March 2021

QuantiFERON® Control Set Blood Collection Tubes Instructions for Use (Handbook)

For Research Use Only
Not for use in diagnostic procedures

REF	626015
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R2 MAT	1122891

Sample to Insight

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Contents

Intended Use

The QuantiFERON Control Set Blood Collection Tubes (QFN Control BCTs) consist of the QuantiFERON Nil and QuantiFERON Mitogen BCTs. QFN Control BCT workflow includes Blood Collection and Processing to generate plasma for the detection of IFN-γ. QFN Nil and Mitogen BCTs are intended to be used as negative and positive controls in conjunction with other QuantiFERON Antigen tubes, when workflow and donor controls are required.

The QFN Control BCTs are for Research Use Only and not for diagnostic use.

Description and Principle

Summary and explanation

The Mitogen tube serves as a positive control. This may be especially warranted where there is doubt as to the individual's immune status. The Mitogen tube may also serve as a control for correct blood handling and incubation for each specimen tested.

A low response to Mitogen may indicate that the blood sample might be nonreactive to antigens. This pattern may occur with insufficient lymphocytes, reduced lymphocyte activity due to improper specimen handling, incorrect filling/mixing of the Mitogen tube, or inability of the patient's lymphocytes to generate IFN-γ.

The IFN-γ level of the Nil tube can be subtracted from the Antigen tube/s and Mitogen tube IFN-γ level to adjust for background or nonspecific IFN-γ signal.

A QuantiFERON test is considered reactive for an IFN-γ response when the Antigen tube reads significantly above the Nil IFN-γ IU/ml value.

It is generally recommended to consider results where Nil > 8.0 IU/ml (high background) and/or Mitogen < 0.5 IU/ml are observed as indeterminate (due to uncertainty about blood handling and/or incubation and/or integrity of the specimen collected).

Materials Provided

Kit contents

Blood Collection Tubes **Catalog no.**		**200 tubes** **626015**
QuantiFERON Nil Tube (gray cap, white ring)	Nil	100 tubes
QuantiFERON Mitogen (purple cap, white ring)	Mitogen	100 tubes
Language Sheet	–	1

QFN Control BCTs are designed to draw the required volume of blood for stimulation. The contents of the BCTs have been dried onto the inner walls, and it is essential that the BCTs be thoroughly mixed with the blood to resolubilize them. Blood collected directly into the QFN Control BCTs must be transferred to a 37°C incubator as soon as possible and within 16 hours of blood collection (see Direct draw into QFN Control BCTs)

Alternatively, blood may be collected into a single lithium-heparin or sodium-heparin tube for storage prior to transfer to QFN Control BCTs and incubation. Blood specimens collected in heparin tubes can be stored at room temperature (17–25°C) but held for no more than 16 hours from the time of collection prior to transfer to QFN Control BCTs and subsequent incubation (see Blood collection into a heparin tube and then transfer to QFN Control BCTs with room temperature storage and handling). Blood specimens in heparin tubes may also be stored at 2–8°C for up to 48 hours prior to transfer to the QFN Control BCTs (see Blood collection into heparin tube and then transfer to QFN Control BCTs with refrigerated storage and handling).

Warnings and Precautions

For Research Use Only. Not for use in diagnostic procedures.

When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. For more information, please consult the appropriate safety data sheets (SDSs). These are available online in PDF format at www.qiagen.com where you can find, view, and print the SDS for each QIAGEN kit or kit component.

CAUTION 	Handle human blood as if potentially infectious. (C1) Observe relevant blood handling guidelines. Dispose of samples and materials in contact with blood or blood products in accordance with federal, state, and local regulations.

Procedure

Stage 1: Blood collection and hold time options

See Blood Collection Options below (Figures 1–3).

Direct draw into QFN Control BCTs

1. Label BCTs appropriately. Ensure that each tube (Nil and Mitogen) is identifiable by its label or other means once the cap is removed.

   Note: It is recommended to record the time and date of blood collection.

   Important: QFN-Control BCTs should be at room temperature 17–25°C (62.6–77°F) at the time of blood collection.

2. For each patient, collect 1 ml of blood by venipuncture directly into each of the QFN Control BCTs. This procedure should be performed by a trained phlebotomist.
   - As 1 ml BCTs draw blood relatively slowly, keep the tube on the needle for 2–3 seconds once the tube appears to have completed filling. This will ensure that the correct volume is drawn.
   - The black mark on the side of the BCTs indicates the validated range of 0.8 to 1.2 ml. If the level of blood in any tube is outside of the indicator mark, a new blood sample should be obtained. Under- or over-filling of the BCTs outside of the 0.8 to 1.2 ml range may lead to erroneous results.
   - If a "butterfly needle" is being used to collect blood, a "purge" tube should be used to ensure that the tubing is filled with blood prior to the QFN Control BCTs being used.
   - QFN Control BCTs can be used up to an altitude of 2650 feet (810 meters) above sea level.
   - If using QFN Control BCTs outside altitude ranges or if low blood draw volume occurs, users can collect blood with a syringe, and immediately transfer 1 ml to each of the BCTs. For safety reasons, this is best performed by removing the syringe

needle, ensuring appropriate safety procedures, removing the caps from the QFN Control BCTs, and adding 1 ml of blood to each (to the black mark on the side of the tube label which indicates the validated range of 0.8 to 1.2 ml). Replace the caps securely and mix as described below. Ensure each BCT (Nil and Mitogen) is identifiable by its label or other means once the cap is removed.

3. Immediately, after filling the BCTs, shake them ten (10) times just firmly enough to make sure the entire inner surface of the tube is coated with blood. This will dissolve antigens on the tube walls.

   Important: Over vigorous shaking may cause gel disruption and could lead to aberrant results.

4. Following labelling, filling, and shaking, the BCTs must be transferred to a 37°C ± 1°C incubator as soon as possible, and within 16 hours of collection. Prior to incubation, maintain BCTs at room temperature (22°C ± 5°C [71.6°F ± 9°F]). If QFN Control BCTs are not incubated at 37°C directly after blood collection and shaking, invert the BCTs to mix 10 times prior to incubation at 37°C.

5. Incubate the QFN Control BCTs UPRIGHT at 37°C ± 1°C for 16 to 24 hours.

   Note: The incubator does not require CO2 or humidification.

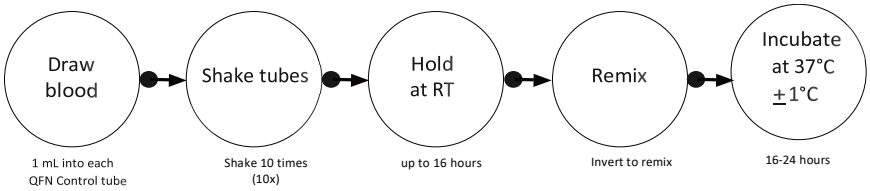

Figure 1. Blood collection option: Direct draw into QFN Control BCTs and hold at room temperature. The total time from blood draw in QFN Control BCTs to 37°C incubation must not exceed 16 hours.

Blood collection into a heparin tube and then transfer to QFN Control BCTs with room temperature storage and handling

1. Blood may be collected in a blood collection tube containing heparin as the anticoagulant and then transferred to QFN Control BCTs. Only use heparin as the blood anticoagulant because other anticoagulants interfere with the assay. Label tubes appropriately.

   Note: It is recommended to label the tube with the time and date of the blood collection.

2. Fill a heparin blood collection tube (≥ 3 ml for the QFN Control BCTs, and additional for any other tubes being tested) and gently mix by inverting the tube several times to dissolve the heparin. This procedure should be performed by a trained phlebotomist.
3. Blood collected in heparin tube must be maintained at room temperature (17–25°C [62.6–77°F]) for no more than 16 hours from the time of collection prior to transfer to QFN Control BCTs and subsequent incubation.
4. Transfer of blood specimen from a heparin tube to QFN Control BCTs.
   - Label each QFN Control BCTs appropriately.
     Note: Ensure each tube (Nil and Mitogen) is identifiable by its label or other means once the cap is removed. It is recommended to transfer the recorded time and date of blood collection from the heparin tubes to the QFN Control BCTs.
   - Samples must be evenly mixed by gentle inversion before dispensing into QFN Control BCTs.
   - Dispensing should be performed aseptically, ensuring appropriate safety procedures, removing the caps from the 2 QFN Control BCTs and adding 1 ml of blood to each tube. Replace the tube caps securely and mix as described below.
5. Mix BCTs. Immediately after filling the QFN Control BCTs, shake them ten (10) times just firmly enough to make sure the entire inner surface of the tube is coated with blood. This will dissolve antigens on tube walls.

   Important: Overly vigorous shaking may cause gel disruption and could lead to aberrant results.

6. Incubate the QFN Control BCTs UPRIGHT at 37°C ± 1°C for 16 to 24 hours.

Note: The incubator does not require CO_2 or humidification.

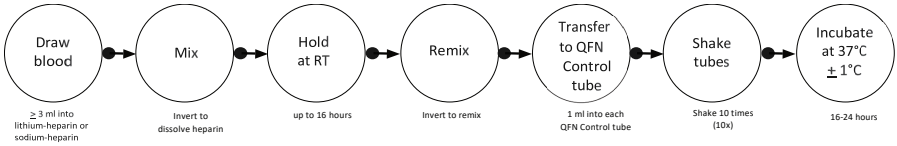

Figure 2. Blood collection option: Draw into heparin tube and hold at room temperature. The total time from blood draw in heparin tube to 37°C incubation must not exceed 16 hours.

Blood collection into heparin tube and then transfer to QFN Control BCTs with refrigerated storage and handling

1. Fill a heparin blood collection tube (≥ 3 ml for the QFN Control BCTs, and additional for any other tubes being tested) and gently mix by inverting the tube several times to dissolve the heparin.

   Important: This procedure should be performed by a trained phlebotomist.

2. Before refrigeration, blood drawn into heparin tube may be held at room temperature (17–25°C) up to 3 hours after blood collection.
3. Blood drawn into heparin tube may be refrigerated (2–8°C) up to 48 hours.
4. After refrigeration, heparin tube must equilibrate to room temperature (17–25°C) for 1 hour prior to transfer to QFN Control BCTs.
   - Aliquoted QFN Control BCTs should be placed in the 37°C incubator within 2 hours of blood of removing heparin tubes from 2-8°C.
   - Label each QFN Control BCT appropriately.
     Note: Ensure each tube (Nil and Mitogen) is identifiable by its label or other means once the cap is removed. It is recommended to transfer the recorded time and date of blood collection from the heparin tubes to the QFN Control BCTs.
   - Samples must be evenly mixed by gentle inversion before dispensing into QFN Control BCTs.
   - Dispensing should be performed aseptically, ensuring appropriate safety procedures, removing the caps from the 2 QFN Control BCTs, and adding 1 ml of blood to each tube. Replace the tube caps securely and mix as described below.
5. Following labeling, filling and shaking, the BCTs must be transferred to a 37°C ± 1°C incubator within 2 hours of removing heparin tube from 2–8°C. If QFN Control BCTs are not incubated at 37°C directly after blood collection and shaking, invert the BCTs to mix 10 times (10x) prior to incubation at 37°C. (See Figures 1–3 for blood collection options.)

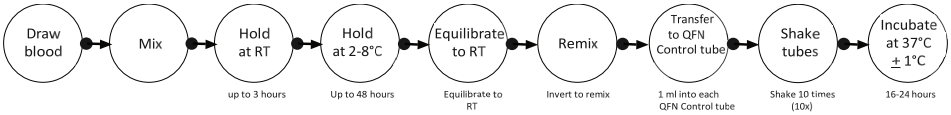

Figure 3. Blood collection option: Draw into heparin tube and hold at 2–8°C. The total time from blood draw in heparin tube to 37°C incubation must not exceed 53 hours. Note: Aliquoted QFN Control BCTs should be placed in a 37°C incubator within 2 hours of removing heparin tube from 2-8°C.

Stage 2: Post-incubation of BCTs and harvesting of plasma

Things to do before starting

- Prior to harvesting plasma, samples in QFN Control BCTs must be incubated at 37°C for 16–24 hours. The incubator does not require CO_2 or humidification.

Procedure

1. After incubation at 37°C ± 1°C, the BCTs may be held between 4°C and 27°C for up to 3 days prior to centrifugation.
2. After incubation of the BCTs at 37°C ± 1°C, harvesting of the plasma is facilitated by centrifuging the BCTs for 15 minutes at 2000 to 3000 RCF (*g*). The gel plug will separate the cells from the plasma. If this does not occur, the BCTs should be re-centrifuged.
3. It is possible to harvest the plasma without centrifugation, but additional care is required to remove the plasma without disturbing the cells.
4. Plasma samples should only be harvested using a pipet.

   Important: After centrifugation, avoid pipetting plasma up and down or mixing plasma by any means prior to harvesting. At all times, take care not to disturb material on the surface of the gel.

   Plasma samples can be stored in centrifuged QFN Control BCTs for up to 28 days at 2–8°C, or harvested plasma samples can be stored for up to 28 days at 2–8°C. Harvested plasma samples can also be stored below –20°C (preferably less than –70°C) for extended periods.

Symbols

The following symbols may appear on the packaging and labeling:

Symbol	Symbol definition
	Legal manufacturer
	Batch code
	Catalog number
	Global Trade Item Number
	Material number (i.e., component labeling)
	Use by
	Temperature limitation
	Consult instructions for use
	Do not reuse
	Sterilized using irradiation
	For research use only. Not for use in diagnostic procedures.
	Caution

Troubleshooting Guide

This troubleshooting guide may be helpful in solving any problems that may arise. For technical assistance and more information, please see our Technical Support Center at www.qiagen.com/support (for contact information, visit www.qiagen.com).

	Comments and suggestions
Underfilling of BCT	
a) BCT removed from the needle too soon.	As 1 ml BCTs draw blood relatively slowly, keep the BCT on the needle for 2–3 seconds once the BCT appears to have completed filling. This will ensure that the correct volume is drawn.
b) Blood drawn outside the recommended altitude of 2650 feet (810 meters) above sea level	QFN Control BCTs can be used up to an altitude of 2650 feet (810 meters) above sea level. If using QFN Control BCTs outside altitude ranges or if low blood draw volume occurs, users can collect blood with a syringe, and immediately transfer 1 ml to each of the BCTs.
c) Tubing not primed while using butterfly needle	If a "butterfly needle" is used to collect blood, a "purge" tube should be used to ensure that the tubing is filled with blood prior to the QFN BCTs being used.
d) BCTs are past their expiration date	BCTs must be used within the expiration date printed on the tube label.
Overfilling of BCT	
Tube not at room temperature during blood collection	BCTs should be at room temperature 17–25°C (62.6–77°F) at the time of blood collection.
Blood clots	
Insufficient mixing	Immediately after filling the BCTs, shake them ten (10) times just firmly enough to make sure the entire inner surface of the BCT is coated with blood. This will dissolve antigens on the BCTs walls.
Plasma not separated by gel	
Insufficient centrifugation speed or time	Harvesting of the plasma is facilitated by centrifuging the BCTs for 15 minutes at 2000–3000 RCF (g). The gel plug will separate the cells from the plasma. If this does not occur, the BCTs should be re-centrifuged.

	Comments and suggestions
Gel disruption	
Tubes shaken too vigorously	Immediately after filling the BCTs, shake them ten (10) times just firmly enough to make sure the entire inner surface of the BCT is coated with blood. This will dissolve antigens on the BCTs walls. Important: Over vigorous shaking may cause gel disruption and could lead to aberrant results.

Contact Information

For technical assistance and more information, please call toll-free 800-362-7737, see our Technical Support Center at www.qiagen.com/contact or contact one of the QIAGEN Technical Service Departments (see back cover or visit www.qiagen.com).

Ordering Information

Product	Contents	Cat. no.
QuantiFERON Control Set	Contains Nil tube and Mitogen tube	626015
Related Products		
QuantiFERON SARS-CoV-2 Starter Pack	Contains QuantiFERON Starter Set (cat. no. 626115 SARS-CoV-2 Ag1 tube and SARS-CoV-2 Ag2 tube) and QuantiFERON Control Set (cat. no. 626015 Nil and Mitogen)	626715
QuantiFERON Monitor Direct	Contains Monitor Direct tube	626315
QuantiFERON ELISA	Contains Microtiter Plate, Conjugate (x100), IFN Gamma Standard, Green Diluent, Wash Buffer (x20), Enzyme Substrate Solution, and Enzyme Stopping Solution	626410

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit handbook or user manual. QIAGEN kit handbooks and user manuals are available at www.qiagen.com or can be requested from QIAGEN Technical Services or your local distributor.

Document Revision History

Date	Changes
R1, November 2020	Initial release
R2, February 2021	Added Description and Principle section Updated Ordering Information section

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For up-to-date licensing and product-specific disclaimers, see the *QuantiFERON Control Set BCT Package Insert*.