Residual Solvents

USP □ 467□ classifies solvents into **Class 1 (to be avoided), Class 2 (to be limited), and Class 3 (low toxic potential)** and prescribes **headspace GC procedures (A, B, C)** for screening, confirmation, and quantification of residual solvents. Testing is required only for solvents used or produced in manufacture or purification; if ingredient-level calculations show compliance, product testing may be unnecessary.

Practical step?by?step procedure (bench?ready, follow your validated SOP)

1. **Decide scope** — Identify which solvents were used/possible in manufacture; test only those or follow full USP panel.
2. **Sample preparation** — Accurately weigh representative sample into **10-mL headspace vials** (typical), seal with appropriate septa; for solids like NaCl, use the mass specified by your SOP to achieve target headspace sensitivity.
3. **Internal standard and diluent** — Add internal standard (e.g., DMSO or other USP-recommended IS) and diluent if required by the chosen procedure; vortex and equilibrate per method.
4. **Headspace conditions** — Place vials in headspace autosampler; equilibrate at the method temperature/time (e.g., 80–100 °C for many matrices) to partition volatiles into the headspace. Use the headspace parameters validated for your matrix.
5. **GC analysis — Procedure A (screening)** — Inject headspace into GC fitted with a USP-specified column (e.g., DB-Select 624 UI) and FID; compare retention times to standards. If any solvent exceeds the screening limit, proceed to Procedure B (confirmation) and/or Procedure C (quantification).
6. **Calibration and standards** — Run multi-level calibration standards and system suitability checks (response factors, resolution). Use USP reference standards where available.
7. **Reporting** — Report concentrations against USP limits for the solvent class; document whether compliance was shown by calculation or by testing. For sodium chloride the monograph notes: “Residual solvents 467: meets the requirements.”

Tips for reliable results

- **Use USP reference standards** and prepare fresh calibration mixes.

- **Validate headspace parameters** (equilibration time/temp) for NaCl matrix to avoid under- or over-estimation.
- **Run blanks and spiked controls** at or near limits to confirm method sensitivity.

Cautions and safety

- **Flammable solvents**: handle standards and samples in ventilated areas; keep ignition sources away. **Dispose** solvent wastes per institutional hazardous-waste rules.
- **Instrument safety**: follow manufacturer guidance for headspace autosampler and GC (pressure, septa, liners).

Bottom line: Test sodium chloride only for solvents relevant to its manufacture or demonstrate compliance by ingredient-level calculation; when testing, follow USP □ 467□ headspace-GC procedures (A/B/C), validated headspace conditions, and USP standards.

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