

TruCulture Custom Tube Development

TruCulture® is a whole blood culture system specifically designed for clinical research and standardized to deliver highly reproducible results. By integrating blood collection and culture into a single, closed system, TruCulture minimizes immune cell manipulation while preserving the full biological complexity of whole blood — including all circulating cells, soluble factors, and Fc receptor-expressing cells that influence immune responses.

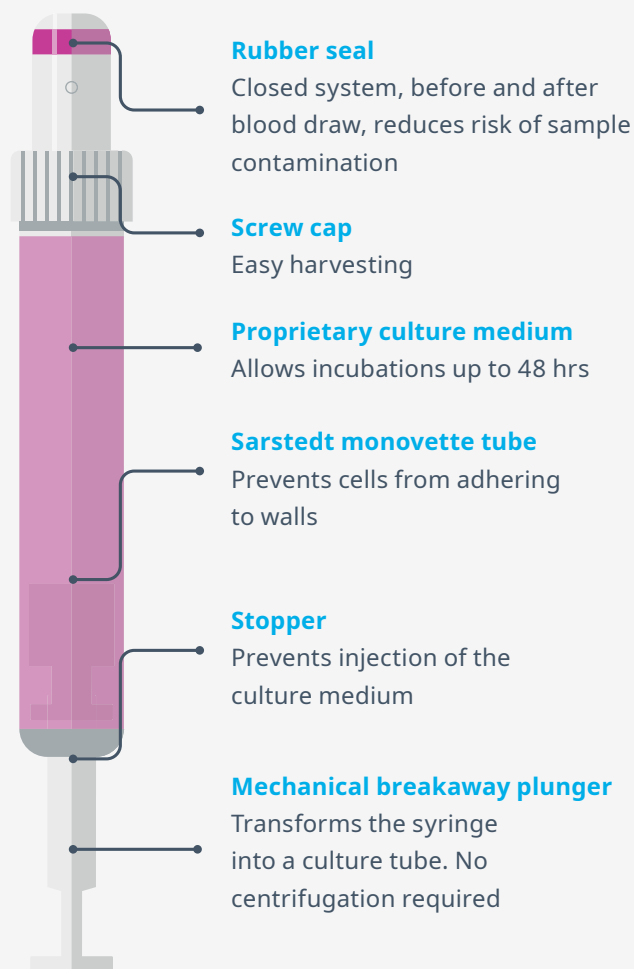
TruCulture provides an ideal ex vivo sample collection and culture solution for clinical trials, enabling a comprehensive assessment of immune function to support:

- Evaluation of dose-dependent effects of immune-modulating therapies
- Assessment of immune-related toxicity
- Monitoring pharmacodynamics (PD) responses

Pharmacodynamic (PD), dosing and safety studies each have distinct objectives and thus require a flexible, customizable culture system. TruCulture medium can be supplemented with a wide range of soluble substances, including immune stimulants and inhibitors targeting specific immune pathways of interest. Standard TruCulture tubes can be pre-loaded with commonly used, optimized stimulants such as LPS, anti-CD3/CD28 and TLR agonists.

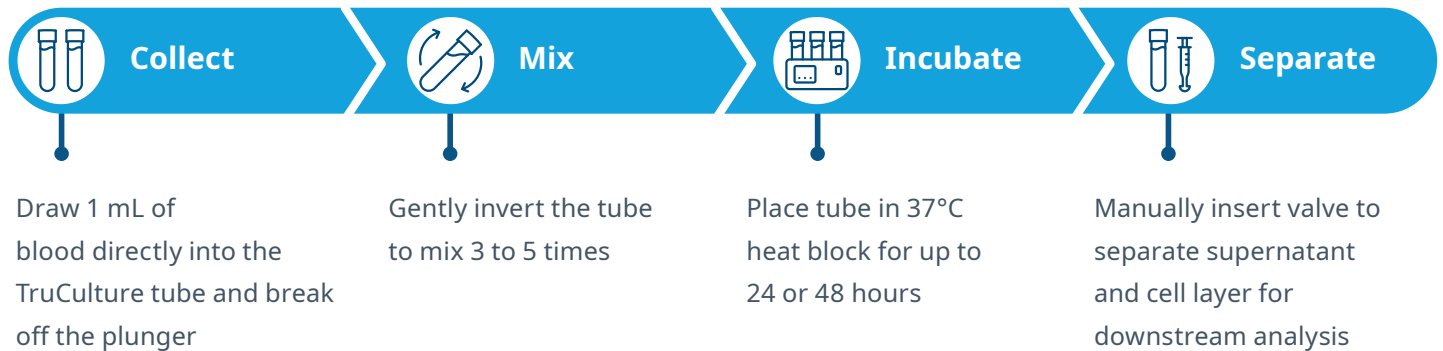
For novel agents — such as antibody-based biologics, small-molecule compounds, immune modulators, proprietary substances or combinations of substances — IQVIA Laboratories Protein Biomarkers team can develop custom TruCulture products through our structured optimization process. This development approach can be tailored to meet specific study objectives and customer requests.

TruCulture Tube



TruCulture procedure

TruCulture tubes are pre-loaded with cell culture media and immune stimulant(s) or drug candidates. Blood is drawn directly into the TruCulture tube and incubated in a dry heat block. Supernatants are collected by simply inserting a valve separator to separate cells from the culture supernatant.



TruCulture custom development process

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Tube design

Custom TruCulture tube development begins with the selection of the test substance(s), usually in consultation with our scientists. The specifics of the custom tube will be determined based on the specific objectives of the study and by the intended study population, including whether samples will be collected from healthy volunteers, patient cohorts or both.

Healthy donor pool

To ensure that TruCulture custom tubes perform as expected in the laboratory, initial validation testing for custom tubes is conducted using whole blood from an established healthy donor pool. The healthy donor pool is comprised of healthy adults (≥ 18 years of age) who meet all the following criteria:

1. No autoimmune diseases;
2. No chronic immune inflammatory diseases;
3. No circulatory problems or diseases;
4. No infection or symptoms of infections within 2 weeks of blood collection;
5. No major or minor surgeries in the last 3 months of blood collection;
6. No recent vaccinations in the last 6 weeks of blood collection;
7. Not on medications that can affect immune function (i.e. steroids);
8. Not pregnant.

General development process

IQVIA Laboratories Protein Biomarkers has a well-established development process for customized TruCulture products that can be further tailored according to customer needs. The general development process includes testing for: solubility, biological activity, stability and donor variability.



Solubility

To ensure that the custom substance is compatible with the TruCulture system, it must be soluble in the TruCulture medium.

Presence of precipitates will inevitably trigger activation of neutrophils (up to 50% of all leukocytes) and monocytes (up to 12% of all leukocytes). This activation could obscure analysis of the immune pathway of interest. Detection of precipitates will be evaluated by microscopy. Solubility will be further examined after a freeze-thaw cycle. If the custom TruCulture system involves a combination of substances, solubility will be examined first individually, then in combination. For substances that require a solvent before dilution into the aqueous medium, a negative control TruCulture tube will be developed with the same volume of the solvent added.



Biological activity

To ensure optimal biological activity is achieved with the custom substance, several doses will be titrated in the

TruCulture tube. Using information on the substance provided by the customer and published resources, a range of concentrations will be tested using whole blood from healthy donors. The optimal concentration of the substance will be decided in collaboration with the customer. If the custom TruCulture tube involves a combination of substances, biological activity will be assessed first individually, then in combination.



Stability

TruCulture tubes are frozen immediately after manufacturing to maximize their shelf life. For custom TruCulture tubes, the stability of the biological activity of the custom compound is investigated after a freeze-thaw cycle. TruCulture tubes should be stored at -20°C until use, and never re-frozen after thawing. Long-term (real-time) stability can be tested for tubes that are stored for months — or even years — based on customer request (at -20°C and thawed once prior to use).



Donor variability

Custom TruCulture tube development is conducted using fresh donor blood. Because immune responses vary due to individual differences, samples from a minimum of 3 healthy donors are tested to ensure optimization of custom products. Donor sample size can be increased upon request.

Data report

Customers can choose between a short report (Excel® file containing the labelled results and a short description of the methods used for these investigations), or an extended version.

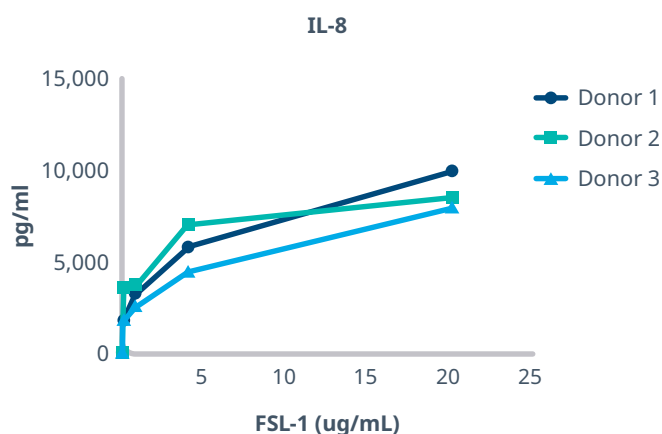
Delivery schedule

The time required to develop a custom tube depends on customer needs, project complexity and current projects in development at our lab. In general, development of custom TruCulture tubes takes 12 to 20 weeks. Once the customer accepts the final development results, the custom tubes can be manufactured within 4 to 6 weeks.

Examples of TruCulture development projects

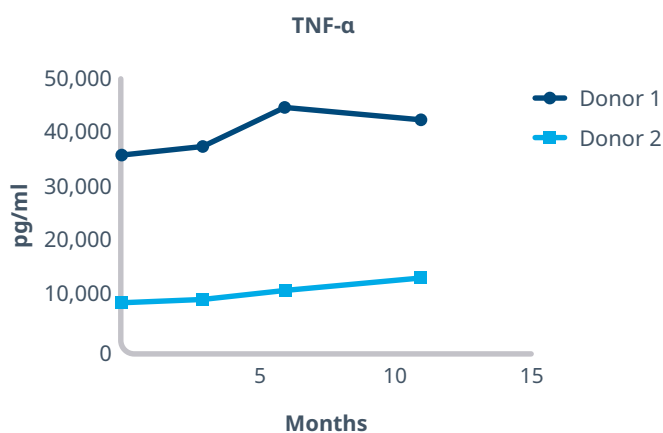
Example 1: Titration of compound

The following example will demonstrate the protocol to determine the optimal concentration of a substance to stimulate whole blood cultured in TruCulture tubes. In this example, the substance titrated is FSL-1 (synthetic diacylated lipoprotein, TLR2/6 ligand) at 5 different concentrations (0, 0.16, 0.8, 4, and 20 µg/mL). Whole blood from 3 healthy donors was drawn into TruCulture tubes supplemented with FSL-1 and incubated at 24 hours in a 37°C heat block, and the supernatant collected for IL-8 analysis. The figure below demonstrated an increase in IL-8 production from whole blood when stimulated with increasing concentrations. The selection of the dose of the stimulant is dependent on customer needs.



Example 2: Long-term stability

The following example demonstrates the typical data generated for TruCulture stability testing. A batch of the LPS+SEB TruCulture tubes were investigated for stability up to 11 months, per customer request. The tubes were manufactured and stored at -20°C. A selection of tubes were thawed and used to culture whole blood from 2 healthy donors at 0, 3, 6, and 11 months. The LPS+SEB tubes were evaluated for activity to stimulate TNF-α production. In the figure below, the data demonstrates that LPS tubes induced similar levels of TNF-α for up to 11 months at -20°C. Longer term stability testing is regularly conducted based on customer request.



Conclusion

IQVIA Laboratories Protein Biomarkers delivers custom TruCulture tube development to support clinical studies that require immune analysis. With decades of experience, our team is adept in customizing tubes for a variety of substances, both known and novel. TruCulture enables the profiling of in vivo immunity, with ex vivo analysis of pharmacodynamics, dosing and safety of pharmaceutical compounds. The versatility of the TruCulture system allows customization to meet unique customer needs and is well suited for efficient and reproducible immune profiling in multi-site clinical trials.