FAQ

INNO-LIPA CFTR

- HOW WERE THE MUTATIONS SELECTED FOR THE INNO-LIPA™ *CFTR*17+Tn UPDATE AND INNO-LIPA™ *CFTR*19 KIT?

  - Based on the ACMG guidelines
  - During design of kit core panel of 25 mutations for population carrier screening in the US, but currently 23 mutations are being recommended*
  - Mutations with worldwide frequency > 0,1%
  - Based on literature, feedback from target sales regions, labs and KOL
  - Define most frequent mutations in Europe
  - Define regional mutations with frequency > 1%
  - Based on competition

  ** The availability of new data from different laboratories, has resulted in a revised recommended panel. More info can be found on the American College for Medical Genetics site http:///www.acmg.net.*

- IS I148T A POLYMORPHISM OR DISEASE-CAUSING *CFTR* MUTATION?

  I148T, currently removed from the INNO-LiPA™ *CFTR*19 strip, was initially classified as a frequent CF-causing mutation. Recent literature describes I148T to be a neutral polymorphism not causing CF disease.*

  ** Castellani C, Cuppens H, Macek JR M et al. J Cyst Fibros 2008; 7:179-196.*

- WHAT IS THE CLINICAL RELEVANCE OF R117H?

  When R117H is detected, the Tn status should also be established:

  - R117H-T5 is considered a mild CF-causing complex allele
  - R117H-T7 is more likely a *CFTR*-related disorder mutation

  When found in compound heterozygosity with a CF-causing mutation, or possibly even in homozygosity, R117H-T5 generally results in pancreatic sufficient CF, while R117H-T7 may result in a mild form of CF, obstructive azoospermia, or no disease at all.

  ** Castellani C, Cuppens H, Macek JR M et al. J Cyst Fibros 2008; 7:179-196*
  Dequeker E, Stuhrmann M, Morris MA et al. Eur j Hum Genet 2008; 1-15

- WHAT IS REFLEX TESTING?

  Some assays can cause a false positive homozygous M.F508del or FI507del result due the presence of non-CF causing variants located at codons 506, 507 and 508.

Each lab should perform additional reflex testing for these variants (ACMG guidelines).

INNO-LiPA™ *CFTR*19 provides a correct clinical interpretation of samples carrying benign variants I506V, I506M, I507V, F508C. The specificity of our assay thus eliminates the need for additional reflex testing.

More information available on “Evaluation F508del probe specificity poster 2002” and in package insert.

- WHAT CONTROLS ARE INCLUDED IN THE INNO-LIPA™ *CFTR* KITS?

Conjugate control line:

- Monitors the color development step meaning the addition and incubation of conjugate and substrate.

Wild type probes:

- For every mutant probe a corresponding wild type probe is coated on the strip. The presence of the wild type probes on the strip verifies a successful amplification.

- WHAT SAMPLE TYPES CAN BE USED IN COMBINATION WITH THE *CFTR* PRODUCT PORTFOLIO?

Internal and external validation studies proved compatibility with whole blood, dried blood spots and buccal brushes for the complete *CFTR* product portfolio.

- WHAT KIND OF TAQ DNA POLYMERASE NEEDS TO BE USED?

The use of a Hot Start Taq DNA polymerase is required, but not provided. Validation studies were performed with Hot Start Taq (Qiagen®), but other Hot Start enzymes can be used.

Initial denaturation temperature (95°C) and time (15 minutes) of the amplification profile included in the package insert should be verified with the Hot Start Taq DNA polymerase manufacturer instructions and potentially adjusted.

- CAN THE STRIPS OF THE DIFFERENT *CFTR* PRODUCTS BE TESTED TOGETHER IN THE SAME TROUGH?

The following strips can be tested in the same trough:

- INNO-LiPA™ *CFTR*17+Tn Update + INNO-LiPA™ *CFTR*19
- INNO-LiPA *CFTR*™ *Italian* Regional + INNO-LiPA™ *CFTR* Deletions + 6

Other strip combinations have not been validated.