Roche Cell Collection Medium

For in vitro diagnostic use

Roche Cell Collection Medium Kit	250 x 20 mL	P/N: 07994745190
Roche Cell Collection Medium Replacement Cap Kit	250 Pieces	P/N: 08037230190
Roche Cell Collection Medium Bottle	4 x 945 mL	P/N: 07994753190
Dispenser for Roche Cell Collection Medium Bottle	1 Piece	P/N: 07994788190

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Intended use

Roche Cell Collection Medium is designed for the preservation and transport of cells to be used in molecular testing and/or for the preparation of cytology slides.

Summary and explanation

Roche Cell Collection Medium is used to collect specimens to be tested by molecular PCR tests including the **cobas®** 4800 HPV Test, the CINtec® *PLUS* Cytology test* and the Pap cytology test. When used with the Roche PCR diagnostic products, it allows for detection of target nucleic acid. When used with the CINtec® *PLUS* Cytology test, it allows for the visualization of cells undergoing transformation as a result of a persistent high risk HPV infection in gynecological preparations for cervical cancer screening. When used with the Pap cytology test, it allows for the visualization of cells in gynecological preparations for cervical cancer screening.

The patient's specimen is collected by the clinician using a cervical sampling device that is immersed and agitated in the Roche Cell Collection Medium vial.

The Roche Cell Collection Medium vial is then capped and sent to the laboratory for processing and testing.

NOTE: Please check with your local Roche representative for the availability of Roche Cell Collection Medium in your country.

*For more information about the CINtec® *PLUS* Cytology test, see the Instructions for Use for the CINtec® *PLUS* Cytology kit, Rev E or later, P/N 06889565001.

Materials and reagents

Roche Cell Collection Medium

Store the unopened kit as recommended in Table 1 through Table 4.

Table 1 Roche Cell Collection Medium Kit

Roche Cell Collection Medium Kit
Store at 15-30°C
250 Vials (P/N 07994745190)

Component	Reagent ingredients	Quantity per kit	Safety symbols and warnings*
Roche Cell Collection Medium	Methanol-based, preservative solution	250 x 20 mL	 Danger H226: Flammable liquid and vapour. H301 + H311 + H331: Toxic if swallowed, in contact with skin or if inhaled. H370: Causes damage to organs. P210: Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P260: Do not breathe dust/ fume/ gas/ mist/ vapours/ spray. P280: Wear protective gloves/ eye protection/ face protection. P301 + P310 + P330: IF SWALLOWED: Immediately call a POISON CENTER/doctor. Rinse mouth. P308 + P311: IF exposed or concerned: Call a POISON CENTER/doctor. P370 + P378: In case of fire: Use dry sand, dry chemical or alcohol-resistant foam to extinguish. P403 + P233: Store in a well-ventilated place. Keep container tightly closed.

*Product safety labeling primarily follows EU GHS guidance

Table 2 Roche Cell Collection Medium Replacement Caps

Roche Cell Collection Medium Replacement Caps
Store at 15-30°C

250 Caps (P/N 08037230190)

Component	Reagent ingredients	Quantity per kit	Safety symbols and warnings
Roche Cell Collection Medium Replacement Caps	N/A	250	N/A

Table 3 Roche Cell Collection Medium Bottle

Roche Cell Collection Medium Bottle
Store at 15-30°C

4 Bottles (P/N 07994753190)

Component	Reagent ingredients	Quantity per kit	Safety symbols and warnings*
Roche Cell Collection Medium Bottle	Methanol-based, preservative solution	4 x 945 mL	 Danger H226: Flammable liquid and vapour. H301 + H311 + H331: Toxic if swallowed, in contact with skin or if inhaled. H370: Causes damage to organs. P210: Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P260: Do not breathe dust/ fume/ gas/ mist/ vapours/ spray. P280: Wear protective gloves/ eye protection/ face protection. P301 + P310 + P330: IF SWALLOWED: Immediately call a POISON CENTER/doctor. Rinse mouth. P308 + P311: IF exposed or concerned: Call a POISON CENTER/doctor. P370 + P378: In case of fire: Use dry sand, dry chemical or alcohol-resistant foam to extinguish. P403 + P233: Store in a well-ventilated place. Keep container tightly closed.

*Product safety labeling primarily follows EU GHS guidance

Table 4 Dispenser for Roche Cell Collection Medium Bottle

Dispenser for Roche Cell Collection Medium Bottle Store at 15-30°C 1 Dispenser (P/N 07994788190)			
Component	**Reagent ingredients**	**Quantity per kit**	**Safety symbols and warnings**
Dispenser for Roche Cell Collection Medium Bottle	N/A	1	N/A

Precautions and handling requirements

Warnings and precautions

- For *in vitro* diagnostic use only.
- The product is highly flammable, and explosive vapour/air mixtures may be formed even at normal room temperatures.
- Avoid contact of the Roche Cell Collection Medium with the skin or eyes. If contact does occur, immediately wash with large amounts of water.
- Not for external or internal use with humans or animals.
- Safety Data Sheets (SDS) are available on request from your local Roche representative.
- Specimens should be handled as if infectious using safe laboratory procedures such as those outlined in Biosafety in Microbiological and Biomedical Laboratories[1] and in the CLSI Document M29-A4.[2]

Good laboratory practice

- Always follow Good Laboratory Practices/Good Clinical Practices (GLP/GCP).
- Wear protective disposable gloves, coats, and eye protection when handling specimens and reagents. Wash hands thoroughly after handling specimens and reagents.

Reagent handling and storage

- Keep container tightly closed in cool, well-ventilated place.
- Do not use past the expiration date.
- Use only with adequate ventilation.
- Follow rules for flammable liquids. Store away from incompatible material.
- Transport and store upright at 15°C to 30°C.

Disposal

- Dispose of unused reagents, waste and specimens in accordance with all applicable regulations.

Spillage and cleaning

- If Roche Cell Collection Medium is spilled, **FIRST** clean with a suitable laboratory detergent and water, and then with 0.5% sodium hypochlorite.

Specimen collection and preparation

Specimen collection

Collect specimens using a broom-type cervical collection device or endocervical brush/spatula combination collection device according to device-specific instructions. Record required patient information in the space provided on the vial label.

To prevent leakage, tighten the closure until the line on cap and line on vial meet or slightly overlap and store upright.

Brush/spatula collection device

Collect specimens according to applicable Instructions for Use for the brush/spatula sampling device being used.

Broom-type collection device

Collect specimens according to applicable Instructions for Use for the broom-type sampling device being used.

Specimen transport and storage

- Following collection, transport the specimen collected in Roche Cell Collection Medium at 2°C to 30°C.
- Specimens collected in Roche Cell Collection Medium can be stored at 2°C to 30°C for up to 6 months prior to testing with the **cobas®** 4800 HPV molecular test.
- Specimens intended for cytology slide preparation may be stored at 15°C to 30°C for up to 6 weeks.
- Transport and store upright.
- Transportation of collected specimens must comply with all applicable regulations for the transport of etiologic agents.[3]

Known interfering substances

The use of lubricants (e.g. K-Y® Jelly) should be minimized prior to specimen collection. Use of over-the-counter products Replens™, RepHresh™ Vaginal Gel and RepHresh™ Clean Balance™ Kit may lead to invalid or false-negative results with the **cobas®** 4800 HPV Test.

Processing instructions

Cellular specimens collected in Roche Cell Collection Medium are to be processed for use with Roche PCR products according to the Roche product Instructions for Use and the Roche Operator's Manuals.

Cellular specimens collected in Roche Cell Collection Medium can be processed for cytology using Hologic's ThinPrep 2000 or ThinPrep 5000 instrument according to Hologic's ThinPrep Operator's Manuals.

Roche Cell Collection Medium in the 945 mL bottle can be used to add volume to specimen vials if required.

Non-clinical performance evaluation

cobas® 4800 HPV Test

A total of 1462 subjects were enrolled to obtain pairs of cervical specimens collected into Roche Cell Collection Medium and PreservCyt® Solution. Each pair of cervical specimens was tested using the **cobas®** 4800 HPV Test to assess the result agreement. In Table 5, specimens with positive results in any of the three HPV detection channels (Channel 1: 12 Other HR HPV, Channel 2: HPV16, Channel 3: HPV18) were considered positive; specimens with negative results in all three of the HPV detection channels were considered negative. The positive agreement between results obtained with Roche Cell Collection Medium and PreservCyt® Solution specimens was 92.1%; the negative agreement was 96.8% and the overall agreement was 95.3%.

Table 5 Summary of cobas® 4800 HPV Test results for cervical specimens co-collected in Roche Cell Collection Medium and PreservCyt® Solution using the "HPV high risk panel" test result

Cervical Specimen Pairs N = 1462		PreservCyt® Solution		
		Positive	Negative	Total
Roche Cell Collection Medium	Positive	408	33	441
	Negative	35	986	1021
	Total	443	1019	1462

Positive Agreement = 408/443 = 92.1% (95% CI: 89.2%, 94.4%)

Negative Agreement = 986/1019 = 96.8% (95% CI: 95.5%, 97.8%)

Total Agreement = 1394/1462 = 95.3% (95% CI: 94.1%, 96.4%)

Study results from these 1462 subjects were also analyzed by combining the results from all three HPV detection channels. In this analysis (Table 6), the results from each of the HPV detection channels 1-3 were combined. The positive agreement between Roche Cell Collection Medium and PreservCyt® Solution specimens was 91.8%; the negative agreement was 99.1% and the overall agreement was 98.3%.

Table 6 Summary of cobas® 4800 HPV Test results for cervical specimens co-collected in Roche Cell Collection Medium and PreservCyt® Solution using the "HPV high risk panel plus genotyping" test result

Cervical Specimen Pairs N = 4386		PreservCyt® Solution		
		Positive	Negative	Total
Roche Cell Collection Medium	Positive	428	35	463
	Negative	38	3885	3923
	Total	466	3920	4386

Positive Agreement = 428/466 = 91.8% (95% CI: 89.0%, 94.2%)

Negative Agreement = 3885/3920 = 99.1% (95% CI: 98.6%, 99.5%)

Total Agreement = 4313/4386 = 98.3% (95% CI: 97.5%, 98.9%)

Pap cytology test

The performance of Roche Cell Collection Medium (RCCM) compared to PreservCyt (PC) solution was assessed by morphological staining of 606 pairs of cervical specimens (cases) using Papanicolau (Pap) stain. Two slides were made from each case, one PC and one RCCM, and were read by a cytotechnologist followed by a pathologist. The Pap diagnostic results comparing PC to RCCM are summarized in Table 7. Cumulative percentages for each category, by collection medium, were calculated by taking the total number of cases in the category and dividing by the total number of cases for the study. Results show a maximum absolute difference between the two sets of cumulative percentages as 2.2% with a with a 1-sided 95% confidence upper limit of 5.2%.

Table 7 Summary of Pap test results for cervical specimens co-collected in Roche Cell Collection Medium and PreservCyt® Solution

		Slides made from samples preserved in PC				
	PAP Diagnosis	**NILM**	**ASC-US /AGC favor reactive**	**LSIL**	**ASC-H /AGC favor neoplastic /HSIL**	**Total**
Slides made from samples preserved in RCCM	**NILM**	94	42	5	7	148 (27.5)
	ASC-US/AGC favor reactive	39	115	30	16	200 (64.7)
	LSIL	8	24	66	19	117 (86.4)
	ASC-H/AGC favor neoplastic/HSIL	6	13	11	43	73 (100)
	Total	147 (27.3)	194 (63.4)	112 (84.2)	85 (100)	538
	% with 1-sided 95% Upper Limit (%)	2.2 (5.2)				

Abbreviations for Diagnoses: **NILM** = negative for intraepithelial lesion or malignancy, **ASC-US** = Atypical Squamous Cells of Undetermined Significance, **AGC** = Atypical Glandular Cells, **LSIL** = Low-grade Squamous Intraepithelial Lesion, **HSIL** = High-grade Squamous Intraepithelial Lesion, **ASC-H** = Atypical Squamous Cells, Cannot exclude High-Grade Squamous Intraepithelial Lesion

Note: Carcinomas can be seen in liquid based Pap tests.[4-7]

Sample adequacy[8] equivalence between PC and RCCM was assessed by calculating the difference of satisfactory rates. Results in Table 8 show that the difference in satisfactory rates for PC and RCCM is 0.0 (-2.3, 2.3).

Table 8 Summary of sample adequacy results for cervical specimens co-collected in Roche Cell Collection Medium and PreservCyt® Solution

Sample Adequacy for RCCM	**Sample Adequacy for PC**		
	Satisfactory	**Unsatisfactory**	**Total**
Satisfactory	538	23	561
Unsatisfactory	23	22	45
Total	561	45	606
n/N, 2-sided 95% CI:	0/606 (0.0) (-2.3, 2.3)		

Table 9 Disposition of non-neoplastic findings for PC and RCCM*

Non-Neoplastic Findings	PC	RCCM
Trichomonas	29	26
Candida	70	79
Coccobacilli	287	276
Herpes	2	2
Reactive changes	310	337
Radiation	2	2
Atrophy	3	5
Inflammation	593	602

*Actinomycetes is also identifiable in liquid based Pap tests.[9]

Table 10 Detection of endometrial cells for PC and RCCM

Endometrial Cells for RCCM	Endometrial Cells for PC		
	Present	**Not Present**	**Total**
Present	9	24	33
Not Present	24	549	573
Total	33	573	606
n/N, 2-sided 95% CI:	0/606 (0.0) (-2.3, 2.3)		

Additional information

Symbols

The following symbols are used in labeling for Roche PCR diagnostic products.

	Ancillary Software		*In Vitro* Diagnostic Medical Device
	Authorized Representative in the European community		Lower Limit of Assigned Range
	Barcode Data Sheet		Manufacturer
	Batch code		Store in the dark
	Biological Risks		Contains sufficient for <*n*> tests
	Catalogue number		Temperature Limit
	Consult instructions for use		Test Definition File
	Contents of kit		Upper Limit of Assigned Range
	Distributed by		Use-by date
	For IVD Performance Evaluation Only		Global Trade Item Number
	This product fulfills the requirements of the European Directive 98/79 EC for *in vitro* diagnostic medical devices.		

Manufacturer and distributors

Manufactured for:

Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany
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Roche Diagnostics
201, boulevard Armand-Frappier
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Pour toute assistance technique,
appeler le: 1-877-273-3433)

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Trademarks and patents

See http://www.roche-diagnostics.us/patents

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Document revision

Document Revision Information	
Doc Rev. 1.0 02/2017	First Publishing.
Doc Rev. 2.0 07/2017	Added cytology claim to **Intended use** section. Added ® to CINtec consistently. Added cytology information and data. Updated RCCM Specimen Stability Claim from 3 to 6 months. Added RCCM Bottle and Dispenser. Changed Legal Manufacturer from Roche USA to Roche Germany. Included corresponding references to align with text added. Removed EC rep symbol. Please contact your local Roche Representative if you have any questions.