DECLARATION OF CONFORMITY

Pharmaline Health Services Ind. Trade Inc. Head Office: Pharmaline Health Services Ind. Trade Inc. operates at the address Sahrayıcedid Mh. Atatürk Street, Atatürk Street Residences No: 43 A-Block Flat: 6 34734 Kadıköy/İSTANBUL as R&D and Production: Batı Sitesi Mh. 2308 Cd. Gersan Site No: 52 06370 Yenimahalle/ANKARA/TURKEY. The conformity assessment of our products has been carried out in accordance with the rules of Annex IX Assessment of Technical Documentation of Regulation (EU) 2017/746. This Declaration of Conformity has been prepared in accordance with Article 17 and Annex IV of Regulation (EU) 2017/746. Pharmaline brand information is given in the table below.

Product Name	**Basic UDI-DI**	**Product Models**	**Catalog (Reference) Number**	**Risk Class**	**GMDN Code**	**EMDN Code**
UniPatogen CerviPan HPV qPCR Screening Kit	869986307PHCPNZM	50 Test	PHCPN-50	Class C Rule 3 Article A; for detecting the presence of, or exposure to, a sexually transmitted agent.	49997 Nucleic acid IVD, kit, nucleic acid technique (NAT) for human papillomavirus (HPV) high-risk strain	W0105041002 Screening High-Risk HPV – NA Reagents
		100 Test	PHCPN-100			
		250 Test	PHCPN-250			
		500 Test	PHCPN-500			
		1000 Test	PHCPN-1000			

Intended Use of the Product: UniPatogen CerviPan HPV qPCR Screening Kit is a qualitative in vitro diagnostic (IVD) test intended for professional use in clinical laboratories.

The measurand of the assay is the DNA sequences of Human Papillomavirus (HPV) genotypes 16, 18, 45, 31, 33, 35, 39, 51, 52, 56, 58, 59, 66 and 68 isolated from cervical swab specimens.

The assay is based on the amplification of specific HPV DNA sequences using real-time Polymerase Chain Reaction (qPCR) technology and the detection of the generated fluorescent signal.

The test is qualitative and is intended to assist in cervical cancer screening by detecting the presence of the specified HPV genotypes.

UniPatogen CerviPan HPV qPCR Screening Kit is intended for professional use in clinical and research laboratories. This kit is based on the detection of HPV types 16, 18, 45 and 11 HPV types by real-time Polymerase Chain Reaction (qPCR). It is performed by detecting fluorescent light obtained by amplification of specific regions of the conserved E6/E7 and L1 genes. The test kit is used to qualitatively detect HPV types 16, 18, and 45 and HPV types 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68 in cervical swab samples. Depending on the primer mix used, a positive test result in the relevant channels; Indicates the presence of one of HPV types 16,18,45 or HPV types 31,33,35,39,51,52,56,58,59,66,68 in the relevant samples.

The kit specifically displays HPV types 16, 18, and 45 in separate channels, while for screening purposes, it displays the presence of one of the following types: HPV 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, or 68 in the corresponding fluorescence reading channel. This allows the kit to aid diagnosis by detecting HPV types 16, 18, and 45, which are frequently associated with cervical cancer. In addition to these types, it can also be used for screening purposes by detecting HPV types 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68 in cervical cancer screening.

The UniPatogen CerviPan HPV qPCR Screening Kit detects HPV types 16, 18, 45, and HPV types 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68. The kit's purpose is to screen individuals for HPV types listed above. This is achieved by detecting fluorescence resulting from amplification of specific regions of the conserved E6/E7 and L1 genes.

The High Risk HPV types that the kit can detect are as follows for Primer Mix-1 and Primer Mix-2:

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Primer Mix-1: 16, 18 and 45. The kit enables simultaneous detection of HPV types 16, 18 and 45 in different channels. It detects HPV16 type in the FAM fluorescence channel, HPV18 type in the HEX fluorescence channel and HPV45 type in the ROX fluorescence channel.

Primer Mix-2: 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, 68. The presence of these HPV types is indicated by increased fluorescence of the FAM and HEX channels.

The RNaseP gene is used as an internal control for DNA extraction quality control and to check for possible qPCR inhibition. RNaseP gene amplification is detected in the Cy5 fluorescence channel. The specially designed molecular design utilizes a novel quencher technology that minimizes nonspecific amplification and provides maximum sensitivity. Taqman probes are used as quenchers.

The UniPatogen CerviPan HPV qPCR Screening Kit detects HPV types 16, 18, and 45, which are most strongly associated with cervical cancer according to the HPV classifications of the World Health Organization (WHO) and recognized expert organizations (e.g., IARC - International Agency for Research on Cancer) (Arroyo Mühr et al., 2024). These three subtypes are considered high oncogenic risk and account for the majority of cervical cancer cases.

In addition, other HPV types, HPV 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68, are detected as present/absent using Primer Mix 2. These HPV subtypes are also classified as “carcinogenic” or “probably carcinogenic” by the IARC and are known to be associated with cervical intraepithelial neoplasia (CIN) and cervical cancer (Moberg, Gustavsson, & Gyllensten, 2003). HPV-68 and HPV-66 are included in the high-risk screening group because they are more carcinogenic than other low-oncogenic pathogens.

Detection of HPV 16, 18 and 45 with Primer Mix 1:
○ Primer Mix 1 detects HPV 16, HPV 18, and HPV 45 separately, and results for each subtype are evaluated independently.

○ FAM channel: Used for HPV 16 positivity. If luminescence is present in the FAM channel, the test is considered HPV 16 positive; if no luminescence is present, the test is considered HPV 16 negative.

○ HEX channel: Used for HPV 18 positivity. If luminescence is present in the HEX channel, the test is considered HPV 18 positive; if no luminescence is present, the test is considered HPV 18 negative.

○ ROX channel: Used for HPV 45 positivity. If luminescence is present in the ROX channel, the test is considered HPV 45 positive; if no luminescence is present, the test is considered HPV 45 negative.

○ The CY5 fluorescence channel is used as the Internal Control (IC). If there is luminescence in the CY5 channel, the patient's sample is considered healthy; if there is no luminescence, the sample is considered unsuitable.

Detection of HPV 31, 33, 35, 39, 51, 52, 56, 58, 59, 66 and 68 with Primer Mix 2:
○ Primer Mix 2 detects the 11 specified HPV types as a single analyte group and does not distinguish between these types.

○ If luminescence is present in the FAM fluorescence channel, the test result is considered positive; if no luminescence is present, the test result is considered negative.

○ Primer Mix 2 does not perform typing.

○ The HEX fluorescence channel is used as the Internal Control (IC). If luminescence is present in the HEX channel, the patient's sample is healthy; if no luminescence is present, the sample is considered inappropriate.

For the sample to be screened, Primer Mix 1 and Primer Mix 2 are used in two separate reactions, not mixed.

Primer Mix 1 provides specific results by detecting HPV 16, HPV 18 and HPV 45 separately.

Primer Mix 2 detects 11 different HPV types as a single group but does not distinguish between specific types.

Samples that do not perform properly for either mix are identified by the absence of corresponding Internal Control (IC) fluorescence and are considered noncompliant.

According to World Health Organization (WHO) guidelines, 70% of women are recommended to be screened with a high-performance test before age 35 and until age 45. HPV screening aims to reduce the risk of cervical cancer by facilitating treatment in early-diagnosed cases. The HPV types with the highest oncogenic potential in the etiology of cervical cancer are HPV 16 (62.4%) and HPV 18 (15.3%) (International Agency for Research on Cancer [IARC], 2002).

UniPatogen CerviPan HPV qPCR Screening Kit contains two primer mixes with different purposes:
○ Primer Mix 1: Provides separate typing of HPV 16, HPV 18, and HPV 45.
For example, if HPV 18 is present in a screening sample, the UniPatogen Cervipan HPV qPCR Screening Kit qualitatively detects the presence of HPV 18 in the sample. The same applies to HPV 18 and HPV 45.

○ Primer Mix 2: Detects HPV 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68 without typing.
For example, if HPV 35 is present in a screening sample, the UniPatogen Cervipan HPV qPCR Screening Kit will qualitatively detect the presence of units from HPV 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68 in the sample. The same applies to HPV 31, 33, 39, 51, 52, 56, 58, 59, 66, and 68.

The main difference here is that the presence of HPV types 16, 18 and 45 can be directly detected in the screening result, while for the remaining 11 types only an aggregate result is obtained as to whether any of these types are present.

The UniPatogen CerviPan HPV qPCR Screening Kit detects HPV types 16, 18, 45, and HPV types 31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68. Accordingly, the device is intended for screening for the presence of high-risk HPV DNA in cervical swab specimens. Screenings performed with both Primer Mix-1 and Primer Mix-2 were qualitative.

The kit performs qualitatively. The UniPatogen CerviPan HPV qPCR Screening Kit is not a fully automated system.

The procedure requires manual steps including specimen preparation, nucleic acid extraction, reaction mixture preparation, and pipetting.

Certain steps of the workflow (e.g., nucleic acid extraction or PCR amplification) may be performed using automated laboratory instruments, depending on the systems used by the laboratory. It works with cervical swab samples received in VTM. The UniPatogen CerviPan HPV qPCR Screening Kit has been validated with the Bio-Rad CFX96 Touch Instrument.

Conformity Assessment Method: Evaluation of Technical Documentation in accordance with Annex IX of Regulation (EU) 2017/746,

We declare that we produce in accordance with EN ISO 13485:2016, TS EN ISO 9001:2015, GMP, EN ISO 15223-1:2021, EN ISO 14971:2019, TS EN TS EN 62366-1 / AC-2016:2018, EN ISO 20417: 2021 standards.
The kit works qualitatively. It is not automated. It is used with cervical swab samples coming in VTM. The UniPatogen CerviPan HPV qPCR Screening Kit has been validated using the Bio-Rad CFX96 Touch RT PCR instrument. It is designed for professional use in clinical and research laboratories. It is designed to be used by qualified clinical laboratory personnel who have been specifically trained and instructed in qPCR techniques and in vitro diagnostic procedures. It is used on cervical swab samples taken from individuals with suspected HPV infection. The test kit can be applied to women of all age groups and racial populations.

This declaration declares that the product listed above, its components and all auxiliary equipment comply with the essential requirements of Regulation (EU) 2017/746. All relevant documents are kept at the manufacturer's site.

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This declaration of conformity has been prepared under the responsibility of Pharmaline Sağlık Hizmetleri San. Tic. A.Ş.

The conformity of our products with the above-mentioned directives and documents has been confirmed by the notified body QMD Services GmbH (Zelinkagasse 10/3 1010 Vienna, Austria) with the CE Certificate given below.

EC Certificate Number	**:**	
Certificate Release Date	**:**	
Certificate Last Publication Date	**:**	
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