Negative

Flowchart 1 (top left):

1st Sample For Antibody Test
→ LIPS U → < 3U/ < 10U → Negative report
→ ELISA → < 35U → Negative report

Flowchart 2 (top right):

1st Sample For Antibody Test
→ LIPS U → < 3U → Negative report
→ ELISA → ≥ 35U → RIA* → All neg.** / < 90U GAD*** / < 9U IA2 / (ZnT8 R/W) → Negative report

Flowchart 3 (bottom left):

1st Sample For Antibody Test
→ LIPS U → ≥ 10U → LIPS I → < 15U → Negative report
→ ELISA → < 10U → Negative report

Flowchart 4 (bottom middle):

1st Sample For Antibody Test
→ LIPS U → ≥ 10U → LIPS I → < 15U → Negative report
→ ELISA → ≥ = 10U → RIA* → All neg.** / < 90U GAD*** / < 9U IA2 / (ZnT8 R/W) → Negative report

Flowchart 5 (bottom right):

1st Sample For Antibody Test
→ LIPS U → ≥ 3U → LIPS I → < 15U → Negative report
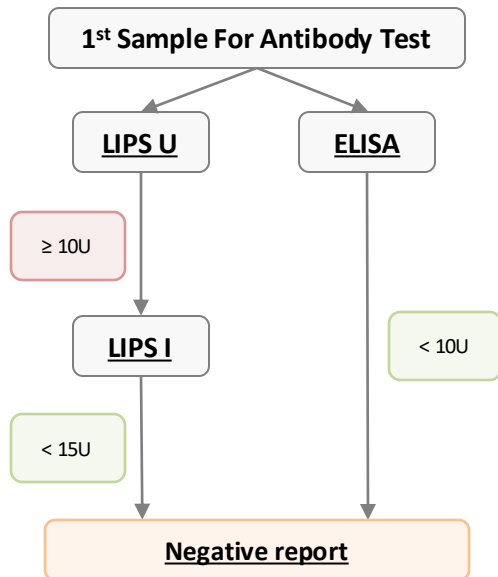→ ELISA → ≥ 35U → RIA* → All neg.** / < 90U GAD*** / < 9U IA2 / (ZnT8 R/W) → Negative report

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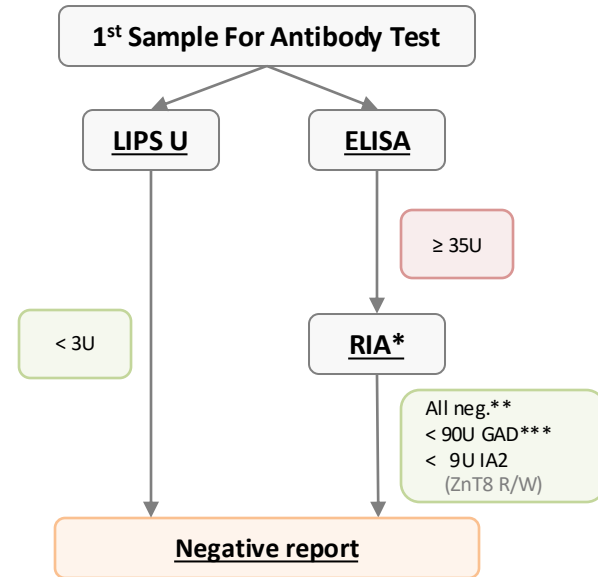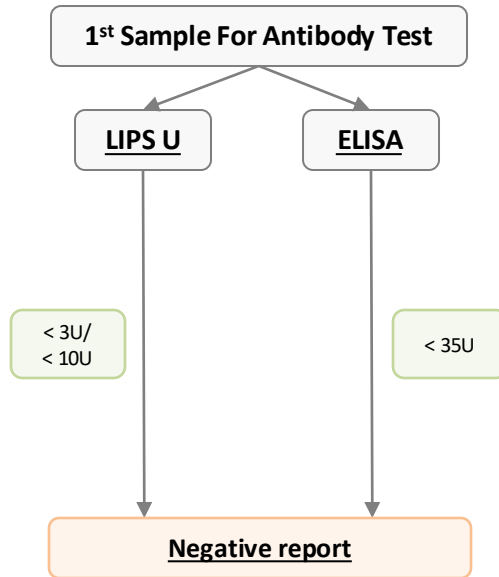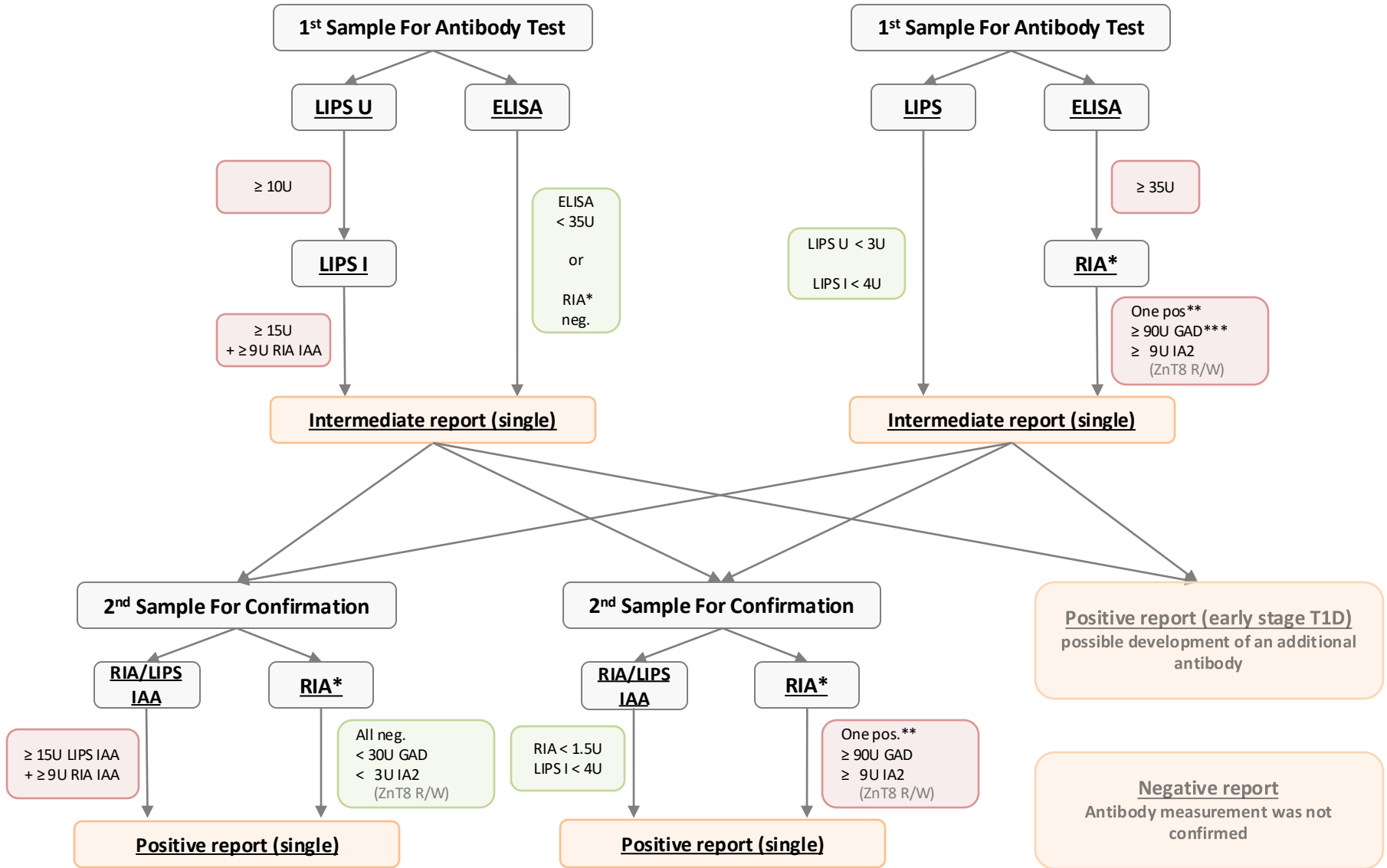
LIPS U = IAA LIPS non-inhibited
LIPS I = IAA LIPS inhibited
ELISA = 3 - Screen ELISA
        (GAD, IA2, ZnT8)
RIA* = GAD, IA2, ZnT8 R, ZnT8 W

1st sample is a capillary sample

** only for Single positive status : at least 3 times higher than regular cut off; ZnT8 AB are not found to be single positive

*** GAD (highest priority); For negative report: Results from IA2 and ZnT8 not necessary if GAD was tested

Fr1da *plus*

Single positive

Left diagram

1st Sample For Antibody Test

- **LIPS U** → ≥ 10U → **LIPS I** → ≥ 15U + ≥ 9U RIA IAA → **Intermediate report (single)**
- **ELISA** → ELISA < 35U or RIA* neg. → **Intermediate report (single)**

Right diagram

1st Sample For Antibody Test

- **LIPS** → LIPS U < 3U / LIPS I < 4U → **Intermediate report (single)**
- **ELISA** → ≥ 35U → **RIA*** → One pos** ≥ 90U GAD*** ≥ 9U IA2 (ZnT8 R/W) → **Intermediate report (single)**

Lower left

2nd Sample For Confirmation

- **RIA/LIPS IAA** → ≥ 15U LIPS IAA + ≥ 9U RIA IAA → **Positive report (single)**
- **RIA*** → All neg. < 30U GAD < 3U IA2 (ZnT8 R/W)

Lower middle

2nd Sample For Confirmation

- **RIA/LIPS IAA** → RIA < 1.5U LIPS I < 4U → **Positive report (single)**
- **RIA*** → One pos.** ≥ 90U GAD ≥ 9U IA2 (ZnT8 R/W)

Lower right

Positive report (early stage T1D)
possible development of an additional antibody

Negative report
Antibody measurement was not confirmed

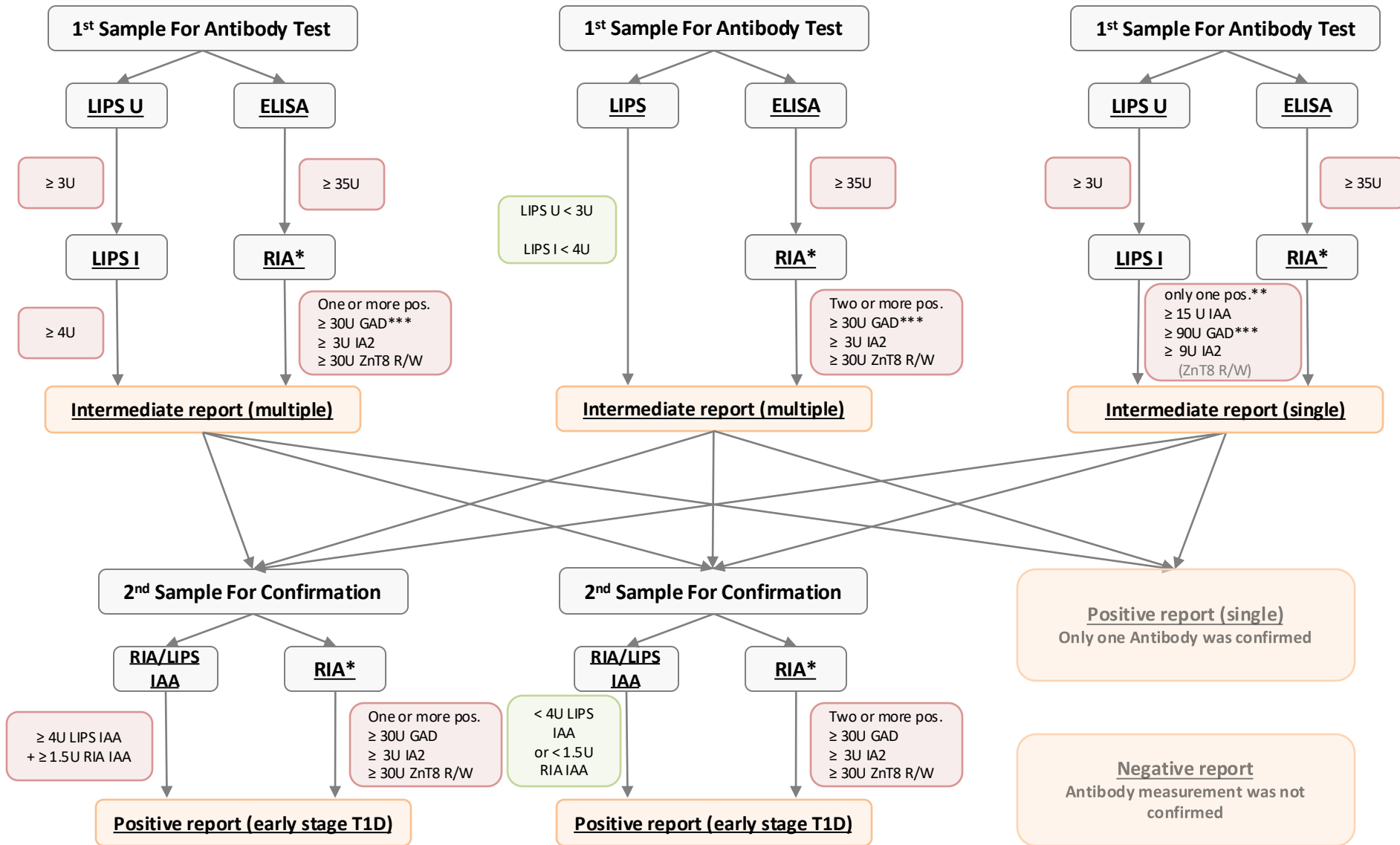1st sample is a capillary sample, 2nd Sample for confirmation is a venous sample (comment in FrontEnd)

LIPS U = IAA LIPS non-inhibited
LIPS I = IAA LIPS inhibited
ELISA = 3 - Screen ELISA
(GAD, IA2, ZnT8)
RIA* = GAD, IA2, ZnT8 R, ZnT8 W

** only for Single positive status : at least 3 times higher (GAD,IA2) and 6 times higher (RIA IAA) than regular cut off; ZnT8 AB are not found to be single positve

*** GAD (highest priority); For negative / single report: Results from IA2 and ZnT8 not necessary if GAD was tested

The final diagnosis will be decided individually in a findings meeting depending on the case

Fr1da plus

Early stage T1D

Column 1

1st Sample For Antibody Test

LIPS U → ≥ 3U → **LIPS I** → ≥ 4U

ELISA → ≥ 35U → **RIA*** → One or more pos. ≥ 30U GAD*** / ≥ 3U IA2 / ≥ 30U ZnT8 R/W

Intermediate report (multiple)

Column 2

1st Sample For Antibody Test

LIPS → LIPS U < 3U / LIPS I < 4U

ELISA → ≥ 35U → **RIA*** → Two or more pos. ≥ 30U GAD*** / ≥ 3U IA2 / ≥ 30U ZnT8 R/W

Intermediate report (multiple)

Column 3

1st Sample For Antibody Test

LIPS U → ≥ 3U → **LIPS I**

ELISA → ≥ 35U → **RIA***

only one pos.** ≥ 15 U IAA / ≥ 90U GAD*** / ≥ 9U IA2 (ZnT8 R/W)

Intermediate report (single)

2nd Sample For Confirmation

RIA/LIPS IAA → ≥ 4U LIPS IAA + ≥ 1.5U RIA IAA

RIA* → One or more pos. ≥ 30U GAD / ≥ 3U IA2 / ≥ 30U ZnT8 R/W

Positive report (early stage T1D)

2nd Sample For Confirmation

RIA/LIPS IAA → < 4U LIPS IAA or < 1.5U RIA IAA

RIA* → Two or more pos. ≥ 30U GAD / ≥ 3U IA2 / ≥ 30U ZnT8 R/W

Positive report (early stage T1D)

Positive report (single)
Only one Antibody was confirmed

Negative report
Antibody measurement was not confirmed

1st sample is a capillary sample, 2nd Sample for confirmation is a venous sample (comment in FrontEnd)

LIPS U = IAA LIPS non-inhibited
LIPS I = IAA LIPS inhibited
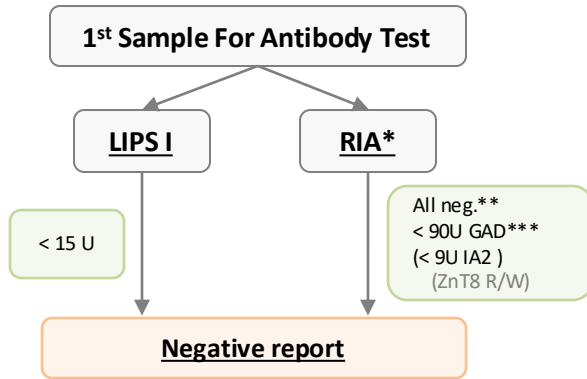ELISA = 3 - Screen ELISA (GAD, IA2, ZnT8)
RIA* = GAD, IA2, ZnT8 R, ZnT8 W

** only for Single positive status : at least 3 times higher (GAD,IA2) and 6 times higher (RIA IAA) than regular cut off; ZnT8 AB are not found to be single positve

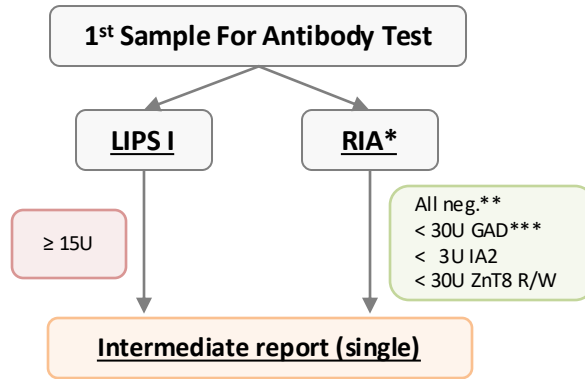*** GAD (highest priority); For negative / single report: Results from IA2 and ZnT8 not necessary if GAD was tested

The final diagnosis will be decided individually in a findings meeting depending on the case

Fr1da plus
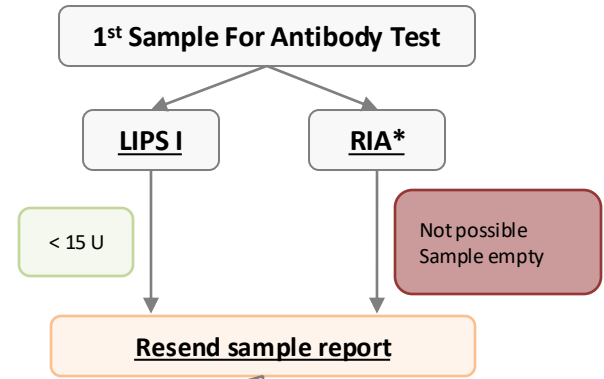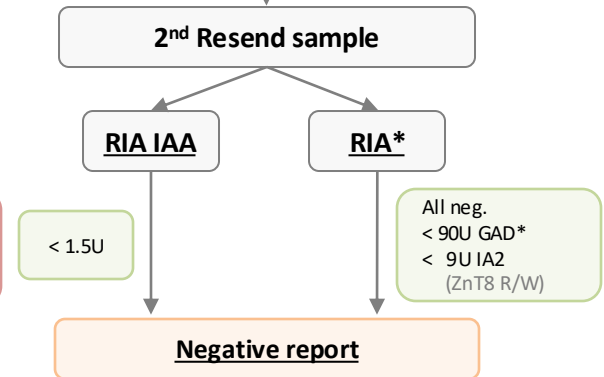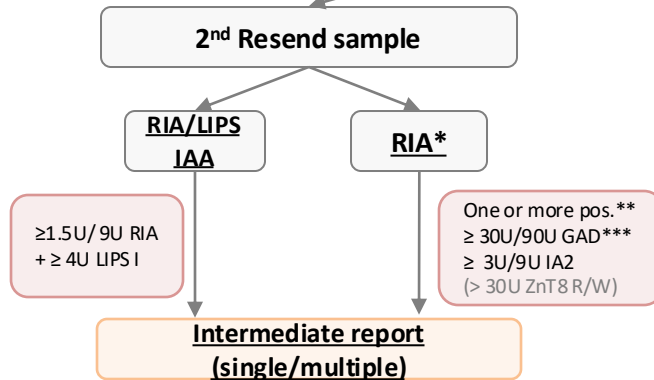
Special cases (not all in use anymore)

Low volume

1st Sample For Antibody Test
→ **LIPS I**
→ **RIA***

LIPS I: < 15 U

RIA*: All neg.**
< 90U GAD***
(< 9U IA2)
(ZnT8 R/W)

→ **Negative report**

Low volume

1st Sample For Antibody Test
→ **LIPS I**
→ **RIA***

LIPS I: ≥ 15U

RIA*: All neg.**
< 30U GAD***
< 3U IA2
< 30U ZnT8 R/W

→ **Intermediate report (single)**

Low volume

1st Sample For Antibody Test
→ **LIPS I**
→ **RIA***

LIPS I: < 15 U

RIA*: Not possible
Sample empty

→ **Resend sample report**

Low volume

1st Sample For Antibody Test
→ **LIPS I**
→ **RIA***

LIPS I: < 4U

RIA*: One pos.
≥ 90U GAD*

→ **Intermediate report (single)**

2nd Resend sample
→ **RIA/LIPS IAA**
→ **RIA***

RIA/LIPS IAA: ≥1.5U/ 9U RIA
+ ≥ 4U LIPS I

RIA*: One or more pos.**
≥ 30U/90U GAD***
≥ 3U/9U IA2
(> 30U ZnT8 R/W)

→ **Intermediate report (single/multiple)**

2nd Resend sample
→ **RIA IAA**
→ **RIA***

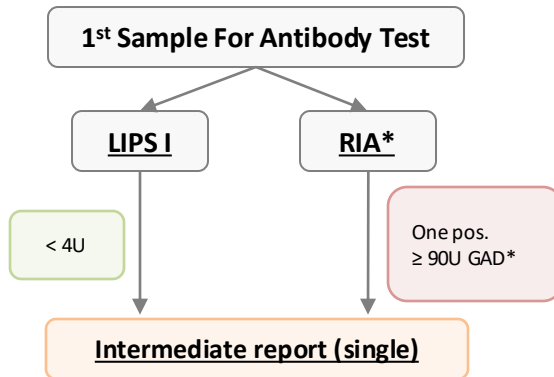RIA IAA: < 1.5U

RIA*: All neg.
< 90U GAD*
< 9U IA2
(ZnT8 R/W)

→ **Negative report**

1st sample is a capillary sample, 2nd Sample for confirmation is a venous sample (comment in FrontEnd)

LIPS U = IAA LIPS non-inhibited
LIPS I = IAA LIPS inhibited
ELISA = 3 - Screen ELISA
(GAD, IA2, ZnT8)
RIA* = GAD, IA2, ZnT8 R, ZnT8 W

** only for Single positive status : at least 3 times higher (GAD,IA2) and 6 times higher (RIA IAA) than regular cut off; ZnT8 AB are not found to be single positve

*** GAD (highest priority); For negative / single report: Results from IA2 and ZnT8 not necessary if GAD was tested

The final diagnosis will be decided individually in a findings meeting depending on the case

Fr1da plus

Cutoffs

- Screening-Cutoffs (Screening and Confirmation samples)
  - **elisa**
    - sample_date <= '2022-01-31' & elisa >= 25 → further testing
    - sample_date > '2022-01-31' & sample_date <= '2024-12-31' & elisa >= 40 → further testing
    - sample_date > '2024-12-31' & elisa >= 35 → further testing
    - further testing: gada_trunc, ia2, znt8_c_arg, znt8_c_tryp
  - **lips_unin_iaa (uninhibited)**
    - if elisa above cutoff and lips_unin_iaa >= 3 → further testing
    - if elisa below cutoff and lips_unin_iaa >= 10 → further testing
    - further testing: lips_in_iaa
  - **lips_in_iaa (inhibited)**
    - in screening sample only if lips_in_iaa >= 15 and other antibodies negative → further testing
    - in confirmation sample always tested; lips_in_iaa >= 4 & m_iaa >= 1.5 → positive
    - further testing: m_iaa

- Screening-Single-Testing- and Follow-Up-Cutoffs: **RIA**-Antibody-Measurements
  - **m_iaa**
    - m_iaa >= 1.5 → positive
  - **gada_trunc**
    - sample_date <= '2016-12-12' & gada_trunc >= 22 → positive
    - sample_date > '2016-12-12' & gada_trunc >= 30 → positive
  - **ia2**
    - sample_date <= '2016-12-12' & ia2 >= 5 → positive
    - sample_date > '2016-12-12' & ia2 >= 3 → positive
  - **znt8 (znt8_c_arg & znt8_c_tryp)**
    - sample_date <= '2016-12-12' & znt8_c_arg >= 16 → positive
    - sample_date > '2016-12-12' & znt8_c_arg >= 30 → positive
    - znt8_c_tryp >= 30 → positive
    - negative only if both znt8_c_arg and znt8_c_tryp are negative; positive if only one or both are positive