

Xpert[®] FFPE Lysis Kit

REF GXFFPE-LYSIS-CE-10

Instructions for Use

IVD CE

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See Section 16, Revision History for a description of changes.

Xpert[®] FFPE Lysis Kit

In Vitro Diagnostic Medical Device

1 Intended Purpose

1.1 Intended Use

The Xpert[®] FFPE Lysis Kit is designed to lyse Formalin-Fixed Paraffin Embedded (FFPE) tissue and preserve nucleic acids for subsequent GeneXpert[®] analysis.

1.2 Intended User/Environment

The Xpert FFPE Lysis Kit is intended to be performed by trained users in a laboratory setting.

2 Principle of Operation

FFPE tissue (from a scroll or slide) is placed into a tube along with the recommended volumes of FFPE lysis reagent and Proteinase K from the Xpert FFPE Lysis Kit. The sample is then incubated in a heat block at 80°C for approximately 30 minutes. During this incubation, the following occurs:

1. The heated solution starts to melt the paraffin wax.
2. The lysis reagent reverses the protein cross-linking formed during the formalin-fixing procedure.
3. The Proteinase K digests proteins and inactivates nucleases (RNases & DNases) that might otherwise degrade the DNA and RNA.

Lastly, Ethanol is then added to the sample and the recommended volume of the prepared sample lysate is added directly to a designated GeneXpert cartridge.

3 Materials Provided

Xpert FFPE Lysis Kit (1 kit, sufficient to prepare 10 lysates)

Each kit contains:

- 1 bag containing 10 x 1.5 mL tubes
- 1 bag containing 10 x 5 mL vials
- 1 bottle containing 13 mL of bulk FFPE Lysis Reagent
- 1 tube containing 250 µL of bulk Proteinase K Reagent

4 Materials and Equipment Required But Not Provided

- Microtome
- Disposable razor blades or scalpels (for macrodissection)
- Pipettes and filter pipette tips suitable to accurately transfer 5 µL, 20 µL, 260 µL and 600 µL
- Heat Block suitable to hold 1.5 mL microcentrifuge tubes (and hold at 80 °C)
- Bench top vortex mixer
- Standard bench top microcentrifuge with fixed angle rotor that fits 1.5 mL microcentrifuge tubes

- ≥95% Reagent Grade Ethanol
- Disposable gloves
- Adhesive labels or sample identification information

5 Warnings and Precautions

- All biological samples should be treated with standard universal precautions. Samples should only be handled by personnel trained in handling biohazardous materials.
- Handle all sample and kit reagents using appropriate techniques to prevent or minimize RNase and/or DNase contamination.
- Do not reuse macrodissection blades, pipette tips or tubes/vials to avoid cross contamination during sample handling.
- Spilled or leaking reagent tubes should be discarded and not be used.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Incomplete removal (scraping) of tumor area from the slide for preparation of the FFPE lysate may result in insufficient material for the assay and therefore a higher than expected indeterminate/**INVALID** rate with Xpert Assays.
- Please refer to the Xpert FFPE Lysis Kit Safety Data Sheet (SDS) available online at www.cepheidinternational.com for detailed safety and disposal information on FFPE lysis kit components. Relevant information from the SDS is provided below.
 - Product Waste –Dispose of content and/or container(s) in accordance with local, regional, national, and/or international regulations.
 - Packaging Waste –Dispose of content and/or container(s) in accordance with local, regional, national, and/or international regulations.

6 Chemical Hazards

Hazard Statement: H319 Causes serious eye irritation

Precautionary Statements:

- P264: Wash thoroughly after handling
- P280: Wear protective gloves/protective clothing/eye protection/face protection
- P302+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
- P337+P313: If eye irritation persists: Get medical advice attention.

7 Kit Storage Requirements

The Xpert FFPE Lysis Kit must be stored at 2-28 °C and used before its expiration date (see outer kit labelling). The kit can be closed and re-opened for additional processing of specimens within 8 weeks after its initial opening.

8 FFPE Tissue Requirements

1. Specimens must have been fixed in only 10% Neutral Buffered Formalin (NBF) for 6 to 72 hours to be tested with any Xpert assay that requires RNA or DNA from FFPE tissue.
2. Some FFPE tissue greater than 10 years old may be of insufficient quality for GeneXpert analysis.
3. The pathologist should select the FFPE tissue/tumor block with the greatest area of visible acceptance tissue/tumor for the assay to run.
4. The Xpert assay requires unstained slide mounted tissue for processing. If macrodissection is required, use an adjacent H&E stained slide from the FFPE tumor block as a guide to ensure the tumor area identified on the H&E stained slide is representative of the tumor area on the unstained slide.
5. Refer to the Xpert assay package insert for additional information.

9 Slide/Scroll Preparation

Preparation of FFPE tissues using this lysis kit requires unstained slide mounted tissue section(s) or scroll(s) for processing and an adjacent H&E stained slide from the same tissue block.

1. Using a microtome, cut a 4 to 5 μm thick section for H&E staining.
2. Cut an adjacent 4 to 5 μm thick section, or scroll, for use in the FFPE Lysis kit.
 - For specimens that require multiple slides/scrolls to meet minimum Xpert assay requirements, all slides/scrolls must be processed together.
3. To prepare tissue section(s), follow standard histology techniques.
 - Ensure that the tissue sections are completely dry.
 - Slide section(s) for FFPE lysis should be stored at 2 °C to 8 °C and processed within two weeks after preparation; however, freshly cut sections will yield highest quality and most reliable results as mRNA degrades more rapidly on slide sections exposed to air than in FFPE blocks.
4. To prepare tissue scroll(s), follow the steps below.
 - Place scroll(s) in a provided 1.5 mL lysis tube. Label the tube for each sample to be processed.
 - Scroll(s) in a 1.5 mL tube should be stored at 2 °C to 8 °C and processed within 2 weeks after preparation.

10 Tissue Removal from Slide

1. Label a 1.5 mL lysis tube (provided) for each sample to be processed.
2. If macrodissection is not required:
 - a. Using a new razor blade or scalpel for each tissue sample to be processed, completely remove (scrape) the entire tissue section from the slide and transfer to a labeled 1.5 mL lysis tube.
 - b. Section(s) in a 1.5 mL tube should be stored at 2 °C to 8 °C and processed within 2 weeks.
3. If macrodissection is required:
 - a. Examine the H&E stained slide (pathologist). Identify (and outline) the tumor area for the assay. Refer to Xpert assay package insert for required number of slides or minimum tumor cellularity requirement.
 - b. Prepare for macrodissection (pathologist). Outline the tumor area to be used for the assay on the backside of the unstained slide(s) by aligning it with the corresponding H&E stained slide and transposing the outlined area.
 - c. Perform macrodissection (pathologist or technician). Using a new razor blade or scalpel for each tissue sample to be processed, completely remove (scrape) the outlined invasive tumor tissue from the slide (see Figure 1) and transfer to the labeled 1.5 mL lysis tube.
 - d. Macrodissected section(s) in a 1.5 mL tube should be stored at 2 °C to 8 °C and processed within 2 weeks.

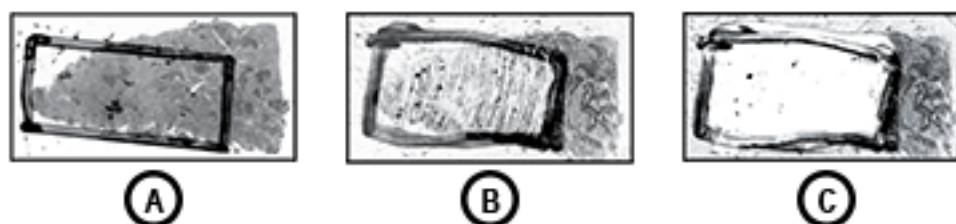


Figure 1. Examples of Proper (Recommended) and Improper (Not Recommended) Tissue Removal from Slide

| | |
|----------|--|
| A | Reference H&E Stained Slide |
| B | Not Recommended (Insufficient Tissue Removed) |
| C | Recommended |

11 FFPE Tissue Processing

1. Add 1200 µL (1.2 mL) of FFPE Lysis Reagent and 20 µL of Proteinase K to the tube containing the FFPE sample, then secure the cap.
2. Vortex the sample for at least 10 seconds, then briefly pulse spin the sample (to remove liquid from the cap).
3. Incubate the sample for at least 30 minutes in a heat block pre-warmed to 80 °C.
4. After the 80 °C incubation, vortex the sample for at least 10 seconds, then briefly pulse spin the sample.
5. Using a pipette, transfer the entire sample (~1.2 mL) to a labelled 5 mL sample vial.
6. Add 1200 µL of >95% Ethanol to the sample and secure the cap.
7. Vortex the sample for at least 15 seconds.

12 FFPE Tissue Processing – Concentrated Lysate
















Follow this protocol if a more concentrated lysate is desired due to insufficient sample (This should be considered for $\leq 6 \times 1 \text{ mm}^2$ area of tumor on scraped slide). Refer to Xpert assay package insert for additional information.

1. Add 260 µL of FFPE Lysis Reagent and 5µL of Proteinase K to a labelled 1.5 mL tube containing the FFPE sample, then secure the cap.
2. Vortex the sample for at least 10 seconds, then briefly pulse spin the sample (to remove liquid from the cap).
3. Incubate the sample for at least 30 minutes in a heat block prewarmed to 80 °C.
4. After the 80 °C incubation, vortex the sample for at least 10 seconds, then briefly pulse spin the sample.
5. Add 260 µL of $\geq 95\%$ ethanol to the same 1.5 mL lysis tube and secure the cap.
6. Vortex the sample for at least 10 seconds, then briefly pulse spin the sample.

13 Sample Storage and Transport

Prepared lysate, with ethanol, should be transported to the laboratory at 2 °C to 8 °C, if testing is to be performed within 1 week. If assay is to be performed at a later time, the FFPE lysate is stable and may be stored up to 4 weeks at ≤ -20 °C before testing.

14 Table of Symbols

| Symbol | Meaning |
|---|---|
|  | Catalog number |
|  | CE marking – European Conformity |
|  | Contains sufficient for n tests |
|  | Manufacturer |
|  | Country of manufacture |
|  | Temperature limitation |
|  | Batch code |
|  | Consult instructions for use |
|  | Biological risks |
|  | <i>In vitro</i> diagnostic medical device |
|  | Authorized Representative in the European Community |
|  | Do not reuse |
|  | Caution |
|  | Warning |
|  | Expiration date |

15 Technical Assistance

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16 Revision History

Description of Changes: 301-5224 Rev. D to 302-6233 Rev. A

Purpose: To align with the requirements of Regulation (EU) 2017/746

| Section | Description of Change |
|---------|--|
| 1 | Updated section to "Intended Purpose" and added subsections "Intended Use" and "Intended User/Environment" |
| 2 | Added new section "Principle of Operation" |
| 4 | Updated section |
| 5 | Added reference to SDS |
| 7 | Expanded section |
| 9 | Updated procedure for preparing slide/scroll |
| 10 | Updated procedure for removing tissue from slide |
| 11 | Updated procedure for FFPE tissue processing |
| 12 | Updated procedure for FFPE tissue processing with concentrated lysate |
| 15 | Updated technical assistance information |
| 16 | Added "Revision History" section |