Guideline for Medical Devices Bundling for Marketing authorization application

April 2021

Addis Ababa, Ethiopia
# Table of Contents

1. Introduction .................................................................................. 3
2. Scope .............................................................................................. 3
3. Definitions ..................................................................................... 4
4. General Principle of bundling ....................................................... 4
5. Bundling Criteria ........................................................................... 5
5.1. Single ....................................................................................... 6
5.2. Family ...................................................................................... 7
5.3. System ..................................................................................... 10
5.4. Set ........................................................................................... 13
5.5. IVD test Kit ............................................................................. 15
5.6. *In vitro* diagnostics cluster .................................................... 17
6. Application submission process .................................................. 19
7. Post registration ........................................................................... 19
8. Annexes ...................................................................................... 21
1. Introduction

The Ethiopian Food and Drug Authority (EFDA) is mandated by proclamation 1112/2019 to regulate medical devices. As part of the regulatory functions, the authority is expected to register and grant marketing authorization after assessing quality, safety & effectiveness of medical devices. Article 19(1) of the same proclamation decrees that “the rigor of regulatory assessment of medicine & medical device shall be commensurate with products type, nature, & potential risk to human health”. Various components or models of medical devices may be marketed individually or in different combinations as required by the end user, as convenient all in one-kit or as an individually customized pack based on the intended purpose. Hence, the authority has devised various mechanisms to carry out the assessments in a feasible and economical way that wouldn’t subject each single medical device to the same rigorous assessment procedure. Therefore, a medical device bundling criteria is needed to guide applicants during application submission for medical devices within one medical devices marketing authorization applications. In order to reduce the application processing time and to facilitate timely access of the products in the market, the authority permits bundling of medical device within a single premarket submission according to the criteria specified in this guideline. This guideline is intended to provide general criteria for bundling medical devices within one medical devices marketing authorization application. All existing pertinent national regulatory requirements and authority’s other guidelines shall be rereferred for all medical devices marketing authorization applications submissions regardless of the way they are grouped. In the event of any contradiction between the contents of this guideline and any written national law (proclamation, regulation and/or directives) the later should take precedence.

2. Scope

This guideline is applicable to all products that fall under the definition of medical devices for which marketing authorization applications are submitted to the Authority by applicants who wishes to bundle or group more than one medical device type, including in-vitro medical device, within one medical devices marketing authorization application. The grouping criteria described in this guideline will also be used as the guiding principles for all other device specialty or function specific grouping guidance documents that have been developed or to be developed in a distinct document.
3. Definitions

All definitions given in relation to medical devices in the proclamation 1112/2019 and subsequent regulation and directives should be applicable.

**Bundling** means the inclusion of multiple medical devices with the same intended purpose in a single premarket submission for the purposes of facilitating review and reasonably cut the user fee payment. Grouping is interchangeably used to describe the same concept.

**Intended purpose** means the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation. Intended use is interchangeably used to describe the same concept.

**Proprietary name** means a unique name given by the product owner to identify a medical device as a whole product, also known as the trade name or brand name. **Generic name** is interchangeably used to describe the same concept.

**In vitro diagnostic** means a medical 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.

**Legal manufacturer** means any natural or legal person with responsibility for design and manufacture of a medical device with the intention of making it available for use, under his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person.

**Surgical instruments** means instruments intended for surgical use by cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or other surgical procedure without connection to any other medical device.

4. General Principle of bundling

The major criteria for the bundlingshould consider the appropriateness of the grouped medical devices based on scientific justification and the cost effectiveness for both the applicant and the authority from the point of view of the suitability for an effective one review process. During bundling, the applicant should also consider devices specific attributes, such as those specific to in vitro diagnostics devices, when categorizing devices for the purposes of grouping. To decide whether an application can be submitted for review in a single medical devices marketing authorization application, the applicant should ensure that
the supporting data are similar; review can be accomplished by primarily one reviewer and the devices are similar.

In general, the following three basic principles should be considered for grouping medical devices in to one marketing authorization application.

- The devices should have one generic name
- The devices should have one trade name (if any).
- The devices should be from one legal manufacturer or product owner.
- The devices should have one intended purpose

Each device or indication in a bundled submission must satisfy the applicable statutory and regulatory premarket requirements.

### 5. Bundling Criteria

The applicant may group medical devices having same or similar intended uses, intended purposes, from the same owner, or commonality of technology and submit in a single application. The grouping of medical devices is for the purpose of submission of single application for getting marketing authorization prior to import or marketing locally manufactured devices. Medical devices can be grouped in to one of the following categories to be submitted in one application for evaluation & marketing authorization.

- i. Single
- ii. Family
- iii. System
- iv. Set
- v. IVD test kits
- vi. IVD Cluster

Summary flow chart for grouped medical devices application submission.
5.1. Single

A. Criteria

Application for marketing authorization of a medical device from a manufacturer identified by a proprietary name with specific intended purpose and sold as a distinct packaged entity is an application for single medical device. An application submitted as a single medical device may be:

a) For a medical device that is to be sold as a distinct packaged entity that may be sold in a range of package sizes, quantity, colour and does not meet the criteria for family, IVD test kit, system, IVD cluster or a set.

b) For a medical device that cannot be assigned to family, IVD test kit, system, IVD cluster or a set and that must be registered separately.

c) For medical device which was a part of a group that needs to be licensed separately before it is sold separately as individual medical devices.

d) Medical device that have different features cannot be bundled/grouped within one marketing authorization application as a single medical device. However, they may be bundled/grouped as a medical devices family (see section 5.2 in this document).

Note: Differences in models may include color, quantity, range of size, number of units.... etc.

B. Examples of medical devices for which MA application might be submitted as a single device

- Condoms to be sold in package of 3, 10 or 16 can be registered as a single medical device application.
- Gloves that are sold in packages of 25, 50, and 100 pieces
- Each medical device supplied individually must be licensed as a single medical device, if a company that assembles a first aid kit that has already registered its products has now decided to also supply each of medical devices in the first aid kit individually.
- If a company manufactures a standalone software program that can be used with a number of CT scanners produced by other manufacturers, although the software cannot function on its own, it can be used on
different scanners. In such instances, the software itself is deemed as a medical device and can be registered as a single medical device.

- A catheter with multi lengths.

5.2. **Family**

A. **Criteria**

A medical device family is a collection of medical devices which might have different features but each medical device family member fulfils the following:

a) each medical device family member is from the same/legal manufacturer or product owner

b) the devices in the family have the same risk classification,

c) has a common intended purpose or use

d) has a common design and manufacturing process

e) has variations that are within the scope of the permissible variants. The characteristics of a medical device may be considered as permissible variant, if
   i. the physical design and material of construction of the medical device are the same or very similar.
   ii. the manufacturing processes, including sterilisation method, for the medical devices are the same or very similar.
   iii. differences in features may include, material, structural characteristic, design, patient groups, energy source, purpose, brand name, model name or device description, area of application, additional function, additional secondary intended use/purpose.
   iv. General and specific acceptable variations are provided in annex I of this document.

f) Surgical instruments that fulfil criteria listed (a) to (c) may be bundled/grouped within a single marketing authorization application as a family of medical devices based on function only if they do not exceed 50 items per application.

g) Dental products that fulfil criteria listed (a) to (c) may be bundled within one marketing authorization application only if they have the same specialty.

h) A special grouping rule is applicable for class I/Reusable surgical instruments (see annex III for this grouping rule).

B. **Examples of medical devices for which the MA might be submitted in a single application as a family**
a) Cardiac catheters that are available in a different numbers of lumens lengths &
diameters can be grouped or bundled with in a single application as a family
medical device
b) IV administration sets that differ in features such as safety features and lengths of
tubing but are manufactured from the same material & manufacturing process and
share a common intended purpose
c) Condoms that differ in colour, size and texture but are manufactured from the
same material and manufacturing process and share a common intended purpose
can be registered a family.
d) Spherical contact lens with additional features of UV protection can be
registered as part of a family, as this feature does not affect the basic design or
manufacturing of the lens. However, contact lens which are available as toric lens
and spherical lens are designed and manufactured differently, and have different
intended purposes and performances cannot be considered as members of a family
due to these differences.
e) Other examples of Medical device family
   i. X-ray and mobile x-ray
   ii. Basic bedside monitor, bedside monitor with EEG module and bedside
       monitor with paper printer
f) Examples of surgical instruments that may be bundled within a single marketing
authorization application as a “family of medical devices” based on function are
as listed in table 1 below.

<table>
<thead>
<tr>
<th>Function</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>cut or incise</td>
<td>scissors, knives, saws and blades</td>
</tr>
<tr>
<td>retract</td>
<td>traction and bone hooks</td>
</tr>
<tr>
<td>grasp, hold or occlude</td>
<td>tissue and bone holding forceps, also needle holders</td>
</tr>
<tr>
<td>dilate or probe</td>
<td>punch</td>
</tr>
<tr>
<td>cannulate or drain</td>
<td>catheters or any instrument used for drain</td>
</tr>
<tr>
<td>aspirate, inject or infuse</td>
<td>instrument to remove unwanted fluids as well as to inject</td>
</tr>
<tr>
<td></td>
<td>fluids such syringes or some needles</td>
</tr>
<tr>
<td>suture or ligate</td>
<td>sutures, clips as well as suture needles and ligating blades</td>
</tr>
</tbody>
</table>
C. Decision flow chart for grouping of medical devices as a family

Medical device for MA application

From same product owner?  

Yes  

Same risk classification?  

Yes  

Common intended purpose?  

Yes  

Common design & manufacturing process?  

Yes  

Variations within the permissible variants  

Yes  

Can be submitted as medical device family  

No  

No

No  

No  

No  

Cannot be submitted as a family
5.3. System

A. Criteria

A medical devices system comprises of several constituent components to complete a common intended purpose. To submit marketing authorization applications as a single application for such members(components) of a medical device, which might have their own distinctive intended uses/purposes but bundled to complete an overall common intended purpose, the following criteria/principles shall apply:

a) General requirements for medical device system
   i. should be sold as medical device system under a single proprietary system name.
   ii. should be from same legal manufacturer/license holder
   iii. should be intended to be used in combination to complete a common intended purpose;
   iv. should be compatible when used as system; and
   v. should have a constituent component labelling instruction for use (IFU) brochures or catalogues which states that each constituent component is intended for use with the medical devicesystem.

b) For a constituent component in a system which is supplied for use in more than one system, such constituent components shall be included in the application for registration of each of other system.

c) If several systems fulfil the following conditions to be grouped as a family, they may be registered as a family:
   i. the systems are from the same manufacturer;
   ii. the systems are of the same risk classification class;
   iii. the systems have a common intended purpose;
   iv. the systems have the same design and manufacturing process; and
   v. key constituent-components of the systems have variations that are within the scope of the permissible variants.
   vi. has the same generic name
   vii. has the same trade name

d) An In Vitro Diagnostic (IVD) Medical Device systems may typically consist of Test kits and instruments (e.g. an analyzer designed to be used with that Test kit).

e) Medical devices and/or accessories from other product owners (or manufacturers) may be incorporated as part of a product owners system to achieve the intended purpose of the
device. These medical devices and/or accessories should be grouped together as a system, and information on all these devices and accessories, such as authorization from their product owners for registration with the system, evidence on use and compatibility with the system shall be submitted.

B. Examples of medical devices for which the MA application might be submitted in a single application as a system

i. A hip replacement system comprising of femoral and acetabular components can be registered as a system. The components must be used in combination to achieve a common intended purpose of total hip replacement. The size of the components may vary.

ii. An electrosurgical unit and its accessories that consist of forceps, electrodes, electrode holders, leads, plug adaptor, when used together for a common intended purpose, can be registered as a system.

iii. Optional accessory such as wireless controller that is part of In-the-ear hearing aid can be registered as a system.

iv. A glucose monitoring system comprising of a glucose meter, test strips, control solutions and linearity solutions can be grouped/bundled with in a single application of marketing authorization and registered as a system.

f) If the items of the system have different risk-classes, the highest risk-class will be considered.

g) If the applicant wishes to market any item of the system separately, he shall apply for another marketing authorization application.
C. Decision flow chart for grouping of medical devices as a system

1. Medical device for MA application
   - From same product owner?
     - No
     - Yes
       - Intended to be used in a combination to achieve common intended purpose
         - No
         - Yes
           - Compatible when used as a system?
             - No
             - Yes
               - Can be submitted as a System
               - No
                 - Sold under a single system proprietary name?
                   - No
                     - Labelling for constituent components is intended for use as a system?
                       - No
                         - Cannot be submitted as a System
                       - Yes
                         - Can be submitted as medical device System
                   - Yes
                     - Can be submitted as medical device System
             - No
               - Can be submitted as medical device System
   - No
     - Medical device for MA application
5.4. Set

A. Criteria

A medical device set is a collection of two or more medical devices, assembled together and supplied in a single package by the same legal manufacturer /license holder.

a. The medical devices set should:

(i) Be sold under a single proprietary name

(ii) Have a common intended use

b. The collection of medical devices in a set may differ in the number and combination of products that comprises each group, while maintaining the same proprietary group name and group's intended purpose.

c. If the medical device in a set is supplied for use in another group, such a medical device shall be included in the application of that other set.

B. Example of medical devices for which the MA application might be submitted in a single application as a set

A first aid kit consisting of medical devices such as bandages, gauzes, drapes and thermometers, when assembled together as one package, can be registered as a set.

Dialysis kit consisting of medical devices such as blood tubing lines and dialysers when packaged together for convenience to meet a specific purpose by a manufacturer can be applied as a set in a single marketing authorization application.
C. Decision flow chart for grouping of medical devices as a set

1. Medical device for MA application?
   - Yes
   - No

2. Collection of two or more medical devices?
   - Yes
   - No

3. Single proprietary group name?
   - Yes
   - No

4. Labelled and supplied in a single package unit by the product owner?
   - Yes
   - No

5. Common group intended purpose?
   - Yes
   - No

6. Cannot be submitted as a set

7. Can be submitted as a medical device set
5.5. IVD test Kit

A. Criteria

An *in-vitro* diagnostics kit that consists of reagents or articles may be bundled/grouped within one marketing authorization application only if:

a. They consist of reagents or articles which are:-
   (i) from same legal manufacturer/ license holder

   (ii) intended to be used in combination to complete a specific intended purpose.

   (iii) sold under single proprietary Test Kit name or the labelling instructions for use (IFU) brochures or catalogues for each reagent or article states that component is intended for use with the IVD test kit; and

   (iv) compatible when used as a Test Kit.

b. An *in-vitro* diagnostics kit does not include the instruments, such as analysers, needed to perform the test.

c. Individual reagents or articles can be supplied separately as replacement items for 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 application of the other Test Kits.

d. Total number of IVD medical device that are grouped/bundled within a single application of grouped medical devices shall not exceed 50 items within a single application.

B. Example of medical devices for which the MA application might be submitted in a single application as IVD

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 Test Kit. These reagents and articles can be supplied separately as replacement items for that particular Test Kit.
C. Decision flow chart for grouping of medical devices as a IVD Test Kit

1. Medical device for MA application
   - From same product owner?
     - No
       - Intended to be used in combination to complete a specific intended purpose?
         - No
           - Reagents & articles compatible as an IVD test kit?
             - No
               - Cannot be submitted as a IVD Test kit
             - Yes
               - Sold under a single IVD Test kit name?
                 - No
                   - Yes
                     - Labelling for reagents & articles stating intended for use with IVD test kits?
                       - No
5.6. *In vitro* diagnostics cluster

A. Criteria

An in-vitro diagnostics cluster comprises of a number of *in-vitro* diagnostics reagents or articles and they should fulfil the following criteria to be submitted as one application.

(i) They should be from same legal manufacturer/license holder;

(ii) They should be sold under single proprietary name;

(iii) They should be within the risk classification of A or B

(iv) They should be intended for a common test methodology;

(v) They should be under the same cluster category

(vi) Should be compatible when used as an IVD cluster.

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

A closed list of common test methodologies and IVD cluster categories is provided in Annex II of this document.
B. Decision flow chart for grouping of medical devices as a IVD cluster

Medical device for MA application

From same product owner?

Yes

Within the risk classification of class A or class B?

Yes

Reagents or articles of common test methodology & with in the listed IVD cluster category?

Yes

Can be submitted as a one IVD IVD cluster

No

No

No

Cannot be submitted as a an IVD Test kit
6. **Application submission process**

a) Applicants shall refer to other relevant guidelines for the administrative and technical documents to be submitted and service fees.

b) The authority will not accept adding more devices or indications for use to a submission which is under review and hence bundling should occur before the application is submitted to the authority. If they have to submit more devices or indications with justifiable scientific reasons and intended use of the grouped medical devices as addition to the submission under review, the applicant can request for such addition provided that the added devices comply with the relevant grouping criteria.

c) Applicants may withdraw a device(s) (or indication for use) from a bundled submission if they have satisfactory reason. But, if they resubmit the device(s) or indication for use in a new application, it will be considered as new application and they will be required to pay the service fee for the resubmission.

d) Applicants should not bundle multiple intended uses of a single test system (or indications for use such as professional and to be used by lay person), because it is unlikely that such multiple uses would be supported by the same data sets.

e) If a submission includes a device or indication that should not be bundled because it presents disparate scientific/clinical or regulatory issues (from the other devices or indications in the submission), the authority will notify the applicant to withdraw the device or indication from the bundled submission. The applicant may resubmit the device or indication for use in a separate submission, withdraw the device or indication for use, withdraw the entire application, or appeal the decision. However, the frequency of resubmissions shall not exceed a maximum of two times.

7. **Post registration**

The registrant is always required to comply with the conditions applicable to the registered medical device and conditions imposed on the MA holder. The MA holder shall undertake the following post-market activities for all medical devices and accessories approved by the authority as part of grouped/bundled medical devices registrations. Such duties and obligations shall include all the constituent-components registered in a group, regardless of whether the constituent components are from the same product owner or no

7.1. **Post approval Notification**
The MA holder shall submit post approval change notifications to the authority for any changes made to the registered medical device in accordance with the guideline for post approval notification. Whenever a product; include a single member of a bundled medical devices, has been withdrawn from the market for any reason (such as deficiencies in product quality defect or ADE reports) in other countries, the local agent or the manufacturer should notify EFDA as per the article 67(17) of proclamation No 1112/2019.

7.2. **Re-registration**

As per article 20(6) of the currently in force EFDA’s law, every medical devices registered in accordance with the proclamation shall have its registration renewed every five years (Marketing authorizations granted by EFDA will be valid for 5 years. Hence, marketing authorization holders should submit applications for re-registration of all medical devices in accordance with the requirements for re-registration stated in the Authority’s guideline for re-registration of medical devices.

7.3. **Retaining Records and reporting**

The registrant is expected to maintain records of supply and any complaints, as well as to report any defects and adverse effects to the Authority. The MA holder shall notify the authority any actions taken concerning field safety corrective action (FSCA), including recall
8. Annexes

Annex 1: Permissible Variants in a Family

The list of permissible variants is a closed and positive list.

<table>
<thead>
<tr>
<th>Specific products</th>
<th>Permissible variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic test</td>
<td>(i) Concentrations</td>
</tr>
<tr>
<td>Catheter</td>
<td>(i) Number of lumens in catheter</td>
</tr>
<tr>
<td></td>
<td>(ii) Material of catheter: PVC (polyvinylchloride), PU</td>
</tr>
<tr>
<td></td>
<td>(polyurethane), nylon and silicone</td>
</tr>
<tr>
<td></td>
<td>(iii) Curvature (straight or pigtail)</td>
</tr>
<tr>
<td></td>
<td>Polymer products-with or without DEPH</td>
</tr>
<tr>
<td></td>
<td>Stent- delivery system, that is over-the –wire or through the scope</td>
</tr>
<tr>
<td>I V cannula</td>
<td>(i) Presence of injection port</td>
</tr>
<tr>
<td></td>
<td>(ii) Presence of safety wing</td>
</tr>
<tr>
<td>Condoms</td>
<td>(i) Texture</td>
</tr>
<tr>
<td></td>
<td>(ii) Flavour</td>
</tr>
<tr>
<td>Contact lens</td>
<td>(i) Diopter,</td>
</tr>
<tr>
<td></td>
<td>(ii) UV protection</td>
</tr>
<tr>
<td>Component</td>
<td>Variants</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Electrophysiological</td>
<td>(i) Electrode spacing</td>
</tr>
<tr>
<td>Catheter</td>
<td>(ii) Number of electrodes</td>
</tr>
<tr>
<td>Suture</td>
<td>(i) Number of strands</td>
</tr>
<tr>
<td></td>
<td>(ii) Pledgets</td>
</tr>
<tr>
<td>Suture passer</td>
<td>(i) Design of jaw, handle or needle</td>
</tr>
<tr>
<td>Dental handpieces</td>
<td>(i) Rotational speed</td>
</tr>
<tr>
<td></td>
<td>(ii) Material of hand-piece</td>
</tr>
<tr>
<td>Dental brackets</td>
<td>(i) Material of bracket</td>
</tr>
<tr>
<td>IVD rapid tests</td>
<td>(i) Different assembly format: cassette, midstream, strip</td>
</tr>
<tr>
<td>IVD urinalysis strips</td>
<td>(i) Different combination of testing configurations</td>
</tr>
<tr>
<td>Polymer Products</td>
<td>(i) With or Without DEHP</td>
</tr>
<tr>
<td>Stent</td>
<td>1) Delivery system, that is over –the-wire or through the scope</td>
</tr>
</tbody>
</table>

**Other permissible variants**

<table>
<thead>
<tr>
<th>Colour</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td></td>
</tr>
<tr>
<td>Flexibility</td>
<td></td>
</tr>
<tr>
<td>Gauge</td>
<td></td>
</tr>
<tr>
<td>Holding force</td>
<td></td>
</tr>
<tr>
<td>Isotope activity level</td>
<td></td>
</tr>
<tr>
<td>Length</td>
<td></td>
</tr>
<tr>
<td>Memory storage</td>
<td></td>
</tr>
<tr>
<td>Print capability</td>
<td></td>
</tr>
<tr>
<td>Radiopacity</td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td></td>
</tr>
<tr>
<td>Width</td>
<td></td>
</tr>
</tbody>
</table>
ANNEX II: 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:

<table>
<thead>
<tr>
<th>S. No</th>
<th>Methodology</th>
<th>Cluster Category (closed list)</th>
<th>Examples of Analytes (non-exhaustive list)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Clinical Chemistry</td>
<td>Enzyme</td>
<td>(i) Acid Phosphatase</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(ii) Alpha-Amylase</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(iii) Creatine Kinase</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(iv) Gamma-GlutamylTransferase</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(v) Lactate Dehydrogenase</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(vi) Lipase</td>
</tr>
<tr>
<td>2</td>
<td>Substrate</td>
<td></td>
<td>(i) Albumin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(ii) Bilirubin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(iii) Urea/Blood Urea Nitrogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(iv) Cholesterol</td>
</tr>
<tr>
<td>Page</td>
<td>Section</td>
<td>Contents</td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>---------</td>
<td>----------</td>
<td></td>
</tr>
</tbody>
</table>
| 3    | Electrolyte 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 |
| 5    | Substrate Electrodes/Biosensors | (i) Creatinine Electrodes  
(ii) Glucose Electrodes  
(iii) GlycatedHemoglobin Electrodes  
(iv) Lactate Electrodes  
(v) Urea Electrodes  
(vi) Bilirubin Electrodes |
| 6    | Immunochemistry | (i) Immunoglobulin A  
(ii) Immunoglobulin D  
(iii) Immunoglobulin G |

Substrate Electrodes/Biosensors:
(i) Creatinine Electrodes  
(ii) Glucose Electrodes  
(iii) GlycatedHemoglobin Electrodes  
(iv) Lactate Electrodes  
(v) Urea Electrodes  
(vi) Bilirubin Electrodes
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Complement Components</td>
<td>(i) Complement Component C1q</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Complement Component C1 inactivator</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Complement Component C3/C3c</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Complement Component for Bb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Complement Component C4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(vi) Complement Component C5a</td>
</tr>
<tr>
<td>8</td>
<td>Transport Protein</td>
<td>(i) Albumin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Ceruloplasmin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Haptoglobin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Hemopixin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Lactoferrin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(vi) Pre-albumin/Transthyretin</td>
</tr>
<tr>
<td>9</td>
<td>Lipoprotein</td>
<td>(i) Apolipoprotein A I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Apolipoprotein A II</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Apolipoprotein B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Apolipoprotein E Sub-typing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Lipoprotein (a)</td>
</tr>
<tr>
<td>10</td>
<td>Other Specific Proteins</td>
<td>(i) a1-Acid Glycoprotein</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) a1-Antitrypsin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) a2-Macroglobulin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>
| 11 | Allergy | (iv) a1-Microglobulin  
(v) Fibronectin  
(vi) Immuno Reactive Trypsin |
|   |   | (i) Immunoglobulin E – Total  
(ii) Immunoglobulin E – Screen  
(iii) Immunoglobulin E – Specific, monotest/monoresult  
(iv) Allergene specific IgA  
(v) Allergene specific IgG |
| 12 | Cancer markers | (i) BR-marker CA15-3  
(ii) GI-marker CA19-9, CA242  
(iii) Carcinoembryonic Antigen  
(iv) Total Prostatic Specific Antigen  
(v) Alphafetoprotein (AFP)  
(vi) 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 Chorionic |
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>Diabetes Assays (Hormones)</td>
<td>(i) C-Peptide</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Glucagon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Insulin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Glycosylated / Glycated Haemoglobin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Islet Cell Ab</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(vi) Proinsulin</td>
</tr>
<tr>
<td>16</td>
<td>Renal metabolism assay</td>
<td>(i) Aldosterone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Angiotensin I / II</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Angiotensin Converting Enzyme</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Cortisol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Renine</td>
</tr>
<tr>
<td>17</td>
<td>Bone and Mineral Metabolism Assays</td>
<td>(i) Bone Alkaline Phosphatase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Calcitonin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Cross-linked C-Telopeptides</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Cross-linked N-Telopeptides</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Cyclic Adenosin Monophosphate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(vi) Hydroxyproline</td>
</tr>
<tr>
<td>18</td>
<td>Endocrine Hormones and Peptides</td>
<td>(i) Adrenocorticotropic Hormone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Human Growth Hormone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Insulin-like Growth Factor I</td>
</tr>
<tr>
<td>Page</td>
<td>Section</td>
<td>Assays</td>
</tr>
<tr>
<td>------</td>
<td>------------------------------</td>
<td>------------------------------------------------------------</td>
</tr>
<tr>
<td>19</td>
<td>Neuroendocrine Function</td>
<td>(i) Bombesin</td>
</tr>
<tr>
<td></td>
<td>Assays</td>
<td>(ii) 17-Hydroxy-Ketosterone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) β-Endorphin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Neurotensin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Somatostatin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(vi) Substance P</td>
</tr>
<tr>
<td>20</td>
<td>Other Individual and</td>
<td>(i) Gastrin</td>
</tr>
<tr>
<td></td>
<td>Specified Hormones</td>
<td>(ii) Gonadotropin-Releasing Hormone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Melatonine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Pepsinogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Adrenalin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(vi) Dopamine</td>
</tr>
<tr>
<td>21</td>
<td>Anaemia</td>
<td>(i) Erythropoietin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Ferritin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) Folate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) Iron</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) Iron Binding Capacity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(vi) Soluble Transferrin Receptor</td>
</tr>
<tr>
<td>22</td>
<td>Vitamins</td>
<td>(i) Vitamin B1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Vitamin B2</td>
</tr>
</tbody>
</table>
| 23 | Non-Immuno Suppressive Therapeutic Drug Monitoring | (i) Phenobarbitol  
(ii) Digitoxin  
(iii) Gentamicin  
(iv) Valproic Acid  
(v) Caffeine  
(vi) Theophylline  
(vii) Methotrexate |
| 24 | Immunosuppressive Therapeutic Drug Monitoring | (i) Cyclosporine  
(ii) Tacrolimus  
(iii) Rapamycin (Sirolimus)  
(iv) Mycophenolate |
| 25 | Toxicology | (i) Amphetamines  
(ii) Cocaine  
(iii) Barbiturates  
(iv) Morphines  
(v) Phencyclidine  
(vi) Acetaminophen  
(vii) Catecholamines  
(viii) Ethanol  
(ix) Salicylate |
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
<th>Details</th>
</tr>
</thead>
</table>
| 26   | 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 |
| 27   | 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 |
| 28   | Liver Function | (i) MEGX  
(ii) Carbohydrate Deficient Transferrin |
| 29   | Cardiac Markers | (i) BNP/proBNP  
(ii) Creatine Kinase - MB  
(iii) Myoglobin  
(iv) Troponin I/T  
(v) Homocysteine  
(vi) High-Sensitivity C-Reactive Protein |
| 30   | Bacterial Infection - Immunology | (i) Bacillus subtilis  
(ii) Escherichia coli |
<table>
<thead>
<tr>
<th>Page</th>
<th>Topic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>Viral Infection – Immunology</td>
<td>(i) Influenza virus</td>
</tr>
</tbody>
</table>
| 32   | Parasitic Infection - Immunology | (i) Entamoebahistolytica  
(ii) Leishmania |
| 33   | Fungal Infection - Immunology | (i) Candida albicans  
(ii) Aspergillus |
| 34   | Haematology (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) |
| 35   | General Coagulation tests | (i) Prothrombin Time  
(ii) Thrombin Time  
(iii) Activated Clotting Time  
(iv) Activated Partial Thromboplastin Time |
| 36   | Haemostasis (Coagulation) | (i) Prothrombin  
(ii) Thrombin  
(iii) Fibrinogen  
(iv) Protein C and Protein S reagents |
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
</table>
| 37   | Other Hematology tests | (i) Complete Blood count  
(ii) Hematocrit  
(iii) Erythrocyte Sedimentation rate |
| 38   | Histology/Cytology | Cytokines (Lymphokines)/Immunomodulators | (i) Interferons  
(ii) Soluble Antigens/Receptors  
(iii) Tumor Necrosis Factors  
(iv) Interleukins  
(v) Colony Stimulating Factors  
(vi) Tumor Necrosis Factors Receptors  
(vii) Interleukins Receptors |
| 39   | Histology/ Cytology Reagents | | (i) Cytochemical Staining  
(ii) Embedding, Fixing, Mounting media  
(iii) Stain solutions  
(iv) Immunohistology kits |
| 40   | Microbiology - | Culture media | (i) Dehydrated culture media |
| 41 | Susceptibility testing | (i) Erythromycin susceptibility test for Staphylococcus aureus  
(ii) Tobramycin susceptibility test for Pseudomonas aeruginosa  
(iii) Fungal susceptibility testing |
| 42 | Biochemical culture Identification (ID) | (i) Gram Negative Manual ID  
(ii) Gram Positive Manual ID  
(iii) Other ID Kits Manual - Anaerobes, Fastidious  
(iv) Mycoplasma |
| 43 | Immunological culture Identification (ID) | (i) Streptococci Grouping Slide tests  
(ii) Serotyping (E.coli, Salmonella, Shigella etc.) |
| 44 | Nucleic Acid (NA) based culture identification (ID) | (i) NA Identification – MRSA  
(ii) NA Identification – Other resistance markers |
| 45 | Serological identification (ID) | (i) For Parasitology and Mycology (Fungi and Yeast) |
| 46 | Molecular Biology | Oncogenes  
Genes, whose mutation or |
| | culture (i)  
Cytochemical Staining (ii)  
Embedding, Fixing, Mounting media (iii) Stain solutions (iv) Immunohistology kits | (DCM)  
(ii) Additives for DCM  
(iii) Prepared Media (Tubes, bottles, Plates)  
(iv) Cells, Media, Serum for Viral culture |
enhanced expression, turns a normal cell into a cancer cell.

(ii) MYC (8q24)
(iii) TERC (3q26)

47
Bacterial Infections (Detection by NA Reagents) (i) Staphylococcal detection
(ii) E.coli detection

48
Viral Infections (Detection by NA Reagents) (i) Influenza and Para-influenza NA Reagents

49
Fungal Infections (i) Fungi NA Reagents

Annex III: Special Grouping Rule for Class I Reusable Surgical Instruments

A special grouping rule is applicable to Class I reusable surgical instruments. The special grouping rule states that reusable surgical instruments can be grouped together as 1 family if they satisfy the following conditions:

- are from the same manufacturer
- same overall intended purpose (This refers to the overall intended purpose of the instrument, regardless of location of the body they are used on).

For example, Class I lung retractor and Class I kidney retractor have the same overall intended purpose as they are both retractors. However, lung forceps and lung retractors do not have the same overall intended purpose and therefore cannot be grouped together as a family.

This special grouping rule is only applicable to Class I reusable surgical instruments. It is not applicable to Class II, III and IV reusable surgical instruments.

Example:

<table>
<thead>
<tr>
<th>Instrument name</th>
<th>Description</th>
<th>Intended purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC Dressing Forceps</td>
<td>Delicate, Serrated Tips, Straight, 4¾&quot;</td>
<td>To pick up or grasp tissue or</td>
</tr>
<tr>
<td>Forceps</td>
<td>Description</td>
<td>Purpose</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------------------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>DEF Kidney Forceps</td>
<td>Half curved, 222 mm length</td>
<td>To grasp renal polyps</td>
</tr>
<tr>
<td>HIJ Lung Forceps</td>
<td></td>
<td>To grasp lung tissue</td>
</tr>
<tr>
<td>XYZ Uterine Biopsy Forceps</td>
<td>Oblong basket jaw, jaw size 3x10mm, shaft length 10”</td>
<td>To grasp tissue during transvaginal or transrectal tissue biopsy</td>
</tr>
</tbody>
</table>

In the example above, the forceps have the same product owners, but have different proprietary names (ABC, DEF, HIJ and XYZ) and different intended purposes. These forceps are Class I medical devices.

These forceps can be grouped as a family and registered as part of one application on the basis of the special grouping rule for Class I reusable surgical instrument because:

- they are Class I reusable surgical instruments,
- the product owner is the same for all instruments, and
- they have the same overall intended purpose (i.e. to grasp).