Proposal for LOINC Lab Committee regarding
PCR-Related *Methods* in LOINC
June 8, 2017

Special topics workgroup goal

To review all of the existing nucleic acid testing *Methods* in LOINC and develop a proposal regarding at what level of granularity these *Methods* need to be distinguished and how best to name them.

Existing Methods in LOINC related to nucleic acid testing

Probe: Target-specific probe (no nucleic acid amplification step)

Probe.amp.tar: Nucleic acid target amplification followed by target-specific probe-based detection of the *Analyte*

Probe.amp.sig: Target-specific probe followed by amplification of the signal so that the signal can be detected (no nucleic acid amplification step)

Probe.mag capture: Magnetic, bead-based nucleic acid capture followed by target-specific probe

Non-probe.amp.tar: Nucleic acid target amplification followed by non-probe based detection method, such as melt curve analysis or turbidity

Process

1. Reviewed all of the existing nucleic acid testing *Methods* and the steps included in each.

2. Looked at different sources, including various lab sites, FDA, CDC, and scientific literature, to get a sense of the level of granularity at which these *Methods* are usually distinguished.

3. Determined what we (the workgroup) thought was the best way forward in light of the impact on LOINC users and stakeholders.

Summary

Each existing *Method* in LOINC contains specific information about one or more of the following steps: 1) nucleic acid isolation; 2) target amplification; and 3) target detection.

Only the **Probe.mag** capture LOINC *Method* actually contains information about the initial nucleic acid isolation step (bead-based). All 34 of the **Probe.mag** capture terms were created for one specific assay that, if we were to assign a *Method* without taking the capture step into account, would be classified as **Probe** (it does not include target amplification as part of the actual assay).

Ultimately, the workgroup felt that distinguishing different methods for nucleic acid isolation should not be part of the LOINC *Method*.

Regarding the target amplification and target detection steps, the workgroup felt that:

1. It is definitely important to distinguish assays that include nucleic acid amplification versus those that do not.

2. It is not as clear whether or not we should distinguish the target detection *Method* (e.g., probe versus melt).

Initially, we considered changing the existing "**Probe.amp.tar**" *Method* to "Nucleic Acid Amplification Test" (NAAT), which most workgroup members felt is a more common term in the lab community than the concept names used in LOINC. With this approach, we would have grouped all nucleic acid amplification methods together regardless of detection method, which would have put **Probe.amp.tar** and **Non-probe.amp.tar** terms in the same *Method* category.

However, such a change would have been more than a simple name change, because we would be changing/broadening the meaning of the existing terms. We briefly considered deprecating all **Probe.amp.tar** and **Non-probe.amp.tar** terms and creating all new "NAAT" terms, but in the end did not think it would be worth the effort to deprecate over 1,300 codes and create new ones.

Recommendations:

1. Deprecate the **Probe.mag** capture terms and create new terms with **Probe** as *Method* where

there is no existing **Probe** term. Also create a new panel term to hold all of the terms in this assay together.

2. Continue to distinguish methods with nucleic acid amplification from methods with no amplification.

3. Continue to distinguish signal amplification from target amplification.

4. Keep the existing *Methods* as is, but add descriptions to the Users' Guide as well as to each *Method* part (can see those descriptions in the RELMA part search) as follows:

a. **Probe**: A hybridization probe is a typically a short nucleic acid segment that binds to a complementary nucleic acid sequence that is the specific to the target of interest. The probe is typically attached to signaling molecule in such a way that a signal is only generated when the probe binds to the target nucleic acid. In LOINC, the **Probe** *Method* is used for assays that do not include either a nucleic acid amplification or a signal enhancement step.

b. **Probe.amp.sig**: **Probe** with signal amplification is a lab method that uses a hybridization probe, which is a typically a short nucleic acid segment that binds to a complementary nucleic acid sequence that is the specific to the target of interest, followed by a signal enhancement step, in which the signal that is generated when the probe binds to the target sequence is multiplied so that it is "brighter" and easier to detect. Signal amplification can be done using difference techniques, including the branched-chain DNA (bDNA) method. In theory, signal amplification is more sensitive than a probe by itself because it generates a brighter signal per each copy of the target sequence that is present. In LOINC, the **Probe.amp.sig** *Method* is assigned to codes for assays that do not include a nucleic acid amplification step.

c. **Probe.amp.tar**: The LOINC **Probe.amp.tar** *Method* is used for assays that include a nucleic acid amplification step, in which many copies of the nucleic acid sequence(s) of interest are made, followed by detection of the target nucleic acid of interest using a hybridization probe. Nucleic acid amplification can be done using different techniques such as polymerase chain reaction (PCR). The primary difference between the **Probe.amp.tar** and **Non-probe.amp.tar** Methods is the

technique used for target nucleic acid detection.

d. **Non-probe.amp.tar**: The LOINC **Non-probe.amp.tar** *Method* is used for assays that include a nucleic acid amplification step, in which many copies of the nucleic acid sequence(s) of interest are made, followed by detection of the target nucleic acid of interest using a method other than a hybridization probe, such as melt curve analysis or turbidity measurement. The primary difference between the **Probe.amp.tar** and **Non-probe.amp.tar** *Methods* is the technique used for target nucleic acid detection.

5. Update the *Long Common Name* and *Short Names* for the *Methods* as shown:

Method	**Current → proposed display name**	**Current → proposed abbreviation**
Probe (includes DNA, RNA etc)	DNA probe → Probe	Prb → Probe (first check to make sure that short names don't exceed 40 char)
Probe.amp.sig	Probe and signal amplification → Probe with signal amplification	bDNA → Probe+sig amp (check 40 char limit)
Probe.amp.tar	Probe and target amplification method → NAA with probe detection	PCR → NAA+probe
Non-probe.amp.tar	Target amplification with non-probe based detection → NAA with non-probe detection	Non-probe PCR → NAA+non-probe
Probe.mag capture	n/a (deprecate)	