# Quality and Testing Standards

CytoPure™ Human Platelet Lysate — PLUS · XF · GI (Research Grade)

## 1. Purpose and scope

This document defines the quality standards, release testing, and manufacturing controls applied to every lot of CytoPure™ Human Platelet Lysate. It applies to CytoPure™ PLUS, CytoPure™ XF, and CytoPure™ GI in all fill volumes.

CytoPure™ products are for research use only, including the culture and expansion of primary cells and other research cell systems. The products are designed to provide consistent, well-characterized supplementation for research applications.

CytoPure™ products are not intended for diagnostic procedures, therapeutic use, administration to humans or animals, or other clinical applications. The quality standards described in this document are established to support consistent product quality, lot-to-lot performance, traceability, and suitability for use.

## 2. Quality management system

Cytologics maintains a documented Quality Management System (QMS) designed to support the consistent manufacture, testing, release, and supply of high-quality research-use-only human biological products. The QMS encompasses all activities from supplier qualification and raw material receipt through manufacturing, quality control testing, product release, storage, shipping, customer feedback, and continual improvement.

The QMS includes documented procedures for:

- Supplier qualification and monitoring
- Raw material acceptance
- Donor traceability
- Manufacturing process control
- Equipment calibration and maintenance
- Environmental controls
- Batch record documentation
- Lot release testing
- Certificate of Analysis generation
- Document control
- Training and competency
- Deviations and CAPA
- Complaint investigations
- Change control
- Record retention
- Risk management

The QMS is designed to support reproducible manufacturing, product consistency, and complete traceability for all Cytologics products intended for research use.

## 3. Release testing standards

Every lot is tested against the following acceptance criteria before release. Results for the specific lot supplied are reported on the accompanying Certificate of Analysis.

The panel is structured on the identity, purity, and biological activity framework described in the joint AABB and International Society for Cell & Gene Therapy publication on human platelet lysate as a cell culture supplement (Bieback et al., Transfusion 2019;59:3448–3460).

| Test | Method | Acceptance criteria | Quality Attribute / Rationale |
|---|---|---|---|
| **Physical** | | | |
| pH | USP <791> | 7.0–7.8 | Confirms the product maintains a pH range suitable for cell culture applications. |
| Osmolality | USP <785> | 250–350 mOsm/kg | Confirms the product is within the physiological range and will not impose osmotic stress when added to basal medium. |
| **Biochemical** | | | |
| Total protein | USP <1057> | 4.0–7.0 g/dL | Verifies total protein concentration, an indicator of the product's capacity to support cellular growth and proliferation. |
| **Microbiological** | | | |
| Sterility (bacteria and fungi) | USP <71> | No growth | Confirms the product is free of bacterial and fungal contamination. |
| Mycoplasma | Enzymatic | Not detected | Confirms the absence of mycoplasma, a contaminant that is not detected by routine sterility testing and that alters cell behavior without visible turbidity. |
| Endotoxin | USP <85> | < 5.0 EU/mL | Confirms low endotoxin levels to minimize adverse effects on cultured cells. |
| **Biological** | | | |
| Cell growth verification | Primary human cell proliferation | Pass | Confirms each lot supports proliferation of primary human cells, verifying biological performance rather than composition alone. |
| **Donor** | | | |
| Donor viral testing | 21 CFR Part 610 | Negative / non-reactive | Documents infectious-disease screening performed on source platelet units by qualified blood-center suppliers. |
| **Product-specific** | | | |
| Gamma irradiation dose | Dosimetry | 25–38 kGy (internal dose) | Confirms each CytoPure™ GI lot received the specified terminal irradiation dose. Applies to CytoPure™ GI only. |

The complete donor infectious disease testing panel, the assays used, and the regulatory basis for each are described in CYT-VSD-009 (Viral Safety and Donor Qualification Statement).

### Lot-to-Lot Consistency

Cytologics routinely trends release results across consecutive production lots to evaluate lot-to-lot consistency and identify potential process variation. The figures below illustrate measured results for representative release parameters across consecutive CytoPure™ XF production lots. No lot pre-screening is applied; every lot manufactured during the stated period is shown.

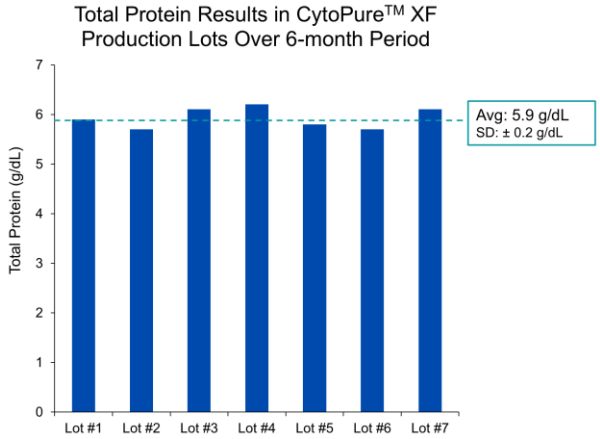


**Figure 1.** Total protein by USP <1057> across seven consecutive CytoPure™ XF production lots released over six months. Mean 5.9 g/dL, standard deviation ± 0.2 g/dL, against a release specification of 4.0–7.0 g/dL. Dashed line, lot mean.

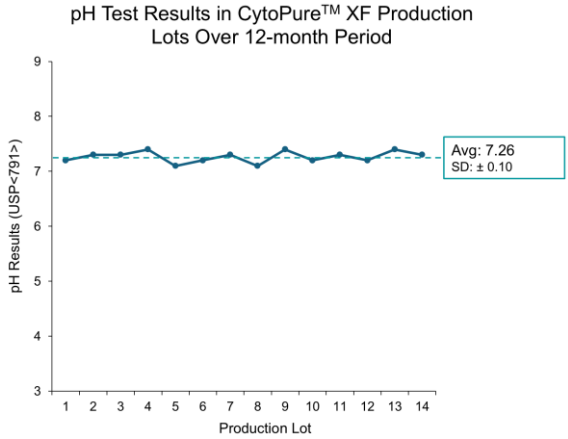


**Figure 2.** pH by USP <791> across fourteen consecutive CytoPure™ XF production lots released over twelve months. Mean 7.26, standard deviation ± 0.10, against a release specification of 7.0–7.8. Dashed line, lot mean.

## 4. Raw material qualification

CytoPure™ is manufactured from platelet units collected at U.S. Food and Drug Administration (FDA)-licensed and AABB-accredited blood centers in the United States. These units were originally intended for use in patient transfusion and met all donor eligibility criteria at the time of collection.

- Blood center suppliers are qualified and monitored under the supplier qualification procedure before any material is accepted.
- Incoming platelet units are inspected and accepted against defined criteria; units that do not meet those criteria are rejected.
- Unit-level identifiers are recorded at receipt and retained, establishing traceability from the finished lot back to the contributing collections.
- Donor pools typically include greater than 300 individuals. Pooling across a large number of donors helps reduce donor-to-donor variability and contributes to lot-to-lot consistency.

## 5. Manufacturing controls

Manufacturing is performed in the United States under documented procedures with batch records completed for every lot. The process comprises multi-donor pooling, controlled lysis to release platelet growth factors, fibrinogen depletion, sterile filtration through 0.2 µm filtration systems, and aseptic filling. Critical manufacturing steps are performed according to controlled procedures and documented in lot-specific batch records.

Heparin sodium (porcine origin) is used in the manufacture of **CytoPure™ PLUS only**. CytoPure™ XF and CytoPure™ GI are not manufactured with heparin at any stage. CytoPure™ GI lots receive terminal gamma irradiation at an internal dose of 25–38 kGy.

### Packaging and product identification

Nalgene™ Square PETG media bottle with a polyethylene closure and tamper-evident seal. Each bottle is inspected for seal integrity prior to release.

| Fill volume | Bottle | Catalog numbers (PLUS / XF / GI) |
|---|---|---|
| 50 mL | 60 mL | 1908-C050 / 1909-C050 / 1910-C050 |
| 100 mL | 125 mL | 1908-C100 / 1909-C100 / 1910-C100 |
| 500 mL | 500 mL | 1908-C500 / 1909-C500 / 1910-C500 |

### Lot identification and records

Lot numbers follow the convention yyC##, where yy is the last two digits of the year of manufacture and ## is the assigned lot number within that year (01 through 99). Lot numbers provide traceability to the applicable production batch and source material records. Batch records, release testing records, and raw material receipt records are retained for 7 years.

## 6. Product handling and stability

| | |
|---|---|
| **Storage** | Store at ≤ –20°C. For storage beyond 12 months, –80°C is recommended. |
| **Shelf life** | 3 years from date of manufacture when stored at ≤ –20°C. The expiration date for each lot is stated on the product label and on the lot-specific Certificate of Analysis. |
| **Thawing** | Thaw in a 37°C water bath until no ice remains. Thawing overnight at room temperature or at 2–8°C is not recommended. |
| **Freeze-thaw** | CytoPure products have been evaluated through up to three freeze-thaw cycles under defined conditions, with less than 5% loss of total protein, minimal precipitate formation, and stable pH. Aliquot on first thaw and return aliquots to ≤ –20°C to avoid repeated cycles. |
| **Complete medium** | Complete medium prepared with CytoPure™ may be stored for up to 30 days at 2–8°C. |
| **Particulates** | Particulates may be observed after thawing and during storage. The presence of visible particulates does not necessarily indicate product failure and may be reduced by centrifugation at 2000 × g for 8 minutes or brief incubation at 37°C. Do not filter the undiluted product. If filtration is desired, dilute CytoPure™ into complete medium first, then filter the complete medium. |

## 7. Documentation

The following documentation is available for CytoPure™ products.

| Document | Number |
|---|---|
| Certificate of Analysis (lot-specific) | CYT-COA-… |
| Product Information Sheet | CYT-HPL-… |
| Safety Data Sheet | CYT-SDS-… |
| Certificate of Origin | CYT-COO-016 |
| Viral Safety and Donor Qualification Statement | CYT-VSD-009 |

| Document | Number |
|---|---|
| TSE/BSE Risk Mitigation Statement | CYT-TSE-002 |
| Quality and Testing Standards (this document) | CYT-QTS-031 |

Lot-specific Certificates of Analysis are provided with each shipment. Additional product and quality documentation is available upon request.

## 8. Non-conformance and technical support

Cytologics does not publish a fixed replacement schedule. Before any product is replaced, Cytologics technical support will work with the customer to determine whether the observed issue may be attributable to media formulation, basal medium selection, supplementation, cell type, culture conditions, or handling procedures. This technical assessment helps identify the likely source of the observed issue and often resolves the issue without requiring product replacement.

When reporting an issue, please provide the following so that the investigation can begin immediately:

- Catalog number and lot number
- Description of the observation
- Cell type, source, and passage number
- Basal medium and supplement concentration
- Seeding density and culture format
- Storage and thawing history of the product

**Note** Complaints and investigations are handled under the documented complaint and CAPA procedures described in section 2, and records are retained for 7 years.

## Related documentation

This document is part of the CytoPure™ technical documentation library. Refer to the following companion documents:

- **CYT-COA-1909** Certificate of Analysis and Release — CytoPure™ XF
- **CYT-VSD-009** Viral Safety and Donor Qualification Statement
- **CYT-COO-016** Certificate of Origin — CytoPure™ Human Platelet Lysate
- **CYT-TSE-002** TSE/BSE Risk Mitigation Statement
- **CYT-TDS-078** Technical Data Sheet — CytoPure™ Human Platelet Lysate

**IMPORTANT** For Research Use Only. Not for use in diagnostic or therapeutic procedures. Not for administration to humans or animals. CytoPure™ contains human-derived material and should be handled as potentially infectious using appropriate biosafety practices and universal precautions.

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