# **Documentation for Equivalence Classes – Flowsheet Use Cases**

## **Rationale**

The equivalence classes (grouper) provide a way to aggregate sets of observations for various purposes.

This document describes producing equivalence classes that define a set of observations that are slightly different but could be displayed in a single line of a flowsheet or aggregated for other purposes, such as in Figure 1. These classes will almost always include only one distinct analyte, but ignore some or all distinctions in methods, some distinctions in specimens, etc. Thus, the tests within one class will, with group clinically similar values. Such an equivalence assumes that the individual LOINC codes and our display names are easily available via “mouse over” or a “click though on a cell” (or some other mechanism) when the flowsheet is a live display, or are included as footnotes at the bottom of the page as shown in Figure 2. The goal is to make flowsheets easier to digest (fewer rows with more data per row), and would allow an organization’s choice to reduce the effort of mapping incoming test results to tests in their local environment that may not be as precisely defined in the receiver’s environment.

In this project, we developed equivalence rules one LOINC class at a time, because we could more easily predict the results when we focused on one class at a time. LOINC terms are constructed from six different types of parts. In general, the approach we took was to first enumerate the distinct parts of each type in a given LOINC class, e.g. the method, specimen, etc. We looked especially closely at the specimen (LOINC system) and the methods together, because the clinical distinctions among some of the sets of method and specimen are small. For example, for most tests, we ignore the distinctions between plasma and blood measurements. For some LOINC classes, we lumped time tests, e.g. 4h, 12h, 24h, together, at least for some concentrations. For some LOINC classes, we ignored distinctions by method except for special LOINC cases. The equivalence classes may also mix tests with categorical values, e.g. positive, negative, and titers, e.g. 1:25L, whose meaning will not be confused with standard numerical values in the same row because their different representations. For some LOINC classes, we also equivalence quantitative titers, arbitrary concentrations, and ordinal values because the displayed values would signal whether they were a concentration, titer, or coded answer. In a few cases, we conditioned the specimen that would be equivalenced to a specific set of analytes.

So, though we equivalence arterial, capillary, venous, mixed venous blood for most chemicals, we could not do that for the analysis of oxygen saturation or oxygen content, and we used different specimen groupings for analytes with distinct values on the arterial versus the venous side of circulation. We equivalence capillary blood to arterial blood, but only for oximeter, because in the case of oxygen saturation is measured peak surge of arterial blood into the capillary bed1, 2, 3.

We have finished the first draft for microbiology, hematology, chemistry, drug/tox, serology, and urinalysis, which constitutes the majority of the lab testing content. We do not plan to address the Chemistry challenge tests (Class Chal) at all, because the tests in that class tend to be exotic, and not congenial to grouping because they are so specialized.

We also have plans to build a unit conversion function into the table, that would convert units of the same property into a locally preferred one, and perhaps, convert some tests with a different mass/molar conversion.

## **Process we followed:**

For each class, we have extracted all of the specimen and method dimensions of the term and defined groups and subgroups via spreadsheets that contains the whole parts. We exclude panels always.

## **Notes on Our Group Labels and Symbols:**

For some classes and terms, we have a set of parts with the word ‘other” at its end. These are used to refer to all of the parts of that type, except those that are not already called out in named groups.

This document is intended for laboratory users, so we refer to the LOINC “Component,” as an “Analyte” because that is what laboratorians usually call it, and we refer to the LOINC “System” as the “Specimen” for the same reason.

We define many named groups of parts, which are “equivalent” for the purpose of this equivalence class use-case. For example, “Intravascular - any” refers to most of the intravascular specimens, e.g. blood, serum, plasma etc. (see the enumeration of the parts it contains in the Cross-Class Specimen Part Groups). So, terms that only differed by different members of the specimen group would be equivalenced. Depending on the class, we might have many sets of part equivalence groups for multiple part types, which we put under Cross-Class Part Groups. And, the same rule would apply across multiple part types, e.g. Method, Specimen, Time. We have attached a sample output in Appendix A, and you can better digest what we are doing from the example output.

Exclude panel terms from all Equivalence classes. Think this will happen automatically because we have most classes are contained in panel classes

## **Exclude panels from the process**

## **Cross-Class Part groups used by more than one class:**

**Cross-Class Analyte (“COMPONENT”) Part Groups:**

Ab and Ag: This group includes all analyte that represent antibodies and antigen tests. However, three proteins include “antigen” as an intrinsic part of their name: Prostate specific antigen, Squamous cell carcinoma antigen, and Tissue polypeptide specific antigen. These three should be treated as a total unit. We use this group to decide when to include method less tests in with the immune assay group. We use this category to put immunology test that are the sane except without a method together with the IA method for the AG or the AB test respectively

**Cross-Class Specimen (“SYSTEM”) Part Groups:**

* Intravascular - any: Bld, BldA, BldC, BldMV, BldP, BldV, Bld.dot, Plas , PlasA, PlasV, Ser, Ser/Bld, Ser/Plas, Ser/Plas/Bld, Ser/Plas.ultracentrifugal- With a few exceptions we equivalence tests with any of these specimen types
* Bld - any: Bld, BldA, BldC, BldMV, BldP, BldV, (we equivalence tests that care about the cells in blood with any of these specimen types. ( we treat cord blood (Taken out of the umbilical cord at birth differently because it has somewhat different content
* BLdCo - any : BldCo,BldCoA, BldCoMV,BldCoV
* DuodGastricFld : "Duod fld/Gast fld", "Duod fld", "Gast fld" (These are close to the same in most cases
* OcularVitrFld: Ocular fluid, Vitreous fluid ( these are close to identical )

**Cross-Class Scale Part Groups**

* OrdNomNarDoc: Ord, Nom, Nar, Doc
  + Narrative, document – these end up being a document without pre-specified in coded structure
  + ORD and NOM– assume most will be distinguished by other properties. Both of these data types have coded answers. ORDs’ are usually yes/no, or rare, few, many, loaded. Noms are us usually names of things identified by the study. They will not be confused in the row of a flowsheet. However the component will almost always be different enough that they won’t collapse into one row.

## **Class: ALLERGY**

**ALLERGY Specimen (“SYSTEM”) Part Groups:**

* Intravascular - any: See the Cross-Class specimen for the definition of this specimen group.

**ALLERGY Method Part Groups:**

* Equivalence all methods (including NULL method)

**Property Part Groups:**

* PrThrACnc: PrThr and ACnc. (This assumes the users just want to know whether the subject has allergies to the compounds in question. Terms with Mass concentrations and percent’s will still be distinguished because mixing the numeric values will not make sense.)

**ALLERGY Scale Part Groups:**

* Use Cross-Class Scale group OrdNomNarDoc, except when the word “RAST” appears in the component. (This may have no effect due to distinctions among other properties.)

## **Class: Antibiotic susceptibility (ABXBACT)**

**ABXBACT Method Part Groups:**

* Method-other: Equivalence all methods (including NULL) except genotyping and method for slow growing mycobacteria.

**ABXBACT Property Part Groups:**

## Treat all properties the same except- almost all are already mixes of ORDQN

ABXBACT- treat all scale value the same except distinguish nom (presume that will make it unnecessary to distinguish PRID from others (not sure if theis is right ??)

## **Class: Blood bank (BLDBK)**

Don’t think there are opportunities to combine any rows . So nothing to do

## **Class: CELLMARK**

**CELLMARK Method Part Groups:**

* Method-other: Equivalence all methods (including NULL)
* Use Cross-Class Scale group OrdNomNarDoc

**CELLMARK Specimen Part Groups:**

* Intravascular - any: See the Cross-Class specimen for the definition of this specimen group.

**NOTEs TO RI:**

* Should see if we can take advantage of panels. If there is not much overlap will provide a nice organization of flow sheet this is just a note to McD

## **Class: CHEM**

**CHEM Analyte (“COMPONENT”) Part Groups:**

For Clem: At present not distinguishing glucose tests done on blood vs ser.plas though maybe should . ditto the different colorimetric methods for protein

* **Oxygen-related**: Oxygen, Oxygen saturation, Oxygen content, Oxygen capacity, Oxyhemoglobin/Hemoglobin.total  Oxyhemoglobin, Deoxyhemoglobin,

Deoxyhemoglobin/​Hemoglobin.total (Paul will want to add the terms that “adjusted for modifiers after the hat, Oxygen ^adjusted to patients actual temperature, Oxygen^^ saturation adjusted to 0.5. No oxygen test should be paired with Intravascular any

* **Group any terms that are the same up to the first ^ character.**

**CHEM Specimen (“SYSTEM”) Part Groups: Lump the categories’ described below the results will remain independent**

* Later- will want to highlight intravascular specimens whose component is Gluose(exactl) se that are Ser or Ser/plas. Will require setting a flag in the table. Will not tackle that now.
* Arterial\*: BldA, BldC, BldCoA
  + EXCEPTION: Only group the Arterial\* specimens when the analyte is contained in the **Oxygen-related** analyte group (see above for the definition of Oxygen-related).. Note also that capillary blood is arterial from the point of view of a pulse oximeter.
* Venous\*: BldV, BldMV, BldCoV, BldCoMV
  + EXCEPTION: Only group the Venous\* specimens when the analyte is contained in the Oxygen-related group (see above for the definition of Oxygen-related).
* DuodGastricFld : See the Cross-Class specimen for the definition of this specimen group
* OcularVitr fld: See the Cross-Class specimen for the definition of this specimen group

**CHEM Property Part Groups:**

* Combining groups with comparable Mass and substance properties – would have to include the appropriate molecular weight in all records with the same analyte. (We have a table with about 1800 of them) users will have to choose whether to prefer S\* or M\* when both are present in an Equiv class .
* Believe we can choose to show units or not. However within a row would prefer to convert all values into the same units. For demonstration purposes would be best to have a control one could set over the whole table so we could see what happens when we turn it on and off. How to decide which to use ? Simplest way would be to pick the first one encountered, but better to allow implementers to set the units in a group explicitly within the template. (For later)
  + Be careful with the length measures and body weight measures . Think we had them working don’t remember the rules
* LOINC also includes Catalitic properties. But these are quite different and would not be combined with the M\* and S\* properties . However there could be scaling issues re units in the same row just as there could be with mass and molar weights
* MCnt and SCnt
* MFr and SFr
* MRto and SRto
* MRat and SRat
* Mass and Sub
* EntMass and EntSub (however almost all of the terms with Ent properties are EntSub
* MFr.DF and SFr.DF
* MCDiff and SCDiff
* MCncSq and SCncSq
* MCrto and SCrto
* RelMCnc and RelSCnc
* RelMRat and RelSRat

**CHEM Time (“TIME\_ASPCT”) Part Groups:**

* TimedSpecimen: 10h, 12h, 18h, 1h, 24h, 2h, 48h, 4h, 5h, 6h, 72h, 8h

**CHEM Method Part Groups:**

* Method-Other: Includes all CHEM methods (and blank ones) except:

“Detection limit\*”, “High sensitivity method”, “screen\*”, “Confirm\*”

(“screen\*” will show up for DRUG/TOX, but not for CHEM)

## **Class: COAG**

**COAG Specimen Part Groups:**

* Intravascular - any: Bld, BldC, ser, plas, PPP, PRP, SerPl, PPP/Bld
* All SuperSystem terms should be distinguished (Be sure we do treat system and super system as unit so that different super systems won’t be mixed
  + NOTE: There is a case discrepancy between what’s in the Part Super System terms which are capitalized (i.e. Control) vs what’s in LOINC which is not capitalized (i.e. PPP^control)

**COAG Method Part Groups:**

* Method\_other: equivalence everything (including NULL methods) except Thromboelastography

**COAG Property Part Groups:**

* PrTitrACnc: Pr, Titr, ACnc

**COAG Scale Part Groups:**

* Scale: treat them all the same--the content will speak for itself

## **Class: CYTO**

**CYTO Specimen Part Groups:**

* Genital-Female: Cvx/Vag with Vag and Cvx
* Resp – Lower: Bal, Broncial, Bronchial brush, sputum

**CYTO Scale Part Groups:**

* Use Cross-Class Scale group OrdNomNarDoc

**CYTO Component Part Groups:**

* MicroCyto: Microscopic observation, cytology report

## **Class: DRUGDOSE**

Fine as is.

## **Class: DRUG/TOX**

Follow rules for class CHEM, except:

**DRUG/TOX Scale Part Groups:**

* Use Cross-Class Scale group OrdNomNarDoc

## **Class: FERT**

**FERT Property Part Groups:**

* PrMCnc: PrThr, MCnc

**FERT Method Part Groups:**

* Method-other: equivalence all methods, including NULL methods

**FERT Scale Part Groups:**

* Use Cross-Class Scale group OrdNomNarDoc

**FERT Property Part Groups:**

* PrNCnc: PrThr, NCnc

Pay attention to classes. (for selected classes may want to order the variables the same way they are ordered in the class- with the class term in front. This won’t work when the classes contain many of the same terms

## **Class: HEM/BC**

**HEM/BC Specimen:**

* Bld-any: See the Cross-Class specimen for the definition of this specimen group
* BldCo-any: See the Cross-Class specimen for the definition of this specimen group
* DuodGastricFld: See the Cross-Class specimen for the definition of this specimen group

**HEM/BC Property:**

* PrTitrNCnc: PrThr, Titr, NCnc

**HEM/BC Method:**

* HEM-BC-Method-Any: NOl HEM/BC methods are distinguishes so all tests of one kind will be in the same group regardless of the methods.

## **Class: MICRO**

**MICRO Analyte/organism (“COMPONENT”)**

* STD-Causing \*: Chlamydia trachomatis, Haemophilus ducreyi, HSV, HSV1 , HSV2 , (Herpes Simplex Virus 1+2), Mycoplasma genitalium, N gonorrhoeae, Trichomonas vaginalis, Ureaplasma urealyticum+Ureaplasma, <HPV high risk>, < HPV probably high risk>, <HPV low risk>, <HPV indeterminate risk>
  + HPV high risk: E6 + E7, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 66, 68
  + HPV probable high risk: 26, 73, 82
  + HPV low risk: 6, 11
  + HPV indeterminate risk: 69

Patterns for STD-Causing, for “COMPONENTCORE” (% means wildcard):

* 1. %HPV E6+E7%
  2. Chlamydia%
  3. Haemophilus ducreyi
  4. Herpes simplex virus%
  5. Human papilloma virus%
  6. Mycoplasma genitalium
  7. Mycoplasma sp%
  8. Neisseria gonorrhoeae
  9. Trichomonas sp
  10. Trichomonas vaginalis
  11. Ureaplasma%

**\***HIV not included because the specimens do not line up with the specimens of the others STD-causing organisms.

**MICRO Property**

* PrACncTitr: PrThr, ACnc, Titr

**MICRO Specimen (“SYSTEM”)**

* Anorectral-Genital-Urinary – The following are only grouped when the analyte is one of the STD-causing organisms (see Micro Analyte group for the definition)
  + AnalRectalStool: Anal, Anogenital, Anorectal, Anorectal/Stool, Rectum, Stool
  + Genital: Genital, Genital fld
  + Genital-Female: Endometrium, Genital Lochia, Vag, Cvx, Genital mucus, Cvm, Vag+Rectrum
  + Genital-Male: Penis, Prostatic fluid, Semen (qualify by STD)
  + UrineUrethra: Urethra, Urine, Urine sediment
* BodyFluid : Body fld, XXX.body fluid
* DuodGastricFld : See the Cross-Class specimen for the definition of this specimen group
* EyeCorneaConjunctiva : Eye, Crn, Cnjt
* Intravascular - any : See the Cross-Class specimen for the definition of this specimen group
* Intravascular-any-BPU : BPU, BPU.autologous, SerPl^bpu
* Intravascular-any-donor : Bld^donor, Bone^donor, Plas^donor, Ser/Plas^donor, Ser^donor
* IntravascularLine: Catheter tip, Line
* LungTissue: Lung, Lung tiss
* OcularVitr fld: See the Cross-Class specimen for the definition of this specimen group
* Resp: Respiratory, Sputum
* Resp-Lower: BAL, Bronchial, Bronchial brush, Respiratory.lower, Sptt, Sputum/Bronchial
* Resp-Upper: Nose, Nph, Pharynx, Respiratory.upper, Thrt
* SmallLargeIntestineBx: TGLI/TSMI, TSMI
* Tissue: Tissue, XXX.tissue
* TubesDrains: Cannula specimen, Drain
* WoundUlcer: Wound, Wound.deep, Wound.shlw, Ulc

**MICRO Method:** For the method, we grouped stains together based on their clinical use.

* Aerobic cult: Aerobic culture, Aerobic culture 25 deg C incubation
* AFB stains: Acid fast stain, Acid fast stain, Acid fast stain.Kinyoun, Acid fast stain.Kinyoun modified, Acid fast stain. Ziehl-Neelsen, Carbol-fuchsin stain, Kinyoun stain, Night blue stain, Rhodamine stain, Rhodamine-auramine fluorochrome stain, Wade stain
* Aggl: Aggl, Aggl.rapid, Aggl.micro, HA, HAI, LA, Sheep cell aggl
* Anaerobic cult: Anaerobic culture , Anaerobic culture 25 deg C incubation
* Anthrax stain: M'Fadyean stain
  + Comment: For information only
* Blood film: Malaria smear
* Blood film – Thick: Malaria thick smear, Thick film
* Blood film – Thin: Malaria thin smear, thin film
* Chlamydia-Rickettsia stain: Macchiavello stain
  + Comment: For information only
* CSF gram negatives stain: Methylene blue stain. Loeffler, Neisser stain
* Cult: Anaerobic+Aerobic Culture, Biopsy Culture, Culture, Culture @1:100, Culture.FDA method, Cytotoxin tissue culture assay, Intravascular line culture, Organism specific culture
* Diphtheria: Alberts stain, Methylene blue stain.Loeffler, Neisser stain
* Elph : Electrophoresis, Immunoelectrophoresis, PAGE, PFGE
* EM Virus stain: Microscopy.electron, Microscopy.electron.negative stain, Microscopy.electron.thin section
* Endospore stain: Malachite green stain
  + Comment: For information only
* Fungal stains: Calcofluor white preparation, Fungus stain
* Giemsa or Acridine orange stains: Acridine orange Giemsa stain, Acridine orange stain, Giemsa stain, Giemsa stain.3 micron, Giemsa stain. May-Grunwald, Modified Giemsa, Wright Giemsa stain
* Gram stains: Crystal violet stain, Gram stain
* HBsAG stain: Orcein stain
  + Comment: For information only
* IA--IF-Null\*: CIE, EIA, EIA.RST, EMIA, IA, IA.rapid, IF, Rapid, RIA, RIPA
  + Comment: We also include null methods in this class but only when the analytes have “Ab” or “Ag” in the name. See the Cross-Class Analyte group for the definition of this group.
* IB\*: IB, IB.test strip
* Immune diffusion: ID, Immune diffusion
* Intestinal parasite stains: Brilliant cresyl blue, Safranin stain, Trichrome stain modified, Trichrome stain, Trichrome stain, Gomori-Wheatley, Trichrome stain.Masson, Trichrome stain.Masson modified
* Leprosy stain: Fite-Faraco stain
  + Comment: For information only
* Light microscopy: Microscopy.light, Microscopy.light.HPF, Microscopy.light.LPF
* Molecular genetics: Amplification/Sequencing, Molgen, Probe.amp, Probe.amp.sig, Probe.amp.tar, Probe.mag capture, Sequencing
* PCP and yeast: Methenamine silver nitrate stain, Methenamine silver stain.Grocott, Methenamine silver stain.Jones
* Resp Cult: ARDS Cult, CF Resp Cult, Resp Cult
* Seratia species: Methyl green stain, Methyl green-pyronine Y stain
* Silver stains: Silver impregnation stain.Dieterle, Silver nitrate stain, Silver stain, Silver stain.Fontana-Masson, Silver stain.Grimelius, Steiner stain, Warthin-Starry stain
* Skin Fungi: KOH Preparation
  + Comment: For information only
* Viral cult: Shell vial culture
* Viral smear-HSV+VZV: Tzanck smear
  + Comment: For information only
* Yersinia pestis stains: Wayson stain
  + Comment: For information only

## **Class: MOLPATH – excludes MOLPATH.MISC**

**MOLPATH Specimen:**

* Amn: amniotic fluid, amniotic fld/CVS, CVS, Fetus, tiss/fetus, POC
* Bld - Bld, Bld/Tiss, Mar, BM (both are bone marrow), buccal, Cells.XXX
* Keep the somatic specimens as is:
  + Cancer specimen
  + Breast cancer specimen
  + Stool
  + CSF
  + Urine
  + Plas (? Only one test maybe could go in with bld etc)

## **Class: SERO**

**SERO Specimen:**

* Intravascular – any: See the Cross-Class specimen for the definition of all interhis specimen group.

**SERO Property:**

* PrTitrACnc: Presence or Threshold, Titer, Arbitrary Concentration. The distinctions among these 3 should be obvious in a flowsheet and they can be diagregated to show them separately when neeeded

**SERO Method:**

* SERO-Aggl: Aggl, Adult RBC Aggl, Cord RBC Aggl, Latex agglutination, Sheep Cell Agglutination
* IA-IF-Null\*: see MICRO for the definition of this method grouper
  + Comment: We also include null methods in this class but only when the analytes have “Ab” or “Ag” in the name. See the Cross-Class Analyte group for the definition of this group.
* SERO-Molecular genetics: molecular genetics, RFLP
* SERO—Method-Other: Lump all methods including null method excpee those that depend on temperature (18 deg C inc, 22 deg C inc, 28 deg C inc, 30 deg C inc, 37 degree C incubation, 4 deg C inc, Cold).

## **Class: UA**

**UA System:**

* UrUrnS: Urine, Urine sediment

**UA Property:**

* PrNaric: PrThr, Naric

**UA Method:** (ignore all methods –that is lump them incluiding the null method

* UA-MicroscopyCount: Microscopy, Microscopy.light, Microscopy.light. HPF, Microscopy.light.LPF, Auto, Automated, Automated count, Computer assisted, Manual Count
* UA-Fat stain: Oil red O stain, Sudan IV stain
* Refractrometry: Refractrometry, Refractrometry.automated
* Strip: Test strip, Test strip.automated

## **GROUP Tallies by Class**

In this draft output, here are the grouping numbers for each class:

* CHEM: 989 tests grouped into 384 groups, with 8976 tests left ungrouped
* DRUG/TOX: 2677 tests grouped into 1240 groups, with 5170 tests left ungrouped
* HEM/BC: 1072 tests grouped into 434 groups, with 1154 tests left ungrouped
* MICRO: 5576 tests grouped into 2215 groups, with 6195 tests left ungrouped
* SERO: 1179 tests grouped into 472 groups, with 1505 tests left ungrouped
* UA: 313 tests grouped into 92 groups, with 135 tests left ungrouped

? include a flag to indicate tests that would not usually be applicatle to clinical records so users could choose to ignore. The drug tox class terms thae are environmental ( e..g Air, , Water and probably XXX0 and the veterinary medicine ( can find with command Veterinary:true would be candidates for such flaggs

**Sources**

1. Bulletin of the World Health Organization Human papillomavirus and HPV vaccines : a review. 2006:1-11.
2. Chansaenroj J, Theamboonlers A, Chinchai T, et al. High-risk human papillomavirus genotype detection by electrochemical dna chip method. *Asian Pacific J Cancer Prev*. 2012;13(4):1151-1158. doi:10.7314/APJCP.2012.13.4.1151.
3. Halec G, Alemany L, Lloveras B, et al. Pathogenic role of the eight probably/possibly carcinogenic HPV types 26, 53, 66, 67, 68, 70, 73 and 82 in cervical cancer. *J Pathol*. 2014;234(4):441-451. doi:10.1002/path.4405.
4. Malatesha G, Singh NK, Bharija A, Rehani B, Goel A. Comparison of arterial and venous pH, bicarbonate, PCO2 and PO2 in initial emergency department assessment. Emerg Med J. 2007;24(8):569-571. doi:10.1136/emj.2007.046979.
5. Mayo Medical Laboratories. Human Papillomavirus (HPV) DNA Detection with Genotyping, High-Risk Types by PCR, ThinPrep. http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/62598.
6. Middleton P, Kelly A, Brown J, Robertson M. Agreement between arterial and central venous values for pH, bicarbonate, base excess, and lactate. Emergency Medicine Journal : EMJ. 2006;23(8):622-624. doi:10.1136/emj.2006.035915.
7. O’Connor TM, Barry PJ, Jahangir A, Finn C, Buckley BM, El-Gammal A. Comparison of arterial and venous blood gases and the effects of analysis delay and air contamination on arterial samples in patients with chronic obstructive pulmonary disease and healthy controls. Respiration. 2011;81:18-25. doi:10.1159/000281879.
8. Yu Z, Kastenmüller G, He Y, et al. Differences between human plasma and serum metabolite profiles. PLoS One. 2011;6(7):1-6. doi:10.1371/journal.pone.0021230.