About SCHOTT pharma services

Analytical Packaging and Development Support

SCHOTT is one of the world's leading suppliers of parenteral packaging for the pharmaceutical industry. The unique combination of specialized analytics and our expertise in materials, products, and processes enables SCHOTT pharma services to support pharmaceutical companies by finding solutions to the most challenging packaging issues. SCHOTT pharma services supports customers worldwide to avoid stability issues resulting from drug / container interaction and provide development support.

Questionnaire for Extractables & Leachables Studies

Contact details
SCHOTT pharma services assists clients with price quotes and contract agreements for projects of all sizes. Please feel free to contact us for your sales and support needs:

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Certifications & Quality
Laboratory Accreditation DIN EN ISO/IEC 17025
FDA registered laboratory

Company and contact information

Company: _____

Company Address:

_____

_____

Contact Name: _____

Phone No.: _____

E-mail: _____

Container closure system or component to be evaluated

- ☐ Glass vial
- ☐ Pre-fillable glass syringe (Luer cone)
- ☐ Pre-fillable glass syringe (staked needle)
- ☐ Glass cartridge
- ☐ Glass ampoule
- ☐ Rubber closure for vial
- ☐ Rubber stopper for syringe or cartridge
- ☐ Tip cap syringe or cartridge
- ☐ Other rubber component
- ☐ Other: _____
- ☐ Polymer syringe
- ☐ Polymer cartridge
- ☐ Polymer vial
- ☐ Polymer container (other)
- ☐ Silicone tube
- ☐ Tube (other material than silicone)
- ☐ Filter
- ☐ IV Bag

Container size: _____ Filling volume: _____ mL

Materials of container closure components (write part number / type, if known)

- ☐ Type I glass (borosilicate)
- ☐ Type II glass
- ☐ Type III glass
- ☐ Bromobutyl rubber
- ☐ Chlorobutyl rubber
- ☐ Rubber (other)
- ☐ Other: _____
- ☐ COC / COP
- ☐ PP
- ☐ Polymer (other): _____
- ☐ Silicone

Part No.: _____ Type: _____

Sterilization conditions

Component: _________ Condition:
☐ ETO
☐ Autoclaving, Condition: ____ °C ____ min.
☐ Terminal sterilization
☐ Gamma, Dose: _____ kGy
☐ Depyrogenization, Condition: ____ °C ____ min.
☐ Other: _________________

Component: _________ Condition:
☐ ETO
☐ Autoclaving, Condition: ____ °C ____ min.
☐ Terminal sterilization
☐ Gamma, Dose: _____ kGy
☐ Depyrogenization, Condition: ____ °C ____ min.
☐ Other: _________________

Component: _________ Condition:
☐ ETO
☐ Autoclaving, Condition: ____ °C ____ min.
☐ Terminal sterilization
☐ Gamma, Dose: _____ kGy
☐ Depyrogenization, Condition: ____ °C ____ min.
☐ Other: _________________

Do you need support for sample preparation / sterilization of samples?
☐ YES ☐ NO

If yes, for the following components:

____

Note: Recommendation for preparation of samples for extractables study to apply for all components the same sterilization conditions as will be applied in the final production process.

Focus of extractables and leachables study

☐ Material characterization

☐ Development

☐ Validation of Packaging

☐ Registration of Packaging of Pharmaceutical Drug Product

☐ NDA submission for human drug

☐ ANDA submission for human drug

☐ Other: _____

Europe (EMEA): ☐ USA (FDA): ☐ Asia (_____): ☐

Other (_____): ☐ Comment: _____

Requirements for extractables and leachables study

☐ AET (Analytical evaluation threshold): ____ µg/unit ____ µg/mL

Support for toxicological assessment

Do you need support for toxicological assessment of the study results?

☐ YES ☐ NO ☐ Maybe

Are you interested in support from toxicological assessment company (partner of SCHOTT pharma services)?

☐ YES ☐ NO

Extractables study *(Please fill out with available information)*

Material information

Glass: Glass type, tubular glass or molded glass, pretreatment:

_____
_____

Rubber and polymers: Additives, cross-linking agents, monomers, catalysts, fillers, residual solvents, adhesives, potential degradation products, curing process (e.g. sulphur):

_____
_____
_____

Guideline requirements

- ☐ USP <1663>
- ☐ ISO 10993-18
- ☐ PQRI
- ☐ ICH Q3D / USP <232>
- ☐ Other: _____

Extraction conditions

Reflux extraction is used as a standard condition.

If other extraction condition than reflux will be required, please mention:

- ☐ 37 °C, 72 h
- ☐ 50 °C, 72 h
- ☐ 70 °C, 24 h
- ☐ 121 °C, 1h (aqueous only)
- ☐ Ultrasonic extraction
- ☐ Exhaustive extraction (ISO 10993-12)
- ☐ Simulated-use extraction
- ☐ Exaggerated extraction

☐ Other extraction condition:

_____
_____
_____
_____
_____

Solvents

The solvents for the extractables study are chosen in alignment with PQRI, USP <1663>, USP <232> and ICH Q3D recommendations.

If specific solvents shall be used for the extractables study, please fill out:

- ☐ Ultrapure water
- ☐ Aqueous buffer solution (acidic), pH: _____
- ☐ Aqueous buffer solution (alkaline), pH: _____
- ☐ Isopropanol (IPA)
- ☐ Hexane (HEX)
- ☐ Dichloromethane (DCM)
- ☐ Other: _____
- ☐ Other: _____
- ☐ Other: _____

Analyses of Volatile Organic Compounds (VOCs)

In a standard protocol headspace analyses by HS-GC/MS on the neat materials (no extraction) are applied

If other methods are requested, please mention:

- ☐ Other: _____

Analyses of Semi Volatile Organic Compounds (SVOCs)

In a standard protocol, the following methods are applied for analyses of SVOCs:

- For aqueous solvents: Liquid-liquid extraction + GC/MS
- For organic solvents (e.g. IPA, hexane, DCM): GC/MS

If other methods are requested, please mention:

- ☐ Other: _____

Analyses of Non Volatile Organic Compounds (NVOCs)

In a standard protocol target screenings by LC/MS, LC/UV are conducted for the following target compounds:
Rubber or polymer additives, anti-oxidants, slip agents, UV-stabilizers, degradation products

If other target substances shall be screened or specific methods are requested, please mention:

- ☐ Other: _____

Analyses of totally extractable silicone

In a standard protocol the following method will be applied: extraction with organic solvent + GF-AAS

Required for extractables study? (Note: Recommended for siliconized components)

☐ YES ☐ NO

Elemental impurities ICH Q3D / USP <232>

In a standard protocol 34 elements of ICH Q3D / USP <232> will be quantified:
Cd, Pb, As, Hg, Co, V, Ni, Tl, Au, Pd, Ir, Os, Rh, Ru, Se, Ag, Pt, Li, Sb, Ba, Mo, Cu, Sn, Cr, Al, B, Ca, Fe, K, Mg, Mn, Na, W, Zn

Characterization of one additional "glass" element recommended: Si *(note: only for glass packaging)*

If further additional elements shall be characterized, please mention:

☐ Additional elemental impurities / metals requested:

_____

Anions

In a standard protocol an aqueous extract is analysed by IC method for some of the following target compounds:
Fluoride, Bromide, Chloride, Nitrate, Sulphate, Phosphate, Formate, Acetate

If other extract solutions shall be characterized, please mention:

☐ Other: _____

Other requirements for specific target substances (e.g. low molecular aldehydes, curing agents, organic acids)

For specific target substances as e.g. low molecular aldehydes (formaldehyde and acetaldehyde), cross-linking agents (e.g. TMP-TMA for needle glue) or organic acids specific methods may be necessary.

If indicated please mention:
Target substance: Name: _____ CAS-no.: _____
Method requirements: _____

Accelerated screening study

Accelerated leachables screening study requested:
☐ YES ☐ NO

Note: An accelerated leachables screening study is recommended to fill the gap between extractables and leachables testing. The accelerated test conditions will be aligned with ICH recommendations.

Leachables study ***(Please fill out with available information)***

Container closure system – short description:

_____
_____
_____
_____
_____

Drug product information

Drug product information with regards to composition of the drug formulation and MSDS is required for identification of suitable analytical methods and due to safety requirements of the laboratory.

Name of the drug product: _____

Name of the active drug substance: _____

CAS No. of the active drug substance: _____

MSDS of active drug substance available: ☐ YES ☐ NO

Composition of the drug formulation:

_____
_____
_____
_____

Does the drug formulation contain any CMR (carcinogenic, mutagenic or reproduction toxic) substances?
☐ YES ☐ NO

pH-range of drug formulation: _____ - _____

Comment: _____

Drug product application

Dosage information: In maximum up to ____ units of ____ mL per day will be administered.

Filling volume of drug product in container closure system: ____ mL

Which is the desired shelf life of the drug product?

_____years

Real-time storage condition of the final drug product:

☐ 2 – 8 °C ☐ 25 °C ____% r.h. ☐ Other: _____ °C, _____ % r.h.

Type of drug product:

☐ aqueous liquid formulation Organic content: ☐ low ☐ high

☐ non-aqueous liquid formulation

☐ lyophilized drug product

Guideline requirements

☐ USP <1664>

☐ PQRI

☐ ICH Q3D / USP <232>

☐ ICH Q1A (R2) (storage conditions shall be aligned with this guideline)

☐ ICH M7

☐ Other: _____

Method development and validation

Validated methods are required for submission of drug product in container closure system.

In other cases please state:

Full method validation required: ☐ YES ☐ NO

Samples for method development and validation:

Sample A: 1000 mL of drug matrix solution filled into a clean glass bottle

Sample B: 100 mL of drug matrix solution filled into a clean polymer tubes or polymer bottle

These samples A and B can be provided:

☐ YES ☐ NO

Comment: _____

Storage Conditions

The storage of the samples will be conducted (or organized) by customer: ☐ YES ☐ NO

The storage of samples shall be conducted by SCHOTT? ☐ YES ☐ NO

Storage conditions for samples:

Condition 1:

☐ Accelerated leachables ☐ Long-term leachables (real time)

T: _____ °C _____ % r.h. Number of time points: _____

Time points: _____

Orientation for storage: ☐ Upright ☐ Inverted ☐ Sideward (horizontal)

Condition 2:

☐ Accelerated leachables ☐ Long-term leachables (real time)

T: _____ °C _____ % r.h. Number of time points: _____

Time points: _____

Orientation for storage: ☐ Upright ☐ Inverted ☐ Sideward (horizontal)

Comment: _____

Number of batches

How many batches shall be tested per each condition and time point? _____

(Note: E.g. 3 different batches are recommended for determination of batch to batch variability)

Blank samples

The following blank samples are required for each time point:

Blank samples A: 500 mL of drug solution stored in a clean glass bottle

Blank samples B: 100 mL of drug solution stored in a clean polymer tubes or polymer bottle

Can these samples be provided for each time point: ☐ YES ☐ NO

Comment: _____

Availability of target compounds

Substance list of target leachables is available and will be provided:

☐ YES ☐ NO ☐ Partially available: _____

Substance list of target leachables will be available after completion of extractables study and toxicological assessment: ☐ YES ☐ NO

Based on the current information the following target leachable compounds shall be determined:

Organic target leachable compounds:

Name:	CAS-no.
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

Inorganic target leachable compounds:

Name:
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Methods for analyses

Depending on the list of target leachables compounds the following methods will be applied:
SVOCs: HS-GC/MS
VOCs: GC/MS
NVOCs: LC/MS, LC/UV
Elemental impurities: ICP (HR ICP-MS, ICP-MS or ICP-OES)
Anions: IC
“Free” silicone: GF-AAS

Specific requirements for methods:

_____

_____

_____

Comment: _____

Additional leachables screening

Note: Additional leachables screening methods are recommended for risk minimization e.g. for identification of “secondary” leachables or other unknown unexpected compounds from the container closure system or secondary packaging

Additional leachables screening requested: ☐ YES ☐ NO

Specific requirements for screening:

_____

_____

Study for label (ink and glue)

Note: For polymer packaging with labels recommended

Shall a label / ink study be included? ☐ YES ☐ NO

Only if yes:

Label with ink and glue used for polymer packaging? ☐ YES ☐ NO

Label study requested for: ☐ Extractables ☐ Leachables

Other requirements

_____

_____

_____

_____