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## 1. VETERINARY CODES

As the NARMS project includes testing done on food and animal isolates, antimicrobials used in veterinary medicine are important. Currently, several animal-specific agents not included in the LOINC lists. I had a meeting last week with Jerry Sable, with the CDC NEDSS project, and he indicated that he believes that you have recently brought someone with a veterinary micro background on-board. That would be great new direction for further LOINC development.

With respect to the NARMS project, the following animal-specific agents are not in the LOINC database:

Avilamycin  
Flavomycin  
Salinomycin  
Tiamulin  
Tilmicosin  
Tylosin  
Virginiamycin

Additional agents missing from LOINC which are included in the NCCLS document M31-A "Performance standards for antimicrobial disk and dilution susceptibility testing for bacteria isolated from animals" (May 2002) include:

Difloxacin  
Orbifloxacin  
Penicillin-novobiocin  
Pirlimycin

## 2. HUMAN ANTIMICROBIALS

The following compounds are listed in the NCCLS document M100-S14 "Performance standards for antimicrobial susceptibility testing" (January 2004), but missing from LOINC.

Cefditoren  
Daptomycin  
Ertapenem

Garenoxacin  
Gemifloxacin  
Telithromycin  
Trospectinomycin  
Cefotaxime/clavulanic acid  
Ceftazidime/clavulanic acid

There are additional NCCLS documents with agents for antifungal, antimycobacterial, and antiviral testing. I am currently in Georgia, so unfortunately don't have these documents with me. When I return to Boston, I will see whether our laboratory has copies and whether any additional compounds should be added to LOINC. As you know, many new antifungals and antiretrovirals have been introduced on the market in the past few years, so it would be good to review the latest documents.

In WHONET, I do include many additional antimicrobial compounds (particularly Japanese drugs, some European drugs, many old "retired" drugs) which do not appear in the LOINC tables, but I am not sure which are still currently used in practice, so I haven't bothered to try including these.

### 3. "GRADIENT STRIP" - ETEST PRODUCTS

In the LOINC tables, there are codes for several agents with "gradient strip" codes which currently do not exist on the market. I would just leave them in for completeness sake in case they are eventually introduced by ABBiodisk or potentially another company.

However, there are other compounds which do not yet have "gradient strip" codes in LOINC, but which are products available from the company ([www.abbiodisk.com](http://www.abbiodisk.com), Product catalog). These include:

Cefdinir  
Cefditoren  
Cefixime  
Cefoperazone.  
Cephalexin  
Enrofloxacin  
Ertapenem  
Fosfomicin  
Gentamicin.High potency  
Mecillinam  
Polymyxin  
Spectinomycin  
Streptomycin.High potency  
Voriconazole  
Sulfonamide

The following Etests do not yet appear in LOINC tables

Cefepime/clavulanic acid

Cefoperazone/sulbactam

Imipenem+EDTA

#### 4. MISSING TEST CODES

Focusing on the antibacterials and the methods “agar diffusion” (disk), “MIC”, and “generic” (blank entry), the following tests have no LOINC code, and should be added. All of the following do have guidelines for test performance and recommendation, either in the United States or in Europe. I have not included theoretical test combinations for which I have no knowledge of use.

Cefdinir – disk

Cefetamet – disk, MIC

Cefotiam – disk, MIC

Ceftibuten – disk, MIC, generic

Ceftiofur - disk, mic

Cefuruxime.oral - disk, generic

Clinafloxacin – disk, MIC

Dirithromycin – disk, MIC, generic

Enrofloxacin – disk, MIC

Fleroxacin – disk

Florfenicol – disk, MIC

Fosfomicin – disk

Grepafloxacin – disk

Isepamicin – disk, MIC

Mecillinam – disk, MIC

Mupirocin – disk, MIC

Nystatin – disk

Pefloxacin – disk

Pristinamycine – disk, MIC

Quinupristin/dalfopristin – disk

Sparfloxacin – disk

Trovafloracin – disk

Voriconazole – MIC

In future, I would recommend that you add “generic”, “agar diffusion”, and “MIC” for all antibacterials by default. For “gradient strip”, you can check the ABBiodisk product catalogue.

I did not paid much attention to the antivirals, antimycobacterials, and antifungals, so these should also be reviewed at some point. I also did not review the entries for SLT and MLC as these are not important tests in routine clinical laboratories. You may wish

to ask a specialist reference center to review those.

## 5. POSSIBLE ERRORS/DUPLICATIONS IN EXISTING LOINC CODES

-- Typing errors

FOSFOMYCINE (French spelling) --> FOSFOMYCIN

CEFMENOXIM (German spelling) --> CEFMENOXIME

CLINACLOXACIN --> CLINAFLOXACIN (which already has a LOINC entry). (In a quick Google search, the only citing to clinacloxacin is the LOINC database)

-- Duplication

MUPIROCIN.TOPICAL --> MUPIROCIN. This is always a topical drug. Especially for susceptibility testing, I don't see any reason for distinguishing this entry from MUPIROCIN.

-- Doesn't exist

IMPENEM+CILASTATIN. Cilastatin is a substance which blocks the human enzyme renal membrane dipeptidase (dehydropeptidase I). In the human body, imipenem is always administered with cilastatin because the renal enzyme very efficiently destroys the antibiotic imipenem. So cilastatin blocks the destruction of imipenem by the kidney, permitting the antibiotic to exert its therapeutic effect. When patients are administered "imipenem", they in fact are administered the imipenem+cilastatin combination.

Consequently, there is no need to use cilastatin in the laboratory. As far as I know, the antibiotic disks and MIC tests contain only the active substance imipenem. You may wish to confirm this by talking to someone else as well.

-- ? Incorrect/incomplete METHOD\_TYP

AZITHROMYCIN+ETHAMBUTOL

This combination is listed as only as an MIC. I am not familiar with the testing of this combination, but I imagine that it is only done for AFB, so you may wish to add an AFB method to this entry.

-- Incorrect synonym

NITROCEFAN. This name is currently listed as a related name and synonym for ceftriaxone (brand name = Rocephin, hence the possible confusion). Nitrocefina is a brand of disks used to test for beta-lactamase production by a bacteria. Thus it should be put as a related name for BETA LACTAMASE.USUAL. Another brand of disk commonly used for doing the same test is "Cefinase", and should also be included as a related name.

## 6. ADDITIONAL COMMENTS ON CURRENT ENTRIES

-- AFB tests. Under METHOD\_TYP are listed the entries AFB and MYCOBACTERIA.SLOW. I wonder whether the individual suggesting the addition of

“Mycobacteria.Slow” in fact wanted a separate option for “Mycobacteria.Fast” or “.Rapid”. The most important AFB (acid-fast bacillus) is *M. tuberculosis*, which is a slow-growing organism. The AFB Method type principally refers to this organism (NCCLS M24-A, “Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes”). As far as I am aware AFB and MYCOBACTERIA.SLOW refer to the same thing.

In contrast, there are many fast-growing mycobacteria, which can be tested using a different method. So MYCOBACTERIA.RAPID may be an entry of interest to some people. Check with the people who suggested the “Mycobacteria.Slow” entry. On the other hand, it is possible that they are referring to some method for other slow growers, for example *M. leprae* (cause of leprosy), and do want the “.SLOW” option.

-- CEFUROXIME.ORAL – this compound is commonly known by its generic name “Cefuroxime axetil”, which you currently have under RelatedNames2. I would suggest adding it to RELAT\_NMS since it is a synonym. Similarly, CEFUROXIME.PARENTERAL is a synonym for “Cefuroxime sodium”.

-- CEFTRIAXONE.MENINGITIS, *etc.*. The meningitis entry is related to MIC and Etest susceptibility testing of *Streptococcus pneumoniae* for the compounds ceftriaxone, cefotaxime, and cefepime (for which there are already LOINC entries). The meningitis interpretative breakpoints in fact are the same as the old *S. pneumoniae* breakpoints for these compounds. What is new is the use of “non-meningitis” breakpoints, so I suggest that you add entries for CEFTRIAXONE.NONMENINGITIS, *etc.*

-- ESBL detection. LOINC has a code for BETA LACTAMASE.EXTENDED SPECTRUM (synonym = ESBL). The combinations cefotaxime/clav., ceftriaxon/clav., and cefepime/clav are used in the detection of ESBL production (but which do not yet appear in the LOINC lists), so you may wish to add “ESBL” to the list of related names for these entries.

## 7. ADDITIONAL TEST METHODS (SCREEN PLATES, ETC.)

In addition to the usual methods discussed above, it is becoming more common to search for specific resistances using specialized tests.

Some are relative low-tech, such as the use of “screen” plates. In a screen plate, a fixed concentration of a certain drug is incorporated into the agar. The isolate is then plated, and examined the next day. If the organism grows, it is resistant to the agent. Common examples of screen plates include “oxacillin screen plate” for detection of MRSA and screen plates for vancomycin, gentamicin (high potency), *etc.* for enterococci. These can be viewed as MIC tests in which only one concentration is tested. Or in computer databases, they are more often treated as distinct special tests. Say you may wish to discuss with your microbiology group how they would like to deal with such plates. The number of distinct plates in routine practice is relatively small, but in research or perhaps in the future, they could be much more common.

Other methods are more high-tech, utilizing PCR or other gene probes to identify specific resistance genes, for example looking for INH resistance in *M. tuberculosis* or the *mecA* gene in MRSA. I know that there are various LOINC codes for gene studies, so one of your micro experts should be able to advise whether any additional modifications/entries for susceptibility testing done with probes should be considered.

There are also specialized lab tests for synergy, killing curves, *etc.* But since they are not used in routine clinical labs, I wouldn't consider them to be high priority for LOINC.