MDA/GD/0054
XXXX 2020
Public comment DRAFT
Due date public comment **27 Mac 2020**

DRAFT MEDICAL DEVICE GUIDANCE DOCUMENT

GUIDANCE ON THE PRODUCT GROUPING FOR IN-VITRO DIAGNOTIC (IVD) MEDICAL DEVICES

Medical Device Authority
MINISTRY OF HEALTH MALAYSIA

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Preface

This Guidance Document was prepared by the Medical Device Authority (MDA) to help the industry and healthcare professionals in their quest to comply with the Medical Device Act (Act 737) and the regulations under it, and/or to facilitate their business endeavour.

In this Guidance Document, the following verbal forms are used:

— “shall” indicates a requirement;

— “should” indicates a recommendation;

— “may” indicates a permission; and

— “can” indicates a possibility or a capability.

Irrespective of the requirements of this Guidance Document, MDA has the right to request for information or material, or define conditions not specifically described in this document that is deemed necessary for the purpose of regulatory control.

MDA has put much effort to ensure the accuracy and completeness of this guidance document. In the event of any contradiction between the contents of this document and any written law, the latter should take precedence.

MDA reserves the right to amend any part of the guidance document from time to time.

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GUIDANCE ON THE PRODUCT GROUPING FOR IN-VITRO DIAGNOTIC (IVD) MEDICAL DEVICES

1 Introduction

The purpose of this document is to provide guidance to determine the appropriate grouping for in-vitro diagnostic (IVD) medical devices in the medical device registration application.

2 Scope and applications

This document applies to all products that fall within the definition of medical device that has been specified in the Guidance Document: The Definition of Medical Device (MDA/GD/0006).

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1 Accessory

For the purposes of this guidance document, an accessory is an article that is intended specifically by its manufacturer to:

a) be used together with a medical device to enable that device to be used in accordance with its intended purpose as a medical device; or
b) augment or extend the capabilities of that device in fulfilment of its intended purpose as a medical device;

and therefore, should be considered as a medical device.

3.2 Component

One of several possibly unequal subdivisions which together constitute the whole medical device to achieve the latter's intended purpose. A component may be known as a part but not a medical device in its own right.

3.3 Proprietary Name

A unique name given by the manufacturer to identify a medical device as a whole product, also known as the trade name or brand name.

3.4 Intended Purpose

The use for which the medical device is intended according to the specifications of its manufacturer as stated on any or all of the following:

a) the label of the medical device;
b) the instructions for use of the medical device;
c) the promotional materials in relation to the medical device.

3.5 Authorised Representative (AR)

a) a person domiciled or resident in Malaysia; or
b) a firm or company constituted under the laws of Malaysia,

and carrying on business or practice principally in Malaysia.

3.6 Manufacturer

Means —

a) a person who is responsible for

(i) the design, production, fabrication, assembly, processing, packaging and labelling of a medical device whether or not it is the person, or a subcontractor acting on the person's behalf, who carries out these operations; and

(ii) assigning to the finished medical device under his own name, its intended purpose and ensuring the finished product meets the regulatory requirement;

Or

b) any other person who-

(i) assembles, packages, processes, fully refurbishes, reprocesses or labels one or more ready- made medical devices; and

(ii) assigning to the ready- made medical device under his own name, its intended purpose and ensuring the finished product meets the regulatory requirement,

but shall not include the following persons:

(A) Any person who assembles or adapts medical devices in the market that are intended for individual patients; and

(B) Any person who assembles, packages, or adapts medical devices in relation to which the assembling, packaging or adaptation does not change the purpose intended for the medical device.

3.7 Medical Device

Refer to MDA/GD/0006: Definition of Medical Device.

3.8 IVD Examination

in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes. Examples are reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles.

3.9 IVD Instrument analyser

IVD instrument analysers are equipment intended to be used with IVD reagents so as to allow the IVD reagents to achieve their intended use.

Note: Devices which produce an analytical result from an applied sample by performing functions beyond the mere analytical reading of a generated signal, such as performed by a simple spectrophotometer, gamma counter, luminometer, fluorometer, etc. The analysers can be further divided into the following three types:

a) Closed-System Analyzer

An analyser that is intended by its manufacturer to be used only in combination with the reagents that it also provides. Closed-system analysers may be batch analysers, random-access analysers or the newer multichannel batch analysers. In many cases, closed-system analysers give the user no programming capabilities other than data management and no access to the assay protocol(s).

b) Open- System Analyzer

An analyser that is manufactured with general purpose features for use only with secondary reagents. Secondary reagents are reagents produced for use with specific analysers by other suppliers. Secondary reagents may be marketed and labelled for one specific analyser or may claim multiple analysers. Most open-system analysers give the user programming capabilities for inputting preferred assay protocols. An example would be an automated microplate analyser that can be adapted by the user to commercially available microplate test kits.

c) Partially-Closed-System Analyzer

An analyser that is intended by its manufacturer to be used both in combination with the reagents that it provides, or with secondary reagents for the analysis of analytes for which the manufacturer does or does not provide reagents. In the latter case, the analyser serves as a general-purpose analyser in an open system.

3.10 IVD Medical Device for Self-Testing

Any IVD medical device intended by the manufacturer to be able to be used by lay persons in home environment.

3.11 Lay Person

Any individual who does not have formal training in a relevant field or discipline.

3.12 Near-Patient Testing

Any testing performed outside a laboratory environment by a health care professional not necessarily a laboratory professional, generally near to, or at the side of, the patient. Also known as Point-of-Care (POC).

3.13 Reagent

Any chemical, biological or immunological components, solutions or preparations intended by the manufacturer to be used as IVD medical devices.

3.14 Specimen Receptacle

An IVD medical device, whether vacuum- type or not, specifically intended by their manufacturer for the primary containment of specimens derived from the human body.

Specimen containers intended for use in self-testing, evacuated or non-evacuated blood collection tubes and specimen containers intended for the collection of urine, faeces, cells or tissue specimens for subsequent in vitro examination.

3.15 Transmissible Agent

An agent capable of being transmitted to a person, as a communicable, infectious or contagious disease.

3.16 Transmission

The conveyance of disease to a person.

4 General Principles of Grouping

4.1 Medical devices that can be grouped into one of the following five categories can be submitted in one application for medical device registration and listing in the Malaysia Medical Device Register (MMDR):

a) SINGLE;
b) SYSTEM;
c) FAMILY;
d) IVD TEST KIT;
e) IVD CLUSTER.

4.2 The three basic rules must all be fulfilled for the grouping to apply. These are:

a) one proprietary name;
b) one manufacturer; and
c) one common intended purpose.

4.3 For the purpose of grouping, the corporate headquarters may be regarded as the manufacturer for its subsidiaries and regional manufacturing sites.

5 Categories

5.1 Single

5.1.2 A SINGLE medical device is a medical device from a manufacturer identified by a medical device proprietary name with a specific intended purpose. It is **sold as a distinct packaged entity**. It may be **offered in a range of package sizes** and **one device with one identifier only.** Example under this grouping is referred in Table 1.

Table 1. Example of grouping as single medical device

No	Example	Explanation
a)	Standalone software for blood-screening assay intended to be used for blood screening open ended analyser.	Medical devices having same intended use or commonality of technology.
b)	Standalone software able to combine a number of IVD results to calculate and report an additional result to be used for clinical purposes. For example, software intended for the interpretation of a series of results obtained as part of a first trimester screening assessment in order to determine foetal risk of trisomy 21.	IVD software that is not intended to drive or influence an IVD instrument (or medical device that is not an IVD) is classified according to its intended purpose. (Please refer to MDA/GD/0001: In-Vitro Diagnostic (IVD) Medical Device Classification System)
c)	Standalone software intended for use in staging or predicting severity of disease by means of an algorithm based on a combination of anthropometric measures and non-invasive biomarkers.	
d)	Cuvette are sold in package of 3, 12 and 30 can be registered as a SINGLE medical device.	sold as a distinct packaged entity. It may be offered in a range of package sizes.
e)	Unassayed Non-Reactive Quality Control Reagent With In Vitro Diagnostic Procedures for Detection of *Chlamydia Trachomatis (Ct)* and *Neisseria Gonorrhoeae (Gc).*	Sold as single reagent designed for use with in-vitro assay procedures for purposes of monitoring assay performance and maintaining quality assurance.
f)	Ovulation Test Kit is a One-Step Immuno-Chromatographic Screening Test designed for the detection of Luteinizing Hormone (Lh) In Urine for Professional and Self-Testing (Home Use) To detect the signal for Ovulation.	Packaging come with single midstream kit.

5.2 System

5.2.1 A medical device SYSTEM comprises of a number of constituent-components that are:

a) from the same manufacturer;

b) intended to be used in combination to complete a common intended purpose;

c) compatible when used as a SYSTEM; and

d) sold under a SYSTEM name or the labelling, instruction for use (IFU), brochures or catalogues for each constituent component states that the constituent component is intended for use with the SYSTEM.

NOTE:

Constituent-components registered as part of a system shall only be supplied specifically for use with that SYSTEM. Any constituent-component that is meant for supply for use with multiple SYSTEMs should be registered together with each of these other SYSTEMs. Alternatively, these constituent-component(s) that are compatible for use with multiple SYSTEMs must be registered separately.

5.2.2 The decision flowchart for grouping of products as a SYSTEM can be found in **Annex A**.

5.2.3 Individual SYSTEM names may contain additional descriptive phrases.

The registration holder has to undertake the following post-market duties and obligations for all the constituent-components in the registered SYSTEM, regardless of whether the constituent-components are from the same manufacturer of the SYSTEM:

a) comply with the conditions applicable to the registered medical device and conditions imposed on the registration holder;

b) submit applications to the Authority for changes made to the registered medical device;

c) maintain records of supply;

d) maintain records of complaints;

e) report defects and adverse effects to the Authority, and

f) notify the Authority concerning field safety corrective action (FSCA), including recall.

5.2.4 An *In Vitro* Diagnostic (IVD) Medical Device SYSTEM may typically consist of TEST KITs and instruments (e.g. an analyser designed to be used with that TEST KIT) that are:

a) from the same manufacturer;

b) intended to be used in combination to complete a common intended purpose;

c) compatible when used as a SYSTEM; and

d) sold under a SYSTEM name or the labelling, instruction for use (IFU), brochures or catalogues for each constituent component states that the constituent component is intended for use with the SYSTEM.

Example of grouping for medical device as a System is as per in **Table 2**.

NOTE:

(1) The interdependence of the instruments and the test methodology prevents the instruments from being assesses separately, even though the instrument itself is still classified as Class A.
(2) The performance of software or instrument that is specifically required to perform a particular test will be assessed at the same time as a system.
(3) Analysers shall be together with its compatible IVD reagents and analyser accessories such as cleaning solutions.
(4) IVD analysers system comprising of test kits, reagents (and compatible analyser accessories) must be submitted in product registration applications.
(5) For automated analysers and their associated reagents or test kits, one or more applications may be submitted based on the risk class of the different assay. For example, ABC HIV-1/-2 EIA, the ABC anti-HCV, the ABC CA125 EIA, and the ABC CK-MB with the ABC ANALYZER. Two applications could be submitted. One Class D application for the ABC HIV-1/-1 EIA AND THE ABC anti-HCV with the ABC ANALYZER and one Class C application for the ABC CA125 EIA, and the ABC CK-MB with the ABC ANALYZER.
(6) Constituent-components registered as part of a system shall only be supplied specifically for use with that SYSTEM. Any constituent-component that is meant for supply for use with multiple SYSTEMs should be registered together with each of these other SYSTEMs. Alternatively, these constituent-component(s) that are compatible for use with multiple SYSTEMs must be registered separately.

Table 2. Example of medical device grouping as a System.

No	Example:	Explanation:
a)	A **glucose monitoring SYSTEM** comprising of a glucose meter, test strips, lancet, control solutions and linearity solutions.	a medical device comprising a number of components or parts intended to be **used together to fulfil some or all of the device's intended functions**, and that is **sold under a single name.**
b)	**LipidScan Lipid Profile Analyzer** contains Analyzer, LipidScan Lipid Profile Test Device, LipidScan Lipid Profile Control Device, Mission Capillary Transfer Tubes and Mission Capillary Transfer Tubes.	**Closed system Analyzer** is an analyzer that is intended by its manufacturer to be **used only in combination with the reagents** that is also **provides by the manufacturer.**
c)	**ABC HEMATOLOGY SYSTEM** contains Automated Hematology Analyzer, Calibrator, Diluent, Lyse solution and Control.	Intended purpose: ABC Hematology System is a quantitative multi-parameter automated hematology analyzer designed for in-vitro-diagnostic use in clinical laboratories for enumeration of the following parameters: WBC, LYM%, LYM#, MID%, MID#, GRA%,GRA#, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV in EDTA anti-coagulated venous whole blood samples. The ABC Hematology System is indicated for use to identify patients with hematologic parameters within and outside of established reference ranges.

d)	**DEF Urine Analyzer** contains Urine Analyzer, Urine Reagent Strips, Urine Detergent and Urinalysis Control	Intended purpose: DEF Urine Analyzer is a semiautomatic urinalysis system intended for in vitro qualitative or semi-quantitative determination of urine analytes, including Specific Gravity (SG), PH, Leukocytes, Nitrite, Protein, Glucose, Ketones, Urobilinogen, Bilirubin, Erythrocytes and Color.
e)	**GHI CRP SYSTEM** contains GHI CRP Instrument, CRP Reagent Cap, Buffer in prefilled cuvettes, CRP Control, Plungers, Capillaries, and CRP Software.	Intended purpose: for quantitative determination of CRP (C REACTIVE PROTEIN) in whole blood, serum or plasma, using the GHI CRP Instrument.

5.3 Family

5.3.1 A medical device FAMILY is a collection of medical devices and each medical device FAMILY member:

a) is from the same manufacturer;

b) is of the same risk classification;

c) has the same medical device proprietary name;

d) has a specific intended purpose*.

*NOTE:

Medical device is intended according to the specifications of its manufacturer as stated on any or all of the following:

i. the label of the medical device;
ii. the instructions for use of the medical device;
iii. the promotional materials in relation to the medical device.

e) has the same design and manufacturing process; and

f) has variations that are within the scope of the permissible variants.

Example of grouping as Family is as per in **Table 3**.

Table 3. Example of medical device grouping as a Family.

No	Example
a)	**IVD Urinalysis Strips-Different combination of testing configuration.** i) Urine Strip with 3 Parameters: Glu, pH, Pro ii) Urine Strip with 10 Parameters: Glu, pH, Pro, Bil, Ket, SG, Blo, Uro, Nit, Leu
b)	**Plain blood tube – Different number of volumes.**

	i) ii)	Plain tube with 6 ml Plain tube with 4 ml

The decision flowchart for grouping of products as a FAMILY can be found in **Annex B**.

5.3.2 A characteristic of a medical device may be considered a permissible variant if:

a) the physical design and construction of the medical devices are the same, or very similar;

b) the manufacturing processes for the medical devices are the same, or very similar;

c) the intended purpose of the medical devices is the same; and

d) the risk profile of the medical devices, taking into account the above factors, is the same.

See **Annex C** for a list of permissible variants in a FAMILY.

5.3.3 Information on all medical devices within a FAMILY must be submitted as part of one medical device registration application. Only members of a FAMILY that are eventually listed on the register shall be supplied on the market. Those that are not listed shall not be supplied on the market.

5.3.4 The medical device proprietary name must appear on the label of each of the member medical devices. Individual medical device names may contain additional descriptive phrase**.**

5.4 IVD Test Kit

5.4.1 An IVD TEST KIT is an in vitro diagnostic (IVD) device that consists of reagents or articles that are:

a) from the same manufacturer;

b) intended to be used in combination to complete a specific intended purpose;

c) sold under a single TEST KIT name or the labelling, instructions for use (IFU), brochures or catalogues for each reagents or article states that the component is intended for use with the IVD TEST KIT; and

d) compatible when used as a TEST KIT.

5.4.2 An IVD TEST KIT does not include the instruments, such as analysers, needed to perform the test.

5.4.3 The decision flowchart for grouping of products as an IVD TEST KIT can be referred in **Annex D**. Example of grouping as IVD Test Kit is as per **Table 4**.

5.4.4 Information on all reagents or articles within an IVD TEST KIT must be submitted as part of one product registration application. Only those reagents or articles within an IVD TEST KIT that are eventually listed on the register shall be supplied on the market. Those that are not listed shall not be supplied on the market.

5.4.5 Individual reagents or articles can be supplied separately as replacement items for the kit. If the reagents or articles in a TEST KIT are supplied for use in more than one TEST KIT, such reagents or articles shall be included in the product registration application of each of the other TEST KITS.

5.4.6 Reagents or articles from another manufacturer may be grouped with the IVD TEST KIT if the applicant furnishes all information on these reagents or articles required for registration, such as authorisation from the other manufacturers for registration and data to substantiate the performance of these reagents when used in the test kit.

Table 4. Example of medical device grouping as IVD Test Kit.

Example	Explanation
A Human Immunodeficiency Virus (HIV) Enzyme Linked ImmunoSorbent Assay (ELISA) TEST KIT may contain controls, calibrators and washing buffers.	All the reagents and articles are used together to detect HIV and therefore can be registered as a TEST KIT. These reagents and articles can be supplied separately as replacement items for that particular TEST KIT.

5.5 IVD CLUSTER

5.5.1 An IVD CLUSTER comprises of a number of *in vitro* diagnostic reagents or articles that are:

a) from the same manufacturer;

b) within risk classification as Class A or Class B;

c) of the *same* methodology, cluster category and test principles*.

Note: *Test principle based on IFU

5.5.2 The IVD CLUSTER may include analysers that are designed for use with the reagents in the IVD CLUSTER.

5.5.3 A closed list of common test methodologies and IVD CLUSTER categories is provided in **Annex E**.

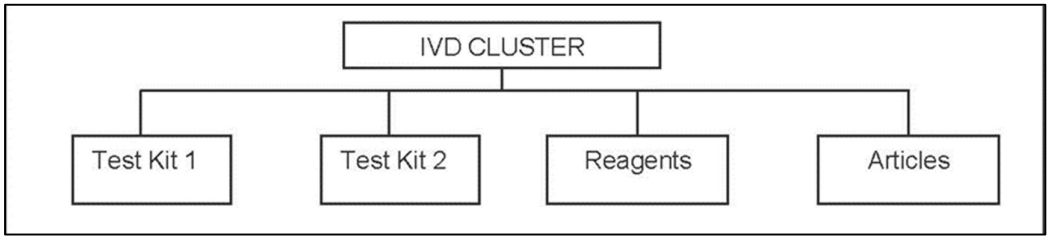
5.5.4 The decision flowchart for grouping of products as an IVD CLUSTER can be found in **Annex F**.

5.5.5 Information on all reagents or articles within an IVD CLUSTER must be submitted as part of one medical device registration application. Only those reagents or articles within an IVD CLUSTER that are eventually listed on the register shall be supplied on the market. Individual reagents or articles that are listed as part of a CLUSTER can be supplied separately.

5.5.6 If a reagent or article is intended for multiple usage categories such that it can be grouped in more than one IVD CLUSTER, the applicant can choose to group the reagent or article as part of any one of the IVD CLUSTERs it qualifies. Information to support all the intended purposes of the reagent or article must be submitted as part of the medical device registration application.

Note: The IVD Cluster grouping is only to be used for medical device registration and would not be applicable as a grouping criterion for the addition of models through a Change Notification.

Table 5. Example of an IVD Cluster.



6. IVD Devices Specific Grouping.

6.1 Immunohistochemistry (IHC) IVD reagents

6.1.1 Immunohistochemistry (IHC) IVD reagents are in vitro diagnostic (IVD) products consisting of polyclonal or monoclonal antibodies labelled with directions for use and performance claims, which may be packaged with ancillary reagents in kits. Their intended use is to identify, by immunological techniques, antigens in tissues or cytologic specimens, and excludes reagents specifically intend to be used with flow cytometry. This section applies to IHC IVD reagents and their accessories only.

6.1.2 The decision flowchart for grouping of Class B only or Class C only IHC IVD can be referred in **Annex G**.

6.1.3 A device specific IHC IVD grouping category comprises of a collection of IVD reagents and their accessories that are:

a) from the same Manufacturer;
b) is of the same risk classification (either all Class B only or Class C only);
c) based on IHC methodology; and
d) within the same IHC IVD Grouping Category as listed below.

When IHC IVD reagents and their accessories satisfy the criteria to be grouped under one of the six prescribed IHC IVD grouping categories, they can be grouped together and submitted in one medical device registration application.

6.1.4 List of IHC IVD grouping categories

The list of IHC IVD categories for the device specific grouping of Class B only or Class C only IHC reagents and their accessories is a closed and positive list is as per in **Table 6**.

a) For grouping of Class B IHC IVD, applicant may choose to group the devices under:
   i. Single
   ii. Family
   iii. System
   iv. IVD Test Kit
   v. IVD Cluster

b) For grouping of Class C IHC IVD, applicant may choose to group the devices under:

i. Single
ii. Family
iii. System
iv. IVD Test Kit

Table 6. IHC IVD grouping categories.

No.	IHC IVD Grouping Category (closed list)	Examples of Analytes (non-exhaustive list)
1	Selective Therapy	(i) HER2/neu (ii) EGFR
2	Hematologic Disorder and Blood Cancer Markers	(i) Immunoglobulin Kappa chain (ii) Immunoglobulin Lambda chain
3	Other Cancer Markers	(i) Alpha fetoprotein (AFP) (ii) Cytokeratins (iii) CD117
4	Pathogen Markers	(i) Escherichia coli (ii) Candida albicans (iii) Herpes simplex virus protein VP22
5	Immune Disorders	(i) Anti-nuclear antibodies (ANAs) (ii) Anti-topoisomerase (iii) Organ-specific autoantibodies (iv) Anti-Streptococcal Hyaluronidase (v) Anti-Streptokinase (vi) Anti-Streptolysin O (vii) C-Reactive Protein
6	Other Pathology Markers	(i) P57 (ii) Growth hormone

6. 2 *Fluorescence in Situ Hybridisation Probes In vitro Diagnostic Reagents.*

6.2.1 Fluorescence in situ hybridization (FISH) probes are in vitro diagnostic (IVD) products that allow for the detection and localisation of the presence or absence of specific DNA sequences on chromosomes, whereby the hybridisation of the probes with the DNA site will be visible using fluorescence microscopy.

6.2.2 A device specific grouping of FISH probes IVD grouping category comprises of a collection of IVD reagents and their accessories that are:

a) from the same Manufacturer;
b) is of the same risk classification (either Class B only or Class C only);
c) based on FISH methodology; and

d) within the same FISH probes IVD Grouping Category as listed below.

6.2.3 The decision flowchart for grouping of Class B and Class C FISH Probes IVD can be referred in **Annex H**.

6.2.4 When FISH Probes IVD reagents and their accessories satisfy the criteria to be grouped in one of the prescribed FISH Probes IVD grouping categories, they can be grouped together and submitted in one product registration application.

a) For grouping of Class B IHC IVD, applicant may choose to group the devices under:
   i. Single
   ii. Family
   iii. System
   iv. IVD Test Kit
   v. IVD Cluster

b) For grouping of Class C IHC IVD, applicant may choose to group the devices under:
   i. Single
   ii. Family
   iii. System
   iv. IVD Test Kit

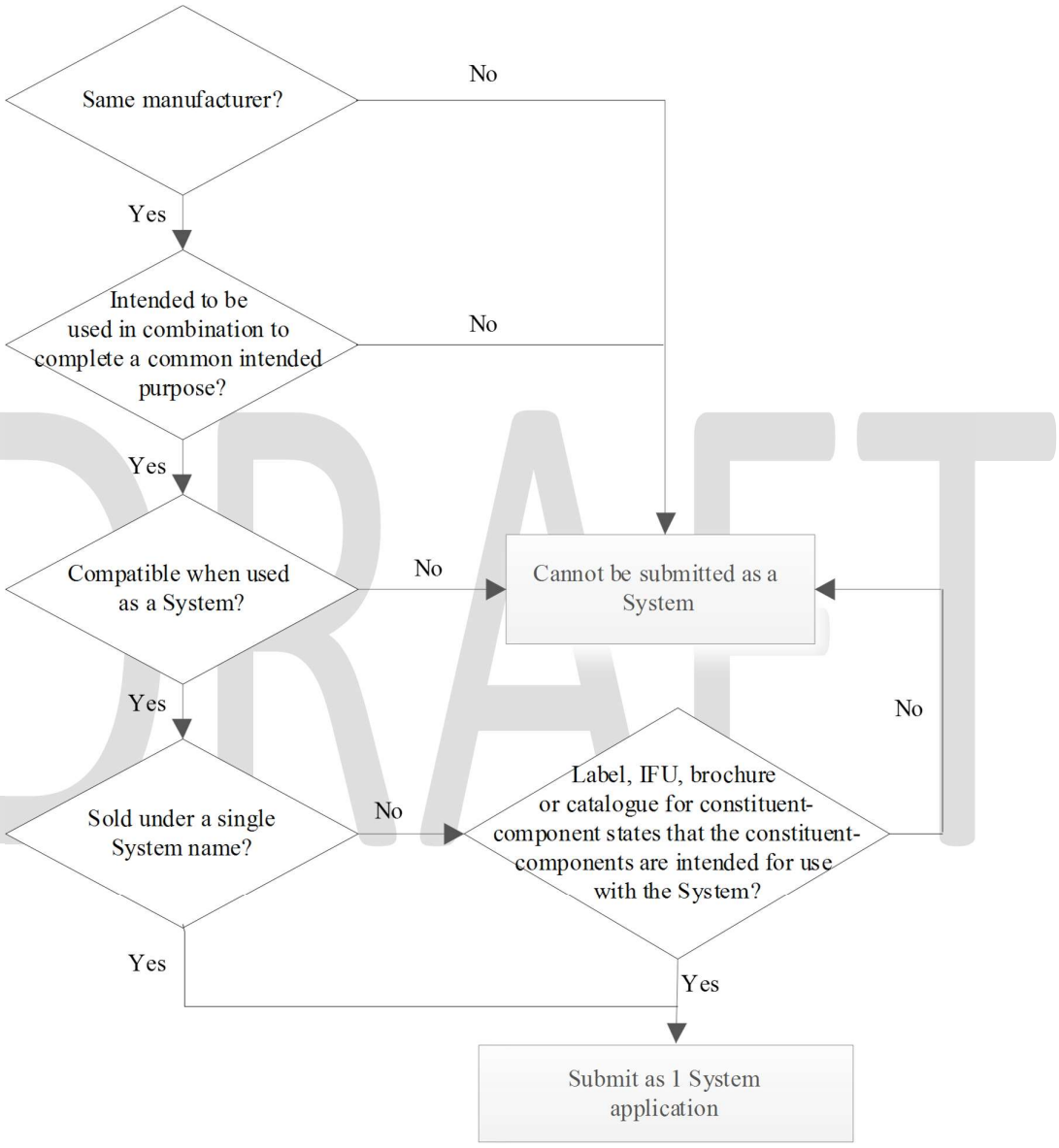
6.2.5 List of FISH probes IVD grouping categories

The list of FISH probes IVD grouping categories for the device specific grouping of Class B only and Class C only FISH probes IVD reagents and their accessories is a closed and positive list are in **Table 7**.

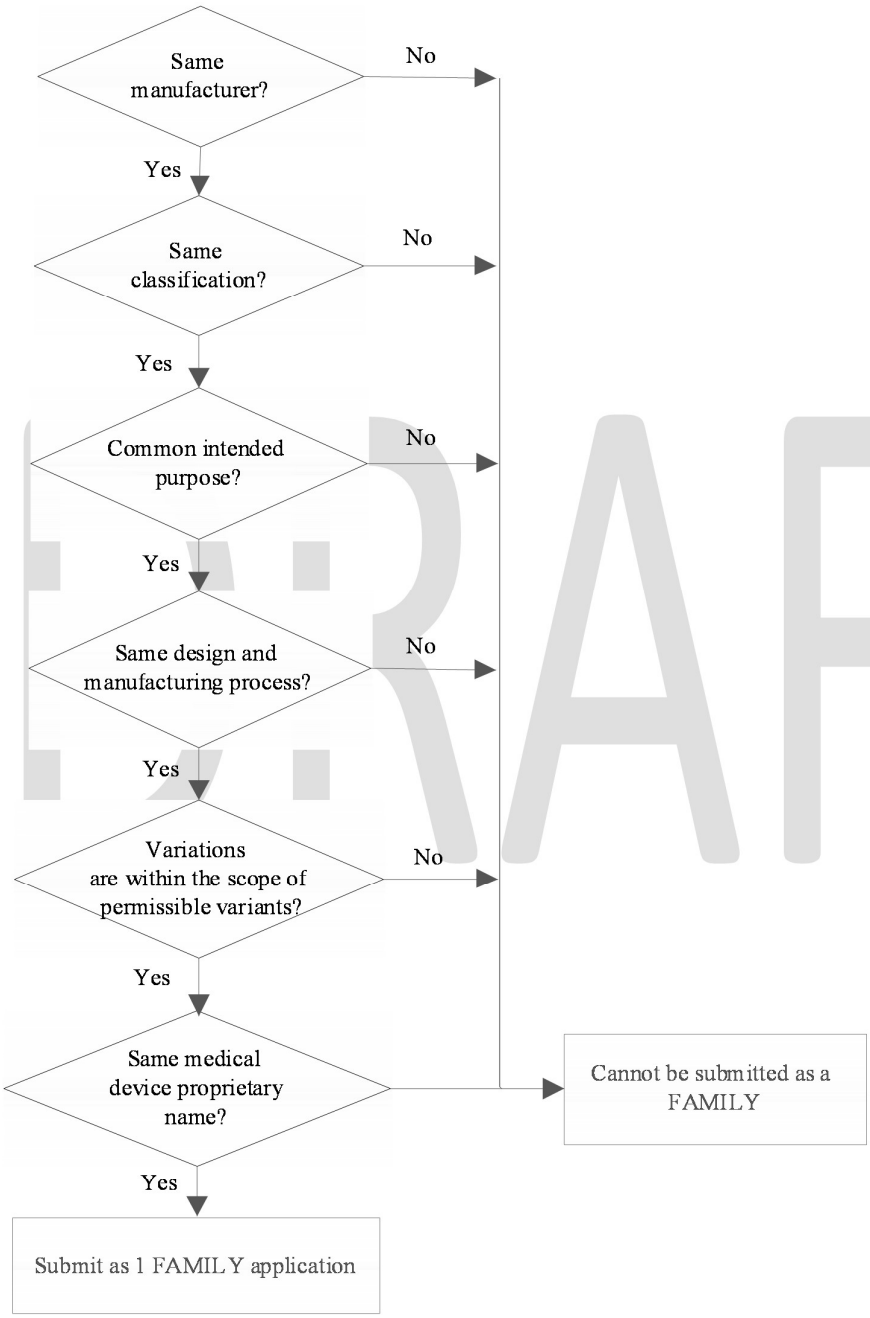
Table 7. IHC IVD grouping categories.

No.	FISH Probes IVD Grouping Category (closed list)	Examples of Gene Targets (non-exhaustive list)
1	Selective Therapy	(i) ALK gene (ii) HER2
2	Pre-natal Testing	(i) Chromosomes 13, 21, 18, X and Y
3	Genetic Testing of Inheritable Disease	(i) ELN gene
4	Pathogen Identification	(i) Mycobacterium tuberculosis complex (MTC) (ii) Escherichia coli
5	Hematologic Disorder and Blood Cancer Markers	(i) Chromosomes 3, 7, 9 and 11
6	Other Cancer Markers	(i) LAMP2 gene (ii) Topoisomerase 2A gene

ANNEX A: Decision Flowchart for Grouping of Products as a System



ANNEX B: Decision Flowchart for Grouping of Medical Devices as a Family

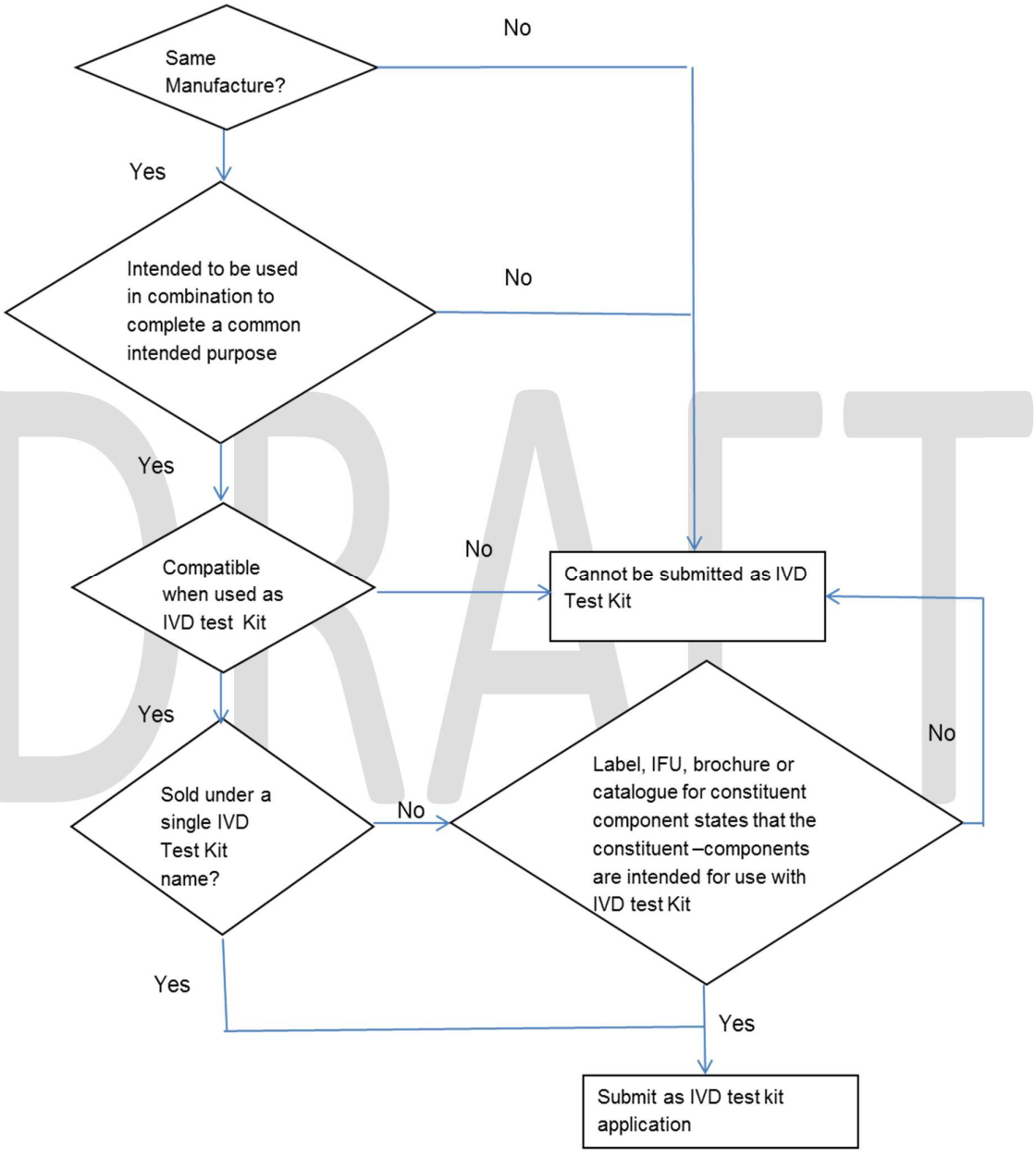


ANNEX C: Permissible Variants in a Family

Specific products	Permissible variants
Antibiotic test	Concentrations
IVD rapid tests	Different assembly format: cassette, midstream, strip
IVD urinalysis strips	Different combination of testing configurations
Blood tubes	Volumes

Other permissible variants in general
Colour
Diameter
Concentrations
Length
Memory storage
Isotope activity level
Print capability
Shape
Size
Volume
Width

ANNEX D: Decision Flowchart for Grouping of Products as an IVD Test Kit



ANNEX E: List of IVD Cluster Categories

This list of IVD CLUSTER categories is only applicable to **Class A and Class B IVD**. It should be clearly stated in the label or IFU of each reagent or article that it is intended for use, whether alone or in combination, for the same category:

No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
1	Clinical Chemistry	Enzymes	(i) Acid Phosphatase (ii) Alpha-Amylase (iii) Creatine Kinase (iv) Gamma-Glutamyl Transferase (v) Lactate Dehydrogenase (vi) Lipase
2		Substrates	(i) Albumin (ii) Bilirubin (iii) Urea/Blood Urea Nitrogen (iv) Cholesterol (v) Creatinine (vi) Glucose
3		Electrolytes Reagents	(i) Ammonia (ii) Bicarbonate (iii) Calcium (iv) Chloride (v) Magnesium (vi) Phosphate Inorganic/Phosphorus
4		Electrolyte Electrodes	(i) Ammonia Electrodes (ii) Carbon Dioxide (Bicarbonate) Electrodes (iii) Calcium Electrodes (iv) Chloride Electrodes (v) Magnesium Electrodes (vi) Potassium Electrodes

No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
5		Substrate Electrodes/ Biosensors	(i) Creatinine Electrodes (ii) Glucose Electrodes (iii) Glycated Hemoglobin Electrodes (iv) Lactate Electrodes (v) Urea Electrodes (vi) Bilirubin Electrodes
6	Immunochemistry	Immunoglobulins (without IgE).	(i) Immunoglobulin A (ii) Immunoglobulin D (iii) Immunoglobulin G (iv) Immunoglobulin M (v) Immunofixation kits
7		Complement Components	(i) Complement Component C1q (ii) Complement Component C1 inactivator (iii) Complement Component C3/C3c (iv) Complement Component for Bb (v) Complement Component C4 (vi) Complement Component C5a
8		Transport Proteins	(i) Albumin (ii) Ceruloplasmin (iii) Haptoglobin (iv) Hemopixin (v) Lactoferrin (vi) Pre-albumin/Transthyretin
9		Lipoproteins	(i) Apolipoprotein A I (ii) Apolipoprotein A II (iii) Apolipoprotein B (iv) Apolipoprotein E Sub-typing (v) Lipoprotein (a)

No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
10		Other Specific Proteins	(i) a1-Acid Glycoprotein (ii) a1-Antitrypsin (iii) a1-Microglobulin (iv) Fibronectin (v) Immuno Reactive Trypsin
11		Allergy	(i) Immunoglobulin E – Total (ii) Immunoglobulin E – Screen (iii) Immunoglobulin E – Specific, monotest/monoresult (iv) Allergen specific IgA (v) Allergen specific IgG
12		Cancer markers	(i) GI-marker CA242 (ii) p53
13		Thyroid Function Markers	(i) Free Triiodothyronine (ii) Free Thyroxine (iii) Thyroid Stimulating Hormone (iv) T – Uptake (v) Thyroglobulin (vi) Neonatal Thyroxine
14		Fertility/Pregnancy Hormones/ Proteins	(i) Androstenedione (ii) Estradiol (iii) Prolactin (iv) Human Placental Lactogen (v) Estriol
15		Diabetes Assays (Hormones)	(i) C-Peptid (ii) Glucagon (iii) Insulin (iv) Glycosylated/Glycated Haemoglobin (v) Islet Cell Ab (vi) Proinsulin

No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
16		Renal Metabolism Assays	(i) Aldosterone (ii) Angiotensin I / II (iii) Angiotensin Converting Enzyme (iv) Cortisol (v) Renine
17		Bone and Mineral Metabolism Assays	(i) Bone Alkaline Phosphatase (ii) Calcitonin (iii) Cross-linked C-Telopeptides (iv) Cross-linkded N-Telopeptides (v) Cyclic Adenosin Monophosphate (vi) Hydroxyproline
18		Endocrine Hormones and Peptides	(i) Adrenocorticotropic Hormone (ii) Human Growth Hormone (iii) Insulin-like Growth Factor I (iv) Insulin-like Growth Factor Binding Protein 1 (v) Vasointestinal Peptide (vi) Vasopressin
19		Neuroendocrine Function Assays	(i) Bombesin (ii) 17-Hydroxy-Ketosterone (iii) β-Endorphin (iv) Neurotensin (v) Somatostatin (vi) Substance P
20		Other Individual and Specified Hormones	(i) Gastrin (ii) Gonadotropin-Releasing Hormone (iii) Melatonin (iv) Pepsinogen (v) Adrenalin (vi) Dopamine

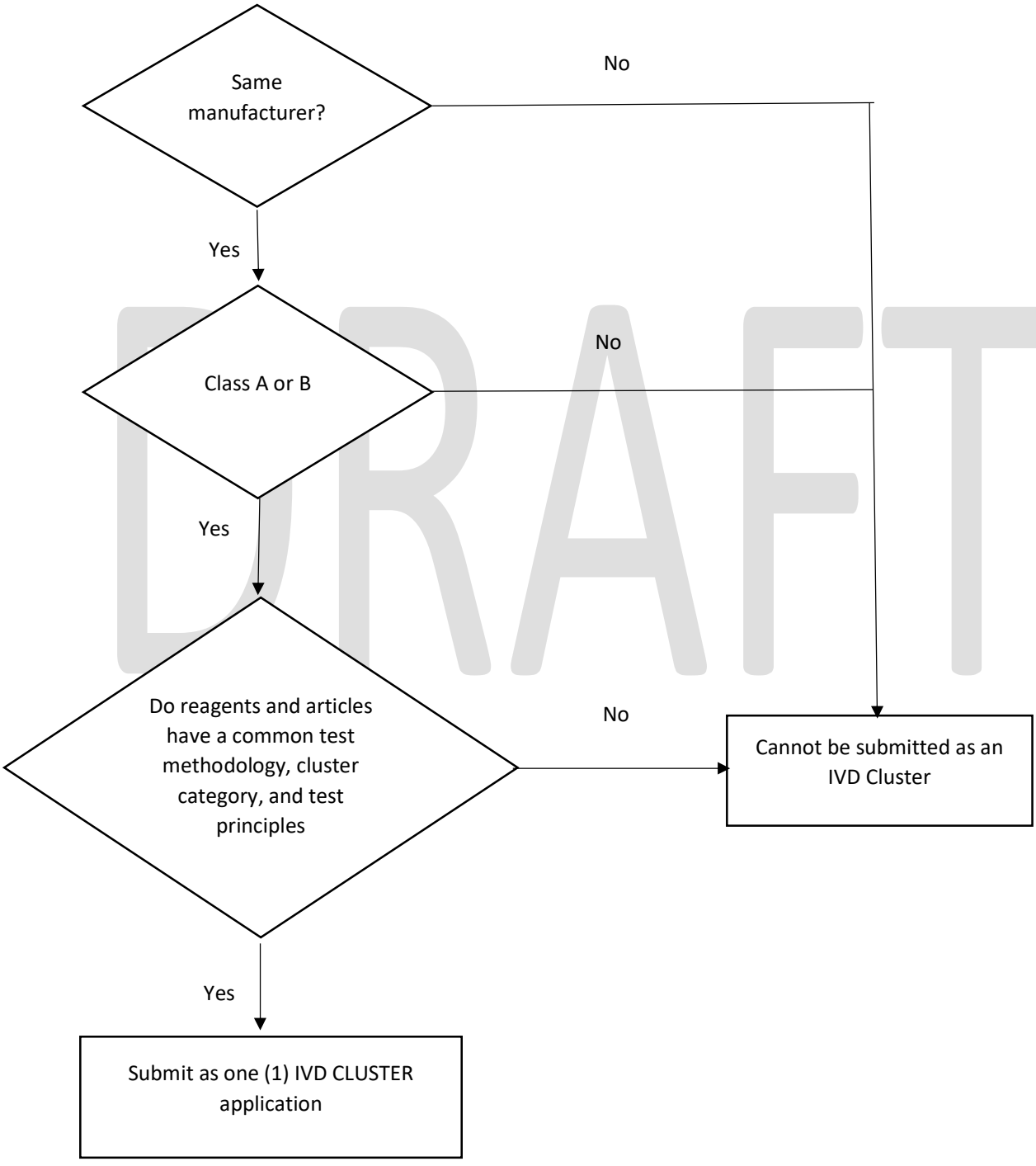
No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
21		Anaemia	(i) Erythropoietin (ii) Ferritin (iii) Folate (iv) Iron (v) Iron Binding Capacity (vi) Soluble Transferrin Receptor
22		Vitamins	(i) Vitamin B1 (ii) Vitamin B2 (iii) Vitamin B6 (iv) Vitamin B12 (v) Vitamin D (Cholecalciferol) (vi) Intrinsic Factor (Blocking Antibody)
23		Drug Monitoring	(i) Caffeine (ii) Benzodiazepines (iii) Penicillins (iv) Tetracyclines
24		Toxicology	(i) Amphetamines (ii) Cocaine (iii) Morphine (iv) Phencyclidine (v) Acetaminophen (vi) Catecholamines (vii) Ethanol (viii) Salicylate
25		Auto-immune Diseases	(i) Anti-nuclear antibodies (ANAs) (ii) Anti-topoisomerase (iii) Organ-specific autoantibodies (iv) Circulating Immuno-complex (v) TSH Receptor antibodies (vi) Anti-Cardiolipin antibodies

No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
26		Rheumatoid-Inflammatory Diseases Markers	(i) Anti-Streptococcal Hyaluronidase (ii) Anti-Streptokinase (iii) Anti-Streptolysin O (iv) C-Reactive Protein (v) Anti-Staphylolysin (vi) Anti-Streptococcal Screening
27		Liver Function	(i) MEGX (ii) Carbohydrate Deficient Transferrin
28		Bacterial Infection - Immunology	*(i) Bacillus subtilis* *(ii) Pseudomonas Aeruginosa* *(iii) Helicobacter Pylori* *(iv) Lactobacillus casei*
29		Viral Infection - Immunology	(i) Norovirus (ii) Hantavirus
30		Parasitic Infection - Immunology	*(i)* Leishmania
31		Fungal Infection - Immunology	*(i) Candida albicans* *(ii) Aspergillus*
32	Haematology/ Histology/ Cytology (Blood tests for transfusions excluded)	Hemoglobin Testing	(i) Hemoglobin determinations (Total Hb) (ii) Fractional oxyhemoglobin (FO2Hb) (iii) Fractional carboxyhemoglobin (FCOHb) (iv) Fractional methemoglobin (FMetHb) (v) Fractional deoxyhemoglobin (FHHb)

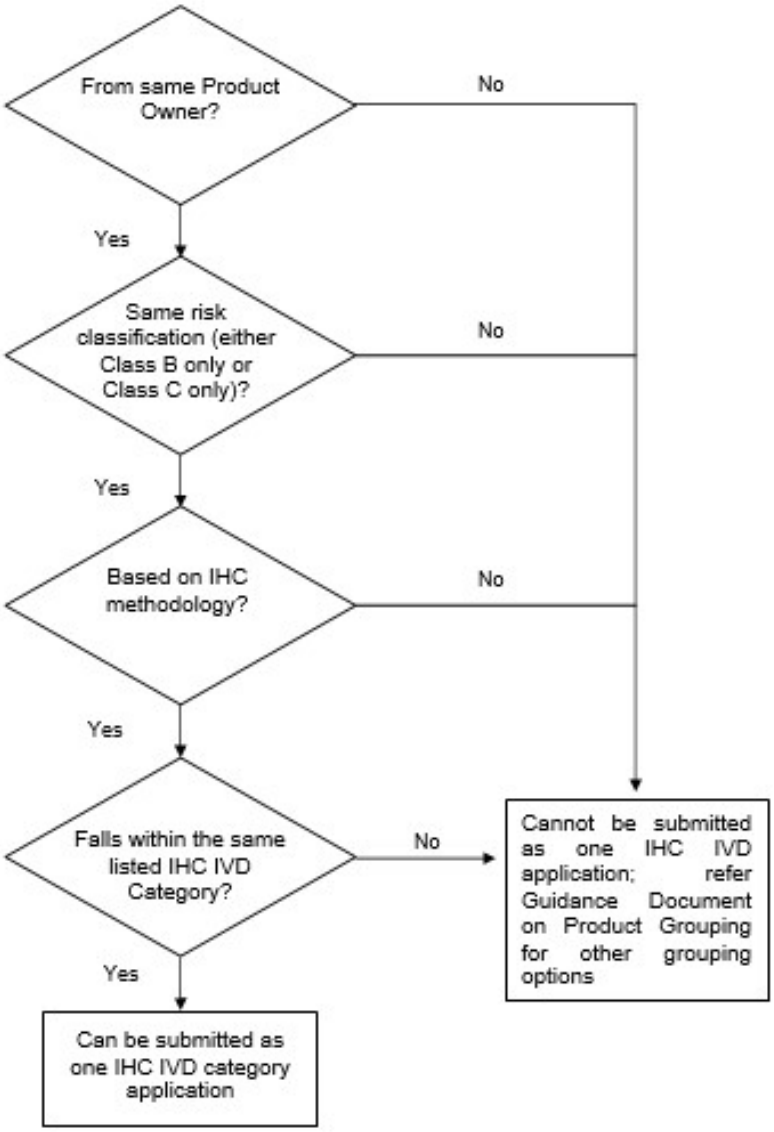
No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
33		Haemostasis (Coagulation)	(i) Fibrinogen (ii) Protein C and Protein S reagents (iii) C1-inhibitors (iv) Alpha-Antiplasmin (v) Fibrin (vi) Factor XIII (vii) Platelet Factor 4 (viii) Plasminogen
34		Other Hematology Tests	(i) Complete Blood count (ii) Hematocrit (iii) Erythrocyte Sedimentation rate
35		Cytokines (Lymphokines)/ Immunomodulators	(i) Interferons (ii) Soluble Antigens/Receptors (iii) Tumor Necrosis Factors (iv) Colony Stimulating Factors (v) Tumor Necrosis Factors Receptors
36		Histology/ Cytology Reagents	(i) Cytochemical Staining (ii) Embedding, Fixing, Mounting media (iii) Stain solutions (iv) Immunohistology kits
37	Microbiology - culture	Culture Media	(i) Dehydrated culture media (DCM) (ii) Additives for DCM (iii) Prepared Media (Tubes, bottles, Plates) (iv) Cells, Media, Serum for Viral culture
38		Susceptibility Testing *Testing for the susceptibility of the bacteria to certain antibiotics.*	(i) Erythromycin susceptibility test for Staphylococcus aureus (ii) Tobramycin susceptibility test for Pseudomonas aeruginosa (iii) Fungal susceptibility testing

No.	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)
39		Biochemical culture Identification (ID)	(i) Gram Negative Manual ID (ii) Gram Positive Manual ID (iii) Other ID Kits Manual - Anaerobes, Fastidious
40		Immunological culture Identification (ID)	(i) Streptococci Grouping Slide tests (ii) Serotyping (Shigella etc.)
41		Nucleic Acid (NA) based culture identification (ID)	(i) Streptococci (ii) Shigella
42		Serological identification (ID)	(i) For Parasitology and Mycology (Fungi and Yeast)
43		Bacterial Infections (Detection by NA Reagents)	(i) Streptococci (ii) Shigella
44		Viral Infections (Detection by NA Reagents)	(i) Para-influenza NA Reagents
45		Fungal Infections	(i) Fungi NA Reagents (ii) Candida albicans (iii) Aspergillus

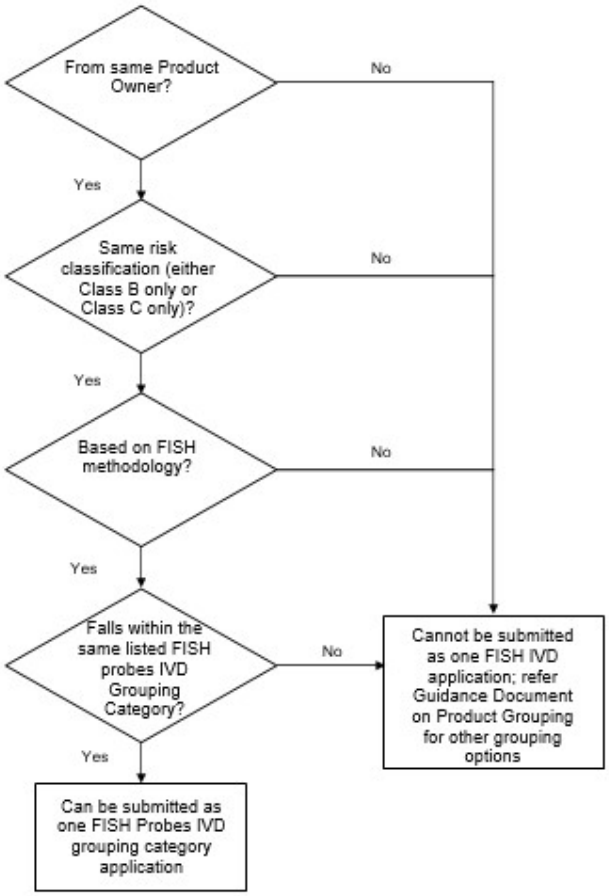
ANNEX F: Decision Flowchart for Grouping of Products as An IVD Cluster



ANNEX G Decision Flowchart for Grouping of Class B only or Class C only IHC IVD Grouping Category



ANNEX H: Decision Flowchart for Grouping of Class B and Class C FISH Probes IVD Grouping Category



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