Risk Classification of *In vitro Diagnostic (IVD)* Medical Devices

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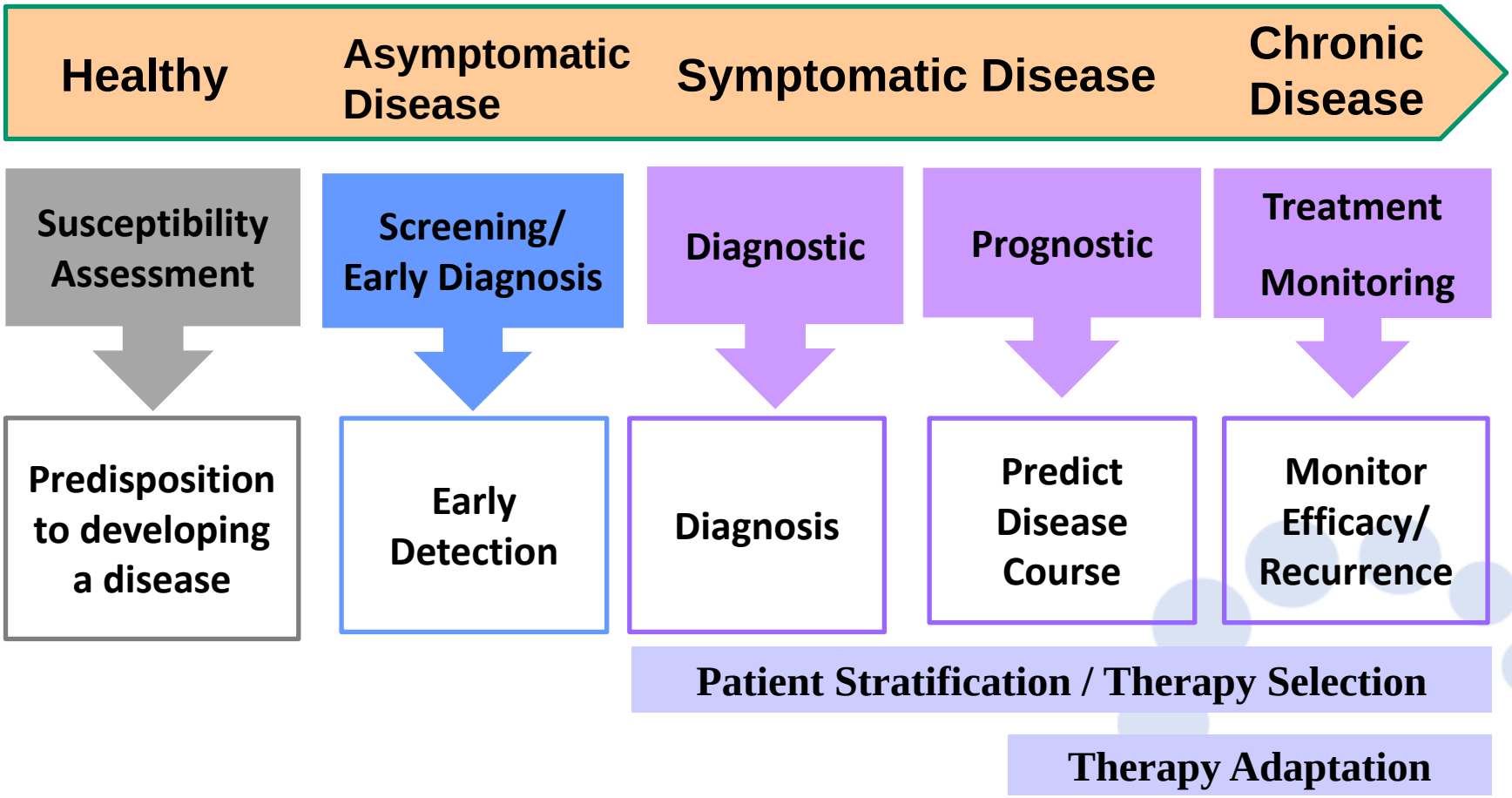
IVD Medical Device Definition

IVD Medical Device: a device, whether used alone or in combination, intended by the manufacturer for the in vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes. This includes reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles

NOTE 1: IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status.

SOURCE: imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-wng64.pdf

IVDs in Healthcare Management



What are IVD medical devices? Examples:

- Immunoassays
  - Early Pregnancy Test Kit
  - Anti-HIV 1/2 ELISA
- Nucleic Acid Amplification Testing
  - Hepatitis C Virus RNA qualitative assay
  - HIV RNA quantitative assay
- Clinical Chemistry
  - Alanine Aminotransferase (ALT)
  - Ion Selective Electrode for Na^+, K^+, Cl^-

These are IVDs…

- Reagent Cartridge
- Calibrator
- Control Materials

- Instrument
- Apparatus
- Analyzers

- Sample collection
- Specimen receptacles
- Storage devices

However, these are NOT IVDs…

Not intended for medical purpose

*For research use only (RUO)

*For detection of biological warfare substances

e.g. Inhalational anthrax; smallpox

*For law enforcement

e.g. drunk driving; drug abuse

*For veterinary use

e.g. bovine viral diarrhea PCR

*General laboratory equipments

e.g. incubator; UV spectrophotometer

NOTE: May differ among jurisdictions

IVD medical device Risk Classification

IMDRF Principles of IVD Classification
imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-wng64.pdf

HSA's Guidance on Risk Classification of IVD Medical Devices
hsa.gov.sg/docs/default-source/hprg-mdb/guidance-documents-for-medical-devices/gn-14-r3-guidance-on-the-risk-classification-of-in-vitro-diagnostic-md-(2023-jul)-pub.pdf?sfvrsn=58f33d7a_2

HSA's Medical Device Risk Classification Tool
https://www.hsa.gov.sg/medical-devices/registration/risk-classification

Risk Associated with the Use of IVDs

To public health

- Spread of infectious disease
- Unsafe blood transfusion

To individual health

- Misdiagnosis/Delayed diagnosis
- Delayed or inappropriate treatment
- Incompatible tissue transplantation

Risk Class	Risk to Individual Health	Risk to Public Health	Examples
A	Low	No or minimal	General culture media
B	Moderate	Low	Vitamine B12, Pregnancy self-testing
C	High	Moderate	Blood glucose self-testing, HLA typing
D	High	High	HIV blood donor screening, HIV diagnostic

How to determine risk classification?

- Intended use/indication for use
  - As specified by the product owner on labelling
- Technical/scientific/medical expertise of the intended user
- The importance of the testing result to the diagnosis
  - sole or key determinant vs ONE of several determinants
- The impact of the result to the individual and/or public health

IVDs for Different Users

Category	Intended User	Testing Environment	Examples
Professional Use Only	Laboratory professionals	✓Hospital/blood-bank Laboratories	✓Anti-HIV ELISA for blood donor screening
Point-of-Care	Other healthcare professionals	✓Medical clinics ✓Patient bed side ✓Land & air transport	✓Rapid HIV Test Kits used in medical clinics ✓Blood Gas Analyzer used in ambulance
Self-testing	Lay-person	✓Home	✓ hCG Pregnancy Test Strip ✓ Blood Glucose Meter, for diabetes management

IVDs for Different Users: Example

Blood Glucose Assay

Higher Risk Associated with Self-testing

Issue 1: The testing environment

May…

- Not be optimal (temperature; moisture)
- Not allow including external control

☞ Special product design (e.g. internal/external controls)

Issue 2: The user: lay person

May…

- Lack basic experimental skills
- Not conduct the test correctly
- Not interpret the test result correctly
- Not be aware of necessary follow-up actions

☞ Special requirements for labeling and instruction for use

☞ Special training for users

CLASS D

Rule 1: IVD medical devices intended for the following purposes are classified as Class D:

- Devices intended to be used to detect the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs or any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration.
- Devices intended to be used to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening, disease with a high or suspected risk of propagation;

Examples

✓HIV, HBV, or HCV test kit for blood donor screening;

✓HIV diagnosis tests

✓COVID-19 Pandemic

CLASS D

Rule 2: IVD medical devices intended to be used for blood grouping, or to determine foeto-maternal blood group incompatibility, or tissue typing to ensure the immunological compatibility of blood, blood grouping for cell administration, blood components, cells, tissue, or organs that are intended for transfusion or transplantation, are classified as Class C, except when intended to determine the presence of the antigen or antibody for any of the following markers:
ABO system [A (ABO1), B (ABO2), AB (ABO3)],
Rhesus system [RH1 (D), RH2 (C), RH3 (E), RH4 (c), RH5 (e), and weak or partial Rh(D)],
Kell system [Kel1 (K)],
Kidd system [JK1 (Jka), JK2 (Jkb)]; or
Duffy system [FY1 (Fya), FY2 (Fyb)],
in which case they are classified as Class D.

Examples

✓Blood typing assay for ABO system

✓Tissue typing for organ transplantation

Rule 3

CLASS C

- in detecting the presence of, or exposure to, a sexually transmitted agent.
  Examples: Sexually transmitted diseases, such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*.

- in detecting the presence in cerebrospinal fluid or blood of an infectious agent with a risk of limited propagation.
  Examples: *Neisseria meningitidis* or *Cryptococcus neoformans*.

- in detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested or to the individual`s offspring.
  Examples: diagnostic assay for CMV, *Chlamydia pneumoniae*, Methicillin Resistant *Staphylococcus aureus*.

- in pre-natal screening of women in order to determine their immune status towards transmissible agents.
  Examples: Immune status tests for Rubella or Toxoplasmosis.

Examples

✓Syphilis/Gonorrhoeae tests

✓MRSA, CMV diagnostic tests

Rule 3

CLASS C

- in determining infective disease status or immune status, and where there is a risk that an erroneous result will lead to a patient management decision resulting in an imminent life-threatening situation or severe disability for the patient or for the patient's offspring.
  Examples: Enteroviruses, CMV and HSV in transplant patients.

- in screening, diagnosis or staging of cancer;
  Examples: PSA, CEA, and CA 125.

- in human genetic testing
  Examples: Huntington's Disease, Cystic Fibrosis.

- to monitor levels of medicines, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in an immediate life-threatening situation for the patient or for the patient's offspring. *Examples*: Troponin, Cyclosporin, Prothrombin time testing.

Examples

✓Genetic testing – Cystic Fibrosis test

✓Cancer markers - PSA, CA125 tests

Rule 3

CLASS C

- in the management of patients suffering from a life-threatening disease or condition. *Examples*: HBV monitoring marker, HCV viral load, HIV Viral Load and HIV and HCV geno- and subtyping

- in screening for congenital disorders in the foetus or embryo.
  Examples: Spina Bifida, Down Syndrome, Glucose-6-Phosphate Dehydrogenase Deficiency, and Tay-Sachs disease.

- in screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities.

Examples

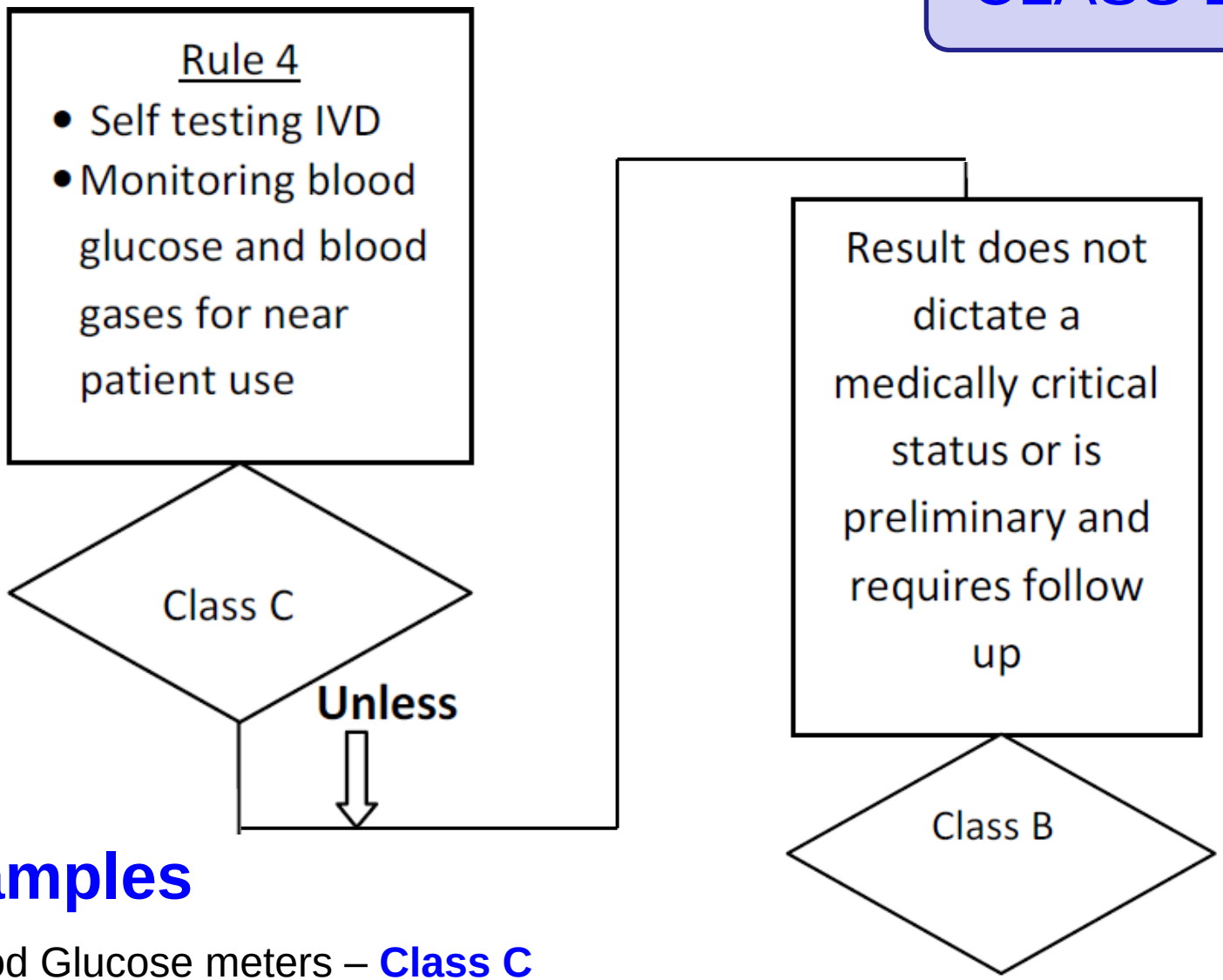
✓Patient Management - HIV viral load tests; HIV/HCV genotyping assays

✓Congenital disorder in foetus– Down Syndrome tests

✓Congenital disorders in new-born – G6PD tests

Rule 4

CLASS B/C



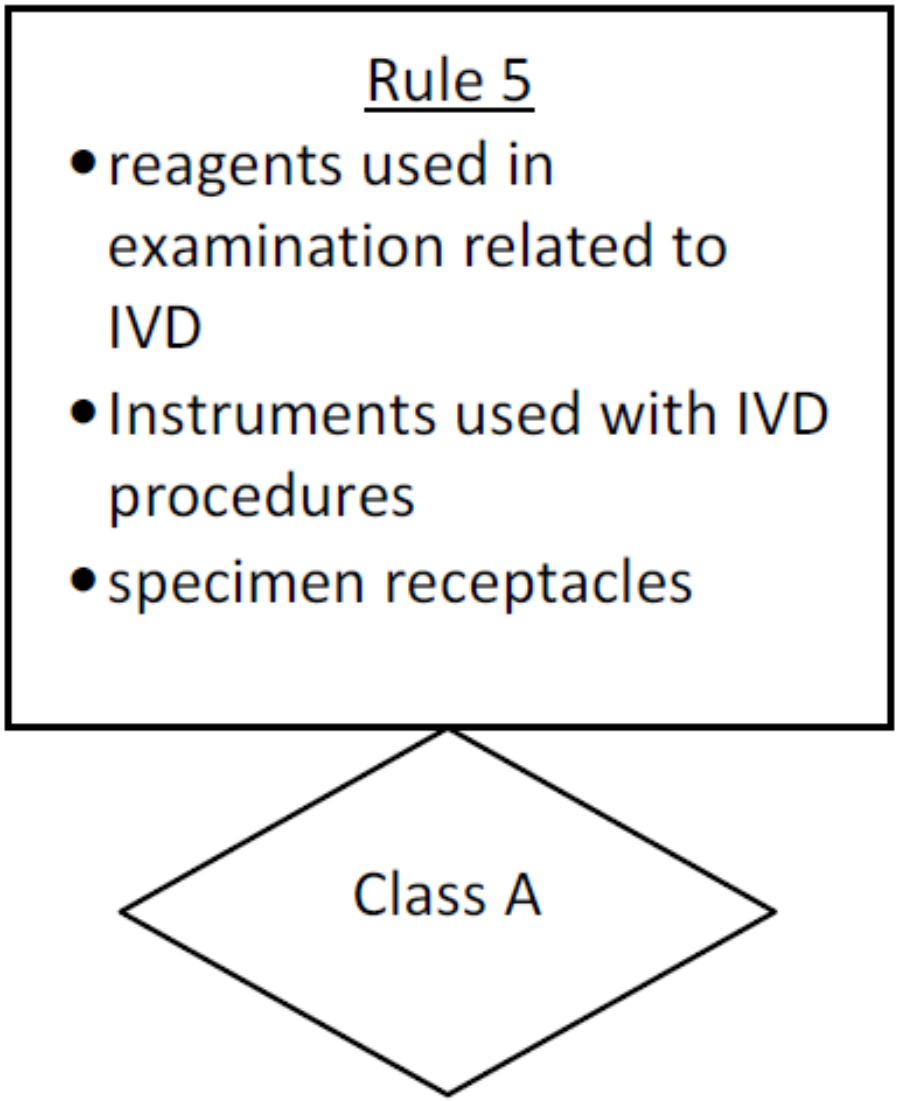
Examples

✓Blood Glucose meters – **Class C**

✓Pregnancy tests, ovulation tests – **Class B**

Rule 5

CLASS A



Examples

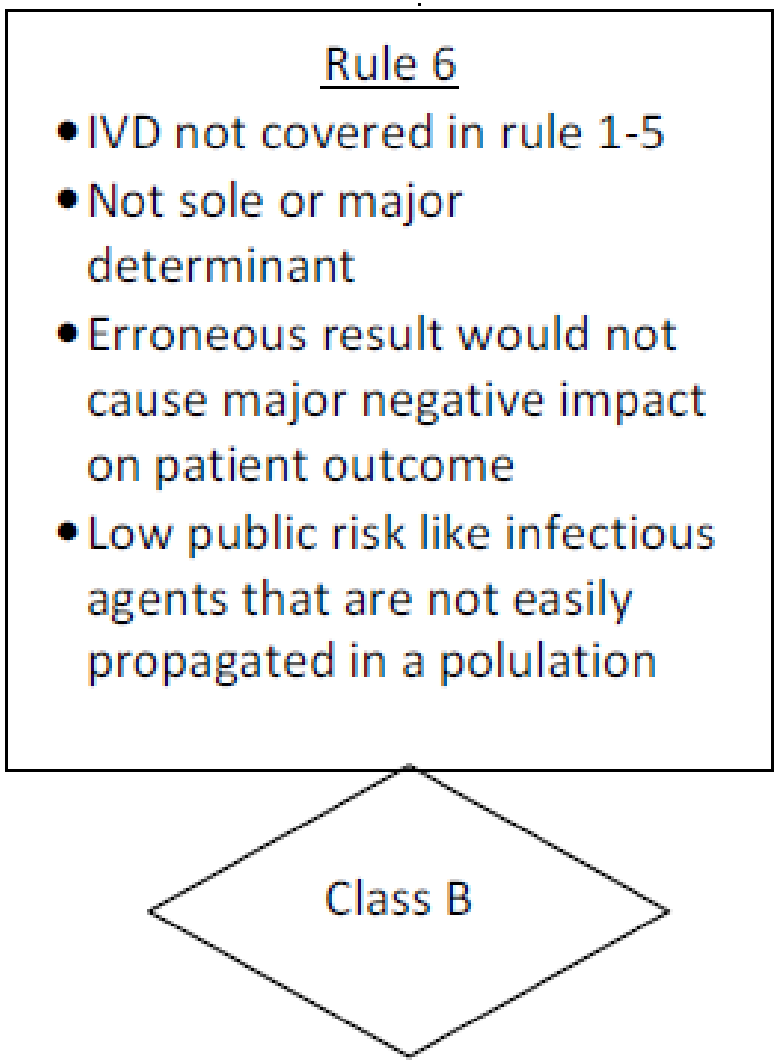
✓Blood collection tubes or vacutainers

✓Analysers not dedicated for any specific reagent/assay
e.g. DNA sequencer

➔ All Class A

Rule 6

CLASS B



Examples

✓Antibiotics assay: gentamicin/vancomycin

✓Urinalysis Reagent Strips

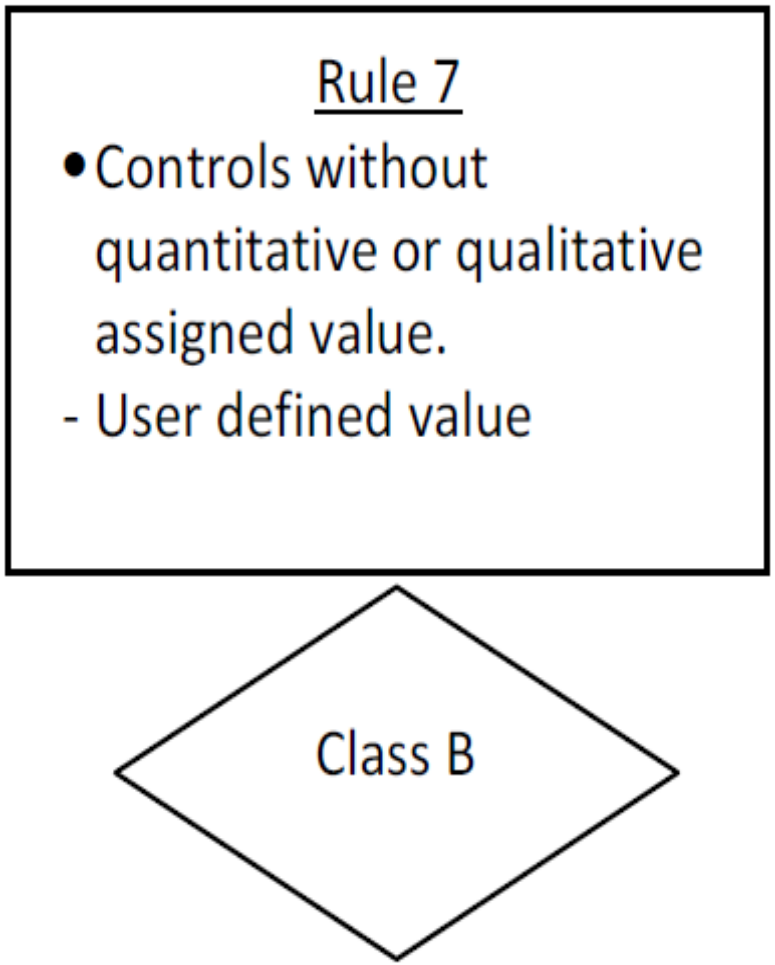
✓Electrolyte electrode

✓*Helicobacter pylori*

➔ Class B

Rule 7

CLASS B



Examples

- Quality control products for clinical chemistry/ urinalysis:
e.g. ALT (Alanine aminotransferase) level control without value assigned Class B.

- Controls with assigned value should be the same risk classification as the correspondent analytes.
e.g. Anti-HIV positive control for blood donor screening assays Class D.

Assigning Risk Classification

- To consider all the seven rules in order
  - If multiple intended purpose/multiple rules apply
    → highest risk applies

Examples

✓ Blood Glucose Meter
- Class C, Rule 4,
- Justification: sole determinant for insulin injection dosage
- High personal risk

✓ Early Pregnancy Detection
- Class B, Rule 4
- Justification: preliminary result requiring follow-up with the appropriate laboratory test)
- Moderate personal risk

Rule 3 vs Rule 6

How to differentiate Class B or Class C?

Critical, or sole determinant
→ Class C

One of several determinants
→ Class B

Thank You