SUMMARY OF SAFETY AND PERFORMANCE (SSP) PapilloDia

1. Introduction

The Summary of Safety and Performance (SSP) is one of the requirements of the new Regulation (IVDR 2017/746), specific for class C and D devices, to enhance transparency and adequate access to information. It intends to provide public access to summarised data on the safety and performance of class C and class D IVD devices to all intended users – professionals and lay persons.

2. Summary of Safety and Performance (SSP)

Requirements based on IVDR Article 29	Potential regulatory sources
Device identification and general information	
Name or trade name including any model number or version	PapilloDia Rapid Test
Manufacturer (name and address)	GaDia SA Route de l'Ile-au-Bois 1A 1870 Monthey Switzerland
Manufacturers single registration number (SRN), if available	CH-MF-000031123
Basic UDI-DI	7649990065CERLR
Intended purpose of the device	
Intended purpose and indications	PapilloDia is a non-automated rapid immunochromatographic test intended to be used for the qualitative detection of HPV 16/18 E6&E7 oncoproteins in female cervical swab samples. This test is for professional use only and is intended to be used as an aid in the diagnosis of Cervical Pre- cancer and Cancer
Target populations	Adult women with suspicion of cervical cancer. Women attending a specific Cervical Cancer screening program.
Contraindications (limitations)	1. The test procedure, precautions and interpretation of results for this test must be followed strictly when testing 2. The test is for professional use only and not for self-testing. 3. This test is a qualitative assay and will not give a quantitative result.

	4. Detection of HPV 16/18 E6&E7 Oncoproteins is dependent on the quantity of proteins present in the specimen. This may be affected by specimen collection methods and patient factors such as age, history of STD, presence of symptoms, etc. The minimum detection level of this test may vary according to serovar. 5. The expression of E6&E7 oncoproteins is only indicative of the risk of cervical cancer and pre-cancer occurs, the positive results do not confirm the cancer or pre-cancer stage and the negative results cannot exclude the happening of cervical cancer and pre-cancer. 6. The test results of this kit should be used as an aid for the rapid detection of E6&E7 oncoproteins. The results must be confirmed with alternative or complementary diagnostic procedures. The clinical management of patients should be comprehensively considered in conjunction with their symptoms, medical history, other laboratory tests and treatment responses.
Device description	
Device description	PapilloDia is a sandwich immunochromatographic assay with one individual test strip containing a conjugate pad impregnated with colloidal gold coupled with monoclonal antibodies specific to HPV 16 & 18 oncoproteins E6 and. E7. The T line is coated with monoclonal antibodies specific to E6 and E7 oncoproteins and the C line is coated with antibodies specific to gold nanoparticles. If the sample is positive, the antigens in the sample react with the nanoparticles and form a complex (Antigen – monoclonal antibody – gold nanoparticles). The mixture then moves upward on the membrane by capillary action. As the sample flows through the nitrocellulose membrane, the specific antibodies present on the membrane (T line) capture the colored conjugate complex and form a red line. If the sample is negative, there is no antigens present or

	the antigens may be present in a concentration lower than the detection limit. The antibodies present on the membrane (Test line) will not capture the antigen-red-colored conjugate complex (not formed), and the red line will not appear. Whether the sample is positive or not, the nanoparticle complex continues to move through the membrane to the immobilized specific antibodies placed in the control line (C line). The antibodies present on the membrane will react with the nanoparticles and capture the complex to form a red line. The presence of this red line serves as: (1) verification that sufficient volume is added, (2) that proper flow is obtained and (3) an internal control for the reagents. The control line must always appear.
Reference to previous generation(s) or variants of the device (as applicable) and a description of the differences	N/A
Description of accessories intended to be used in combination with the device (as applicable)	N/A
Description of other devices and products intended to be used in combination with the device (as applicable)	Materials Required but Not Supplied 1. Cervical swab (eg. #25–806 1PD, Puritan Medical Products) 2. Timer 3. Protective equipment
Standards Reference	
Harmonised standards and Common Specifications (CS) applied	IVDD 98/79/EC EN ISO 13485:2016 EN ISO 15223-1:2021 EN ISO 17511:2021 ISO 14971:2019 ISO 18113-1:2009 ISO 18113-2:2009 ISO 20417:2021 ISO 13975:2003 ISO 13612:2002 ISO 23640:2011

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	ISO 20916:2019 IEC 62366-1:2015+A1:2020

Summary of the Performance Evaluation

A retrospective performance evaluation study was conducted on 142 cervical swab samples. PapilloDia rapid test was compared to immunohistochemical assay (IHC) [6]. The performance of the test is strongly dependent of the stage of the cervical cancer. The 71 positive samples were all collected from patient with CIN2 or CIN3 (cervical intraepithelial neoplasia grade 2 or greater).

		IHC	
		+	-
PapilloDia	+	58	8
	-	13	63

Sensitivity	**81,7%**	(CI95%: 70.4-89.5%)
Specificity	**88,7%**	(CI95%: 78.5-94.7%)
PPV	**87,9%**	(CI95%: 77.0-94.3%)
NPV	**82,9%**	(CI95%: 72.2-90.2%)

Summary of the Post-Market Performance Follow-Up

The aim of this study conducted at the University Hospital of Geneva (Switzerland) is to assess the performance of lateral flow HPV testing for CIN2+ diagnosis. To do this, we will evaluate the test's feasibility in a gynaecological visit setting (colposcopy clinic) through a pilot study, examining the test's performance compared to PCR testing. If lateral-flow HPV testing proves feasible and shows promising results for CIN2+ diagnosis, it may help render cervical precancerous diagnosis more easily accessible.

Before launching a large, prospective trial to evaluate these new devices, a small pilot study to assess feasibility and preliminary results of the test is appropriate. As the test should theoretically only target HPV genotypes 16 and 18, we wish to assess whether there is cross reactivity with other HPV genotypes, alongside determining whether the tests show promising results for the detection of oncoproteins produced by HPV 16 and 18 in women attending for colposcopy or conisation.

Results of the rapid HPV test will be assessed to see whether there is diagnostic concordance with the HPV PCR test. Sensitivity and specificity will be calculated for the sensitivity of the test in participants with CIN2+, and this is the primary endpoint. PCR testing will be used as the reference, and the gold standard will be histological diagnosis.

The study population is women attending for colposcopy in the University Hospitals Geneva

Inclusion criteria:

- Women who have had a recent cervical biopsy or cytology result within past 3 months or need to have a cervical biopsy or cytology as part of the regular patient visit
- Women who have had a recent HPV test within past 3 months or who need to have a HPV test as part of the regular patient visit
- Able to give informed consent as documented by signature
- Older than 20 years old

Exclusion criteria

- Pregnant women
- History of hysterectomy

40 women are recruited in the following groups:

a) 20 CIN2+ on biopsy (including 10 HPV 16/18 positive and 10 positive for other genotypes)

b) 20 <CIN2 on biopsy or cytology (including 10 HPV 16/18 positive and 10 who are HPV negative)

Preliminary results are presented in the following table.

Age	HPV PCR*	Histopathology	PapilloDia Result
41	Positive - HR other	CIN3	Positive
30	Negative	6h squamous epithelium without lesion, 3h chronic inflammation	Negative
36	Positive – HPV 16	CIN3 conisation	Positive
36	Positive – HPV 16	epidermoid cancer of vulva	Positive
26	Positive – HPV 16	Histology not available as patient is pregnant Cytology: HSIL	Positive
60 (post menopausal)	Positive – HPV 18	Cytology – ASC-H	Low Positive
35	Positive - HR other	CIN2	Low positive – cut-off
38	Positive group A (31, 33, 52, 58)	CIN2	Positive
38	Positive - HR other	Histopathology result: not done (cytology result ASC-US)	Positive

This rapid test showed very interesting results in diagnosing quickly the Oncoproteins E6/E7 of HPV 16 & 18. Cross-reaction with other high-risk HPV was observed. These preliminary results are very encouraging and suggest good performance of the rapid test for the use a screening method.

Metrological traceability	
Metrological traceability of assigned values	N/A
Users	
User Profile	The tests can be performed by health care workers, nurses, medical doctors, gynecologist, or laboratory technicians with appropriate training in sample collection, biosafety and in the use of the test. The test can be run in doctor or gynecologist office or pharmacies. Sampling can be realized by the patient (self-collected samples).
User Training	Appropriate training in sample collection, biosafety and in the use of rapid tests.
Device Risks Information	

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Residual risks and undesirable effects	- Contamination of the user by infected samples - Wrong interpretation of the test results - False negative - Interference - Cross-reactivity
Warnings and precautions	1. Read the instruction for use carefully before using the test. 2. This product is for in vitro diagnostic and professional use only. 3. Do not reuse the test or kit components 4. Do not use the test after expiry date and do not freeze the test. 5. Read the test results within the specific time to avoid wrong interpretation. 6. Do not use the components from different batches or different types of reagents. 7. Properly dispose the specimen and used materials following the local biohazardous disposal regulation. 8. Use protective equipment when using the test and handling samples as they may contain infectious agents, human or animal components 9. Humidity and temperature can adversely affect results, use the test in standard laboratory humidity and temperature conditions. 10. The Extraction buffers (A & B) contain acid and alkaline solutions. Avoid eyes and skin contact. In case of contact with eyes, rinse immediately with plenty of water. 11. Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.