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Chlorhexidine Gel 7.1% Gel Job Aid to Assist the Laboratory Testing

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usp®

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The Promoting the Quality of Medicines Plus (PQM+) Program is a five-year cooperative agreement between USAID and USP to sustainably strengthen medical product quality assurance systems in low- and middle-income countries. The program works to improve medical product quality through cross-sectoral and systems strengthening approaches and the application of international quality assurance standards across the pharmaceutical system. By sharing scientific expertise and providing technical support and leadership, PQM+ helps create resilient and robust local health systems that address diseases such as HIV/AIDS, tuberculosis, malaria, and neglected tropical diseases, as well as improve maternal, newborn, and child health.

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Contents

Acronyms

CHX	Chlorhexidine
GSK	GlaxoSmithKline
HPLC	high performance liquid chromatography
N/A	not applicable
Ph. Eur.	The European Pharmacopoeia
PQM+	Promoting the Quality of Medicines Plus
TFA	Trifluoroacetic acid
USAID	U.S. Agency for International Development
USP	U.S. Pharmacopeial Convention
UV	ultraviolet
water R	Purified water as defined in Ph. Eur.
Titan Yellow Paper R	Paper that has been impregnated with Titan Yellow test solution

This lab aid is a compilation of information to assist in the testing of Chlorhexidine (CHX) Gel 7.1% Gel. The information should be used as to facilitate testing that can be found in the original GlaxoSmithKline (GSK) Chlorhexidine Technology Transfer Report (May 2019) and complements the The European Pharmacopoeia (Ph. Eur.) and USP pharmacopeial test procedures for appearance, identification, relative density, assay, and pH.

Chlorhexidine Gel 7.1% Gel

Tests	Ph. Eur.	GSK	USP
Appearance	• Almost colorless or pale-yellowish liquid	• Visually examine 1.0 g of gel product against a white background. • Where lower grades of guar gum were used, GSK has observed small dark particles, which were in fact guar seed husks. If necessary, confirm with microscopy. **Acceptance criteria:** A colorless to yellow, translucent gel essentially free from visible particles	N/A
Identification	**By IR:** 1. To 1 mL add 40 mL of purified water as defined in Ph. Eur. (water R). 2. Cool in iced water. 3. Make alkaline to Titan yellow paper R by adding dropwise, and with stirring, strong sodium hydroxide solution R adding 1 mL in excess. 4. Filter; wash the precipitate with water R until the washings are free from alkali. 5. Recrystallise from ethanol (70% V/V) R. 6. Dry at 100–105°C. 7. Examine the residue. 8. Compare to CHX chemical reference substance. **Acceptance criteria:** **The IR spectrum of sample should be the same as that of**	**By ultraviolet (UV):** • UV maxima of CHX should be within ±3 nm relative to reference. **By high-performance liquid chromatography (HPLC):** • Retention time of CHX should peak within ± 3% of that in reference solution.	**By UV:** • The retention time of the UV spectrum of the major peak of the sample solution corresponds to that of the standard solution obtained in the assay. **By HPLC:** • The retention time of the major peak of the sample solution corresponds to that of the standard solution obtained in the assay.

	the reference standard spectrum.		
Relative Density	Follow the procedure under section 2.2.5 of Ph. Eur. and measure relative density of the liquid sample using a calibrated densitometer. **Acceptance limit: (1.06–1.07)**	N/A	**Specific gravity** **USP <**841>** **Acceptance criteria: 1.06–1.07**
Assay	1. Determine the density (2.2.5) of the preparation to be examined. 2. Transfer 1.00 g to a 250 mL beaker and add 50 mL of anhydrous acetic acid R. 3. Titrate with 0.1 M perchloric acid, determining the end-point potentiometrically according to section 2.2.20 of the Ph.Eur. 4. 1 mL of 0.1 M perchloric acid is equivalent to 22.44 mg of CHX gluconate. **Acceptance criteria: 190 g/L–210 g/L**	**Mobile Phase Preparation** • Acetonitrile / Water / Trifluoroacetic acid (TFA) • Measure out individual volumes. • Do not add solvents into each other and make up to volume. You will obtain different ratios of solvents. • Do not filter the mobile phases to degas because TFA is volatile. Sonicate instead. **Sample Preparation** ~1.13g of CHX gel (~80mg of CHX digluconate), into 100 mL 1. Add approximately 50 mL of diluent. 2. Disperse by vortexing for 5 minutes. 3. Sonicate for 15 minutes with intermittent shaking. 4. Bring to volume. Filter through a 0.45µm nylon filter directly into an HPLC vial. **Note:** All samples will not be dissolved after sonication. Aim for a well-dispersed solution. Avoid a gel-like ball formation, which can negatively impact extractability. **Acceptance criteria:**	

		6.75–7.45% w/w (95.0%–105.0% of label claim)	
pH	Dilute 5.0 mL to 100 mL with carbon dioxide-free water R and measure pH of the solution. **Acceptance criteria: 5.5–7.0**	• Test directly. • Use a pH probe containing a gel-filled reference, such as the Mettler Toledo Inlab ExpertPro (P/N51343153). • Standard liquid-filled probes will not accurately measure the pH in the gel product. **Acceptance limit: 5.5–6.5**	**USP <**791>**:** when diluted 1 in 20 with water **Acceptance criteria: 5.5–7.0**

References

Web site
GSK Chlorhexidine Technology Transfer Report (May 2019) https://www.usp-pqm.org/sites/default/files/pqms/article/gsk-chx-gel-tech-transfer-report-6-20-2019.pdf

United States Pharmacopeia – National Formulary (USP 43–NF 38)

European Pharmacopeia (Ph. Eur.) 10th Edition