Calibration, Set PID	Setup Regu	Execute Experiment	New Experiment	Open Experiment	Printout Export	Audit Trail	Set Auto Shutdown	DAC Calibration
GrpR01	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR02	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR03	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR04	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR05	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR06	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR07	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR08	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR09	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR10	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GrpR11	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Project No.: 4621
Customer No.: D14379

OECD guidelines and GLP compliance...



...inhalation toxicological study system

Thank You!

Questions/ Comments?



Valentin Makarov



БГА

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