# PreventID® **Dermatophyte**

Manual (FOR PROFESSIONAL USE)

REF KSTDE001GP

## Intended use
The **PreventID® Dermatophyte** is an immunochromatographic rapid test for the qualitative determination of dermatophyte-derived antigens in nails.

## Introduction
A fungal infection of nails, also nail mycosis or onychomycosis, is an infection of the toenails or fingernails, usually caused by dermatophytes (filamentous fungi). Internal (endogenous) disposition factors could be for example metabolic diseases, genetic predispositions causing a susceptibility to onychomycosis, and immune deficiencies. Especially patients with diabetes mellitus, circulatory disorders, nail eczema and nail psoriasis are susceptible for fungal infections. Favouring is a moist-warm environment, toenails, therefore, are more frequently affected than fingernails. Another cause might also be a prolonged therapy with antibiotics.

## Test Principle
The **PreventID® Dermatophyte** is based on an immunochromatographic method for the determination of dermatophyte-antigens in nails infected with dermatophytes. The test device contains a fixed antibody against dermatophyte antigen in the test zone and a gold-conjugated monoclonal antibody against dermatophyte-antigen in the reagent zone. With the extraction solution the dermatophyte antigen is solubilised from the nail substance before the test run.

In case there is dermatophyte-antigen in the extraction solution this antigen binds during the test run to the colloidal-gold antibody. This complex migrates to the fixed second monoclonal antibody forming a coloured precipitate at the test line and indicating a positive result – an infection with dermatophytes. A coloured control line is formed as internal control and proves the correct test run.

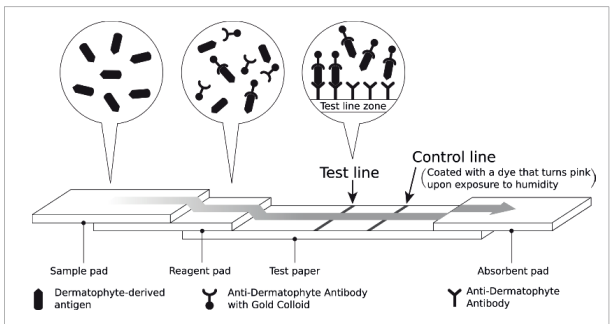


*Fig. 1*: **PreventID® Dermatophyte** Test Principle

## Material
**Material Provided:**
- test strips, single packed* TEST
- extraction buffer BUF
- test tube TUBE
- stir rods
- manual

**Material Required but not Provided:** Timer or stop watch, gloves, clippers or scissors

* To prevent the test strip from kinking, the test pack contains a stabilising cardboard strip that can be disposed of together with the packaging after having taken out the test strip.

## Storage and Stability
Store the test between 2 °C and 30 °C; do not freeze. The test device is sensitive to humidity, direct sunlight as well as to heat. Perform the test immediately after removing the test device from the pouch. Do not use it beyond the expiry date.

## Precautions
⚠ If the extraction buffer comes in contact with the eyes, mouth, or skin, rinse thoroughly with running water as first aid, and seek medical treatment if necessary.
1. For *in vitro* diagnostic use only.
2. Do not eat or smoke while handling specimen.
3. Wear protective gloves and wash hands thoroughly after performing the test.
4. Avoid splashing or aerosol formation while handling specimen and performing the test.
5. All samples and materials used should be treated as potentially infectious and disposed in a biohazard container. Clean all contaminated objects and surfaces carefully.
6. Do not use test if the pouch is torn or if the membrane of the test device is visibly damaged.
7. Read the instruction carefully before performing the test.
8. Do not mix reagents from different lots.
9. If you have any questions please contact Preventis GmbH.

## Specimen Preparation and Specimen Collection
This kit is intended for the detection of Dermatophyte-derived antigen in nails. Scales, scalp specimens, hair or other specimens cannot be used.

1. Preparation for specimen collection: Take a specimen of 1 mg or more according to the guidelines for diagnosis and treatment of cutaneous fungal infection (1, 2, 3).
   An inappropriate procedure for specimen collection or an insufficient amount of specimen taken may lead to false negative results or an incorrect judgment.
   Use clean nail clippers or scissors when taking a specimen and place it in a test tube from the kit.
2. Specimen collection must be performed by a professional who is qualified by appropriate education, training and/or experience according to the guidelines for diagnosis and treatment of cutaneous fungal infection. The procedure for specimen collection stated in the guidelines is partially shown below.
   a) Distal and Lateral Subungual Onychomycosis
   Remove the area of onycholysis or the tip of the nail, and take a specimen from the deep portion of the nail, as close to the nail bed as possible *(Fig. 2)*. If a specimen cannot be taken from the deep portion of the nail, take a specimen from the surface of the skin (actually the nail bed), where onycholysis is present.
   b) Superficial White Onychomycosis
   Remove a whitish superficial spot on the nail plate using nail clippers or scissors, and use it as a specimen *(Fig. 3)*.
3. Influence of Drugs
   The influence of oral antifungals[1] (terbinafine, itraconazole) that are commonly used for the treatment of tinea unguium on this assay were evaluated. When the negative control specimen, the positive control specimen and the weakly positive specimen which was prepared by diluting the positive control specimen with the negative control specimen was mixed with the antifungals and subjected to this kit, no influences of these drugs were observed. The concentration of each drug added was approximately 100 times the MIC (minimum inhibitory concentration).

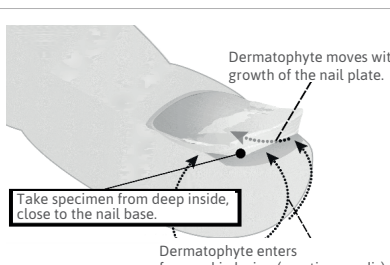


*Fig. 2*: **PreventID® Dermatophyte** sample collection in case of onychomycosis

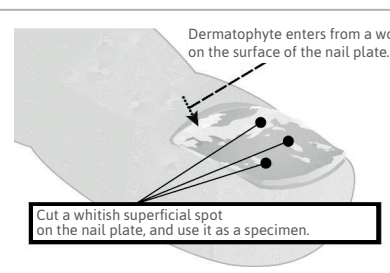


*Fig. 3*: **PreventID® Dermatophyte** sample colleciton in case of superficial white onychomycosis

| Antifungal | Concentration (µg/mL) | Influence |
|---|---|---|
| Terbinafine | 0.5 | Not observed |
| Itraconazole | 100 | Not observed |

*Table 1:* Influence of Antifungals coexisting in Specimens

## Test Procedure
1. Specimen and test device should be at room temperature and the following procedure should be performed at room temperature.
2. Prepare the required quantities of test strips, stir rods and extraction buffer. Do not touch the sample pad (*Fig. 4*).
3. Label tubes and test strips with patient name or number.
4. Add 0.25 to 0.5 mL of the extraction buffer to the test tube (*Fig. 4*). Put the specimen in the test tube and stir at least 20 times with a stir rod while pushing the specimen down. After stirring, stand the test tube in a test tube rack for at least 1 minute.
5. Stand the test strip in the test tube with the sample pad down. Confirm that the sample pad has reached the bottom of the test tube.
6. Let the test strip stand for at least 5 minutes and determine the result (positive, negative or invalid) by visually checking the presence or absence of coloured bands in the control line zone and the test line zone, within 30 minutes after standing the test strip in the test tube.

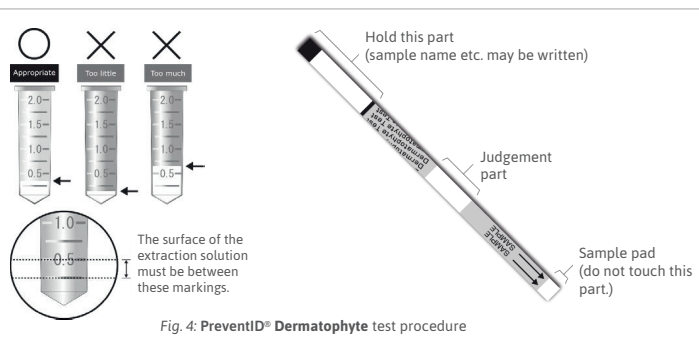


*Fig. 4:* **PreventID® Dermatophyte** test procedure

## Test Interpretation *(Fig. 5)*
**Positive:** If a pink line appears in the control line zone and a purple line appears in the test line zone, it indicates a dermatophyte-derived antigen positive result.

**Negative:** If a pink line appears in the control line zone and no visible line appears in the test line zone, it indicates a negative result. If a line appears in the test line zone after 30 minutes or longer, it indicates a negative result.

**Invalid:** If no pink line appears in the control line zone after 5 to 30 minutes, the test is invalid.

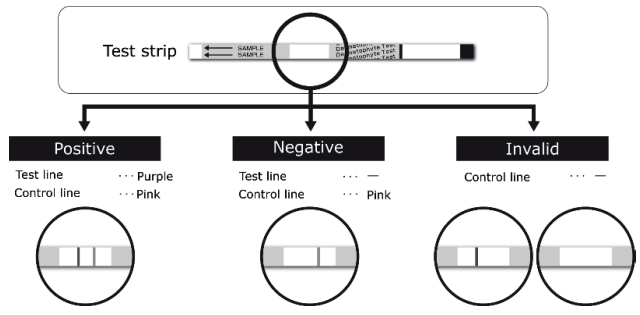


*Fig 5*: **PreventID® Dermatophyte** Test interpretation

**Precautions for interpretation:** If the amount of dermatophyte in the nail specimen is small, the result may become negative. The user should comprehensively evaluate the result of this assay in conjunction with other test results and clinical symptoms.
This kit is cross-reactive with other fungi than dermatophyte, such as Aspergillus and Penicillium. These fungi may be present in the soil or other environments and infect the skin of immune-compromised patients. Professionals should be careful when making a diagnosis.

## Test Characteristics
1) Results of Clinical Performance Study (5):
   In 222 patients (at 11 centers) suspected of having tinea unguium on visual inspection, a specimen was collected from a foot or hand nail according to the guidelines for diagnosis and treatment of cutaneous fungal infection. The specimen was aliquoted into three portions and subjected to measurement with **PreventID® Dermatophyte**, direct microscopy and PCR (only specimens for which the results of **PreventID® Dermatophyte** and direct microscopy were inconsistent), respectively. Specimen collection, direct microscopy, **PreventID® Dermatophyte** and PCR were performed by different persons under blinded conditions.
   a) Comparison between the results of **PreventID® Dermatophyte** and PCR incorporating direct microscopy. Analyses were performed on 222 patients. In 5 patients in whom the results of **PreventID® Dermatophyte** and direct microscopy were inconsistent and PCR could not be performed because the amount of specimen was insufficient, the result of direct microscopy was used.

| | | PCR incorporating direct microscopy | | |
|---|---|---|---|---|
| | | Positive | Negative | Total |
| PreventID® Dermatophyte | Positive | 196 | 5 | 201 |
| | Negative | 6 | 15 | 21 |
| | Total | 202 | 20 | 222 |

- Sensitivity: 97.0%
- Specificity: 75.0%
- Accuracy: 95.0%
- Negative predictive value: 71.4%
- Positive predictive value: 97.5%

*Table 2:* Comparison between the Results of **PreventID® Dermatophyte** and PCR incorporating Direct Microscopy

   b) Comparison between the results of **PreventID® Dermatophyte** and the dermato-logist's final diagnosis (based on the results of direct microscopy, PCR, clinical manifestation, specimen collection site, etc.). Analyses were performed on 217 patients, excluding 5 patients in whom PCR could not be performed because the amount of specimen was insufficient and a final diagnosis could not be made.

| | | Final Diagnosis | | |
|---|---|---|---|---|
| | | Dermatophytes | Non-Dermatophytes | Total |
| PreventID® Dermatophyte | Positive | 196 | 2 | 198 |
| | Negative | 4 | 15 | 19 |
| | Total | 200 | 17 | 217 |

- Sensitivity: 98.0%
- Specificity: 8.2%
- Accuracy 97.2%
- Negative predictive value: 78.9%
- Positive predictive value: 99.0%

*Table 3:* Comparison between the Results of **PreventID® Dermatophyte** and the Final Diagnosis

2) Sensitivity and Accuracy: When a negative control specimen was tested, this kit provided a negative result. When a weakly positive specimen and a positive control specimen were tested, this kit provided positive results.
3) Within-run reproducibility: When a negative control specimen was tested 4 times, the kit provided a negative result every time. When a weakly positive specimen and a positive control specimen, respectively, were tested 4 times, the kit provided a positive result every time.
4) Minimum Detectable Sensitivity:Trichophyton rubrum (NBRC 9185), 0.5 µg dry weight/mL
5) Reference Standard for Calibration: Dry cells of Trichophyton rubrum (NBRC 9185)
6) Cross-reactivity: Autoclaved dry cells of various other fungi than Dermatophyte were added to the extraction buffer at a concentration of 300 µg/mL to evaluate the influence of each fungus on the assay. In addition, colonies of various bacteria grown on agar plates were added to the extraction buffer to evaluate the influence of each bacterium on the assay.
   This kit was **not reactive with** the tested fungi (non dermatophyte) shown below: *Aspergillus nidulans, Penicillium citrinum, Scopulariopsis brevicaulis, Alternaria alternate, Pseudallescheria boydii, Scedosporium apiospermum, Prototheca wickerhamii, Schizophyllum commune (1 nucleus), Schizophyllum commune (2nuclei), Absidia corymbifera, Basidiobolus ranarum, Cunninghamella bertholletiae, Mortierella isabellina, Mucor circinelloides, M. racemosus, Rhizomucor pusillus, Rhizopus microsporus var. rhizopodiformis, R. oryzae, R. stolonifer var. reflexus, Syncephalastrum racemosum, Zygorhynchus exponens, Candida albicans, C. dubliniensis, C. tolopicalis, C. parapsilosis, C. guilliermondii, C. glabrata, C. krusei, Geotrichum candidium, Trichosporon asahii, Cryptcoccus neoformans serotype A, C. neoformans serotype B, C. neoformans serotype C, C. neoformans serotype D, C. neoformans serotype AD, Sporothirix schenckii, Fonsecaea pedrosoi, Exophiala. jeanselmei, Phialophora verrucosa, P. richardsiae, Rhinocladiella atrovirens, Cladophialophora bantiana, Malbranchea albolutea, M. aurantiaca, M. chrysosporioidea hrysosporioidea, M. cinnamomea, M. dendritica, M. filamentosa, M. flava, M. flocciformis, M. fulva, M. graminicola, M. gypsea, M. multicolor, M. pulchella, Malassezia furfur, Gymnoascoideus petalosporus, Auxarthron reticulatum, Gymnoascus intermedius, G. petalosporus, G. reessii, G. udagawae, Emmonsia parva var. crescens, E. parva var. parva, Phanerochaete chrysosporium, Apinisia queenslandica, Arthroderma multifidum, Uncinocarpus reesii, Chrysosporium carmichaelii, C. indicum, C. keratinophilum, C. pseudomerdarium*

   The kit was reactive with the fungi (non dermatophyte) shown below: *Aspergillus flavus, A. fumigatus, A. niger, A. terreus, Neosartorya fischeri, Paecilomyces lilacinus, Penicillium griseofulvum, Veronaea botryosa, Fusarium solani, Exophiala dermatitidis (M-Y form), E. dermatitidis (G form), E. spinifera, Hortaea werneckii, Malbranchea circinata, M. flavorosea*

   The kit was not reactive with the bacterium shown below: *Escherichia coli, Bacillus subtilis, Staphylococcus aureus, S. faecalis*
7) Reaction with dermatophyte: Autoclaved dry cells of dermatophyte were added to the extraction buffer at a concentration of 300 µg/mL to evaluate the reactivity of the assay. The kit was reactive with the dermatophyte shown below: *Trichophyton mentagrophytes, T. rubrum, T. tonsurans, T. violaceum, T. verrucosum, Microsporum gypseum, M.canis, Epidermophyton floccosum*

## Clinical Significance
**PreventID® Dermatophyte**, unlike direct microscopy, does not require special skills to determine whether dermatophyte is present or absent[4], and this kit, unlike PCR, does not require special equipment. **PreventID® Dermatophyte**, which is easy to use and provides quick results, is an effective assay for the rapid diagnosis of Tinea unguium.

## Test Limitations
Test results are only reliable if you follow the instructions for use carefully. The test is limited to the detection of dermatophyte in human nails. Use the test only once. Although the test is very accurate, a low incidence of false results can occur. If negative or questionable results are obtained, the test should be repeated on a fresh specimen using a new test device.
As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.


**References**
1. Ameen M, Lear JT, Madan V, Mohd Mustapa MF, Richardson M. British Association of Dermatologists' guidelines for the management of onychomycosis 2014. Br J Dermatol 2014; 171: 937–958.
2. Guidelines of care for superficial mycotic infections of the skin: onychomycosis. Guidelines/Outcomes Committee. American Academy of Dermatology. J Am Acad Dermatol 1996; 34: 116-121.
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4. Screening for tinea unguium by Dermatophyte Test Strip, Y. Tsunemi, et al., Br. J. Dermatol. , 170, 328-331, 2014
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|---|---|---|---|
| | Temperature limitation | | Manufacturer |
| IVD | *In vitro* diagnostic device | LOT | Lot number |
| REF | Catalogue number | | Expiry date |
| | Keep away from sunlight | | Do not reuse |
| | Read user instructions | n | Contains sufficient for <n> tests |

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Status: 2019-02-28


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