

HEALTH SCIENCES AUTHORITY

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MEDICAL DEVICE GUIDANCE

GN-34: Guidance Document for IVD Analysers

Revision 1.2



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PREFACE

This document is intended to provide general guidance. Although we have tried to ensure that the information contained here is accurate, we do not, however, warrant its accuracy or completeness. The Health Sciences Authority (HSA) accepts no liability for any errors or omissions in this document, or for any action/decision taken or not taken as a result of using this document. The information contained in this document should not be a substitute for professional advice from your own professional and healthcare advisors.

REVISION HISTORY

<u>Guidance Version (Publish Date) [3 latest revisions]</u>	<u>Revision</u>
GN-34: Revision 1 (01 December 2017)	R1
R1.1 ► GN-34: Revision 1.1 (01 June 2018)	R1.1
R1.2 ► GN-34: Revision 1.2 (19 September 2018)	R1.2

**Where applicable, changes and updates made in each document revision are annotated with or within the arrow symbol "►". Deletions may not be shown*

1. INTRODUCTION

1.1. Purpose

This document provides guidance to product owners and registrants concerning *in vitro* diagnostic devices (IVD) analysers and their associated accessories.

1.2. Background

HSA has made updates for IVD analysers concerning their risk classification, grouping, listing options on the Singapore Medical Device Register (SMDR) and Change Notification (CN) for all listings containing IVD analysers.

1.3. Scope

This guidance document addresses the following for IVD analysers:

- Risk classification
- Grouping of medical devices for product registration
- Product registration and SMDR listing options
- Change Notification

The affected guidance documents are as follows:

Affected Guidances	Title
GN-12-1	Guidance on Grouping of Medical Devices for Product Registration – General Grouping
GN-12-2	Guidance on Grouping of Medical Devices for Product Registration – Device Specific Grouping Criteria
GN-14	Guidance on the Risk Classification of In Vitro Diagnostic Medical Devices
GN-15	Guidance on Medical Device Product Registration
GN-21	Guidance on Change Notification for Registered Medical Devices
GN-22	Guidance for Dealers on Class A Medical Devices Exempted from Product Registration

Analysers that are not manufactured, sold or represented by manufacturers for use in IVD applications are not considered to be IVDs. This includes products sold for general laboratory applications and products that are labelled 'For Research Use Only' (RUO).

1.4. Definitions

Definitions that do not indicate they are set out in the Health Products Act (*Act*) and Health Products (Medical Devices) Regulations 2010 (*Regulations*) are intended as guidance in this document. These definitions are not taken verbatim from the above legislation and should not be used in any legal context. These definitions are meant to provide guidance in layman terms.

ACCESSORY: for the purposes of this guidance document, an accessory is an article that, is intended specifically by its product owner to:

- be used together with an IVD medical device to enable that device to be used in accordance with its intended purpose as an IVD medical device.
- or to augment or extend the capabilities of that device in fulfilment of its intended purpose as an IVD medical device.

and therefore should be considered an IVD medical device.

INTENDED PURPOSE/INTENDED USE (*as set out in the Regulations*): in relation to a medical device or its process or service, means the objective intended use or purpose, as reflected in the specifications, instructions and information provided by the product owner of the medical device.

IN VITRO DIAGNOSTIC (IVD) PRODUCT (*as set out in the Regulations*): means any reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination, that is intended by its product owner to be used *in vitro* for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:-

- concerning a physiological or pathological state;
- concerning a congenital abnormality;
- to determine the safety and compatibility of donations, including blood and tissue donations, with potential recipients; or
- to monitor therapeutic measures,

and includes a specimen receptacle but not a product for general laboratory use, unless that product, in view of its characteristics, is specifically intended by its product owner to be used for *in vitro* diagnostic examination.

IVD ANALYSER: IVD analysers are equipment intended to be used with IVD reagents so as to allow the IVD reagents to achieve their intended use. IVD analysers are typically instruments that analyse the reaction and yield a result of positive, negative, amount of analyte detected, etc.

PRODUCT OWNER (as set out in the Regulations): in relation to a health product, means a person who —

- supplies the health product under his own name, or under any trade mark, design, trade name or other name or mark owned or controlled by him; and
- is responsible for designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the health product, or for assigning to it a purpose, whether those tasks are performed by him or on his behalf.

PROPRIETARY NAME: for the purposes of this guidance document, 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.

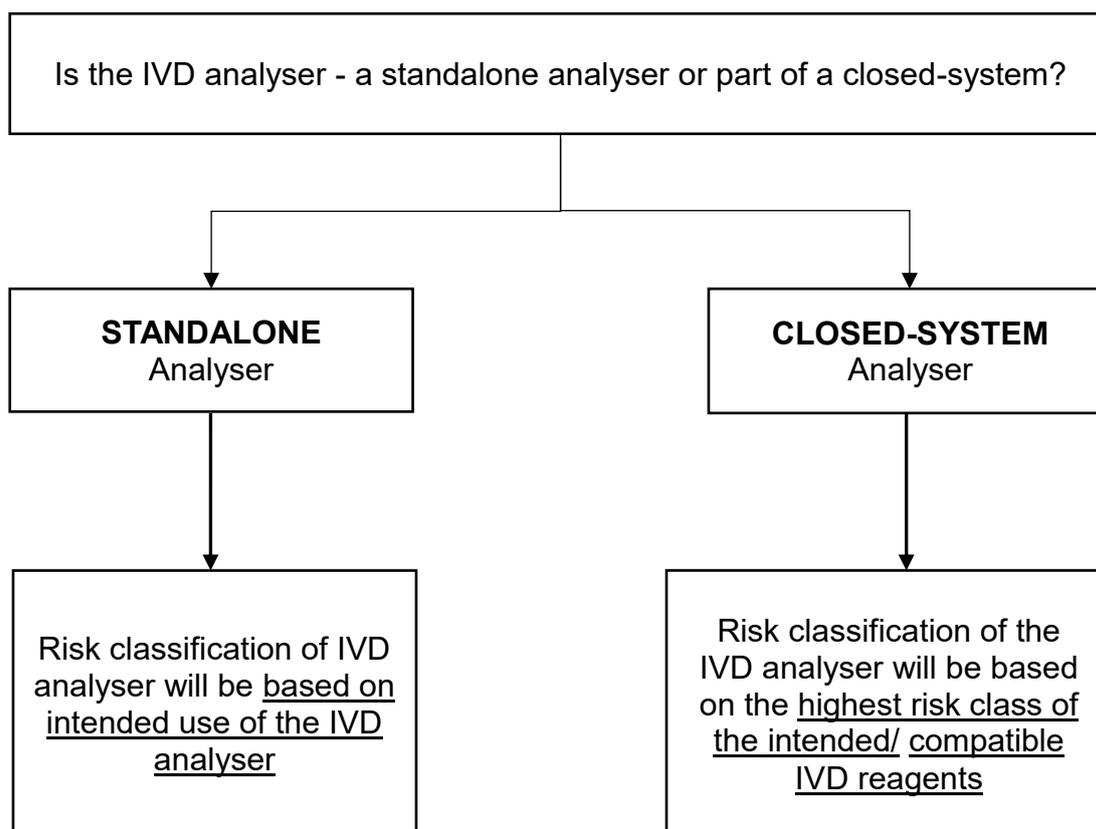
2. RISK CLASSIFICATION OF IVD ANALYSERS

The risk classification of an IVD analyser (inclusive of software) depends on the intended purpose of the analyser and whether it is intended to be used as a standalone analyser or as part of a closed IVD system.

Standalone analysers are instruments that are not intended by their product owners to be used with specific reagents. Typically, these instruments can be used with reagents from different product owners.

Closed-system analysers are instruments that are intended by their product owners to be used with specific reagents, which typically come from the same product owner. Refer to Flowchart 1 for the risk classification of IVD analysers.

Flowchart 1: Risk Classification approach for of IVD Analysers



Example of the risk classification for a closed-system analyser:

IVD reagents X, Y and Z have different intended uses and the highest risk class among them is Class C. All 3 reagents are compatible and intended for use with IVD analyser P. Therefore, IVD analyser P is a closed-system analyser and its risk class shall be Class C.

Example of the risk classification for a standalone analyser:

IVD analyser Q is used for the automation of an enzyme immunoassay. The product owner does not intend for the analyser to be used with specific reagents; and its labels and user manual does not indicate the performance characteristics of any reagents using the automated protocol of the analyser. Therefore, IVD analyser Q is a standalone analyser and its risk class shall be Class A.

Risk classification Rule 5 from GN-14 Guidance on the Risk Classification of In Vitro Diagnostic Medical Devices will be revised to capture the updates to the risk classification made to analysers, along with the examples and rationale. Refer to Table 1 for the updates for Rule 5.

Table 1: Clarifications Made to Rule 5 of GN-14

Rule 5	Revised Rule 5
<p>The following IVD medical devices are classified as Class A:</p> <ul style="list-style-type: none"> • Reagents or other articles that possess specific characteristics, intended by the product owner to make them suitable for in vitro diagnostic procedures related to a specific examination. 	<p>The following IVD medical devices are classified as Class A:</p> <ul style="list-style-type: none"> • Reagents or other articles that possess specific characteristics, intended by the product owner to make them suitable for in vitro diagnostic procedures related to a specific examination.

<p>[Amended]</p> <ul style="list-style-type: none"> Instruments intended by the product owner specifically to be used for in vitro diagnostic procedures. Specimen receptacles. <p>[Amended]</p> <p>Note: Any product for general laboratory use not manufactured, sold or represented for use in specified in vitro diagnostic applications are not deemed to be IVD medical devices.</p> <p>Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These IVD medical devices present a low individual risk and no or minimal public health risk.</p> <p>Examples: Selective/differential microbiological media (excluding the dehydrated powders which are</p>	<p>[Updated to]</p> <ul style="list-style-type: none"> Standalone instruments (inclusive of software) intended by the product owner specifically to be used for in vitro diagnostic procedures, not intended for use in specific medical diagnostic purposes. <p>Example: sample-preparation instruments</p> <ul style="list-style-type: none"> Specimen receptacles. <p>[Updated to]</p> <p>Examples: Wash solutions, and plain urine cup.</p> <p>Note: Any product for general laboratory use not manufactured, sold or represented for use in specified in vitro diagnostic applications are not deemed to be IVD medical devices.</p> <p>Rationale: The application of this rule as defined above for Class A IVD medical devices should be in accordance with the rationale for this rule which is as follows: These IVD medical devices present a low individual risk and no or minimal public health risk.</p>
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considered not to be a finished IVD medical device), identification kits for cultured microorganisms, wash solutions, instruments and plain urine cup.

NOTE: The performance of software or an instrument that is specifically required to perform a particular test will be assessed at the same time as the test kit.

NOTE: The interdependence of the instrument and the test methodology prevents the instrument from being assessed separately, even though the instrument itself is still classified as Class A.

3. DEVICE-SPECIFIC ‘FAMILY’ GROUPING CRITERIA FOR IVD ANALYSERS

IVD analysers that meet the ‘FAMILY’ grouping criteria indicated in GN-12-1 Guidance on Grouping of Medical Devices, may be grouped together under one device listing on SMDR if they also fulfil the additional grouping requirements of the list of permissible variants as shown in Table 2 below. The non-permissible variants are also specified in Table 2.

Any requests to reconsider or review the grouping criteria for IVD analysers shall be submitted via email to hsa_md_info@hsa.gov.sg with subject header “Request for review of IVD analyser grouping criteria”. The email should include detailed information regarding:

- (i) Device description
- (ii) Existing grouping options and their limitations (if any)
- (iii) Proposed grouping criteria and rationale
- (iv) Technical/ scientific information to support the proposal

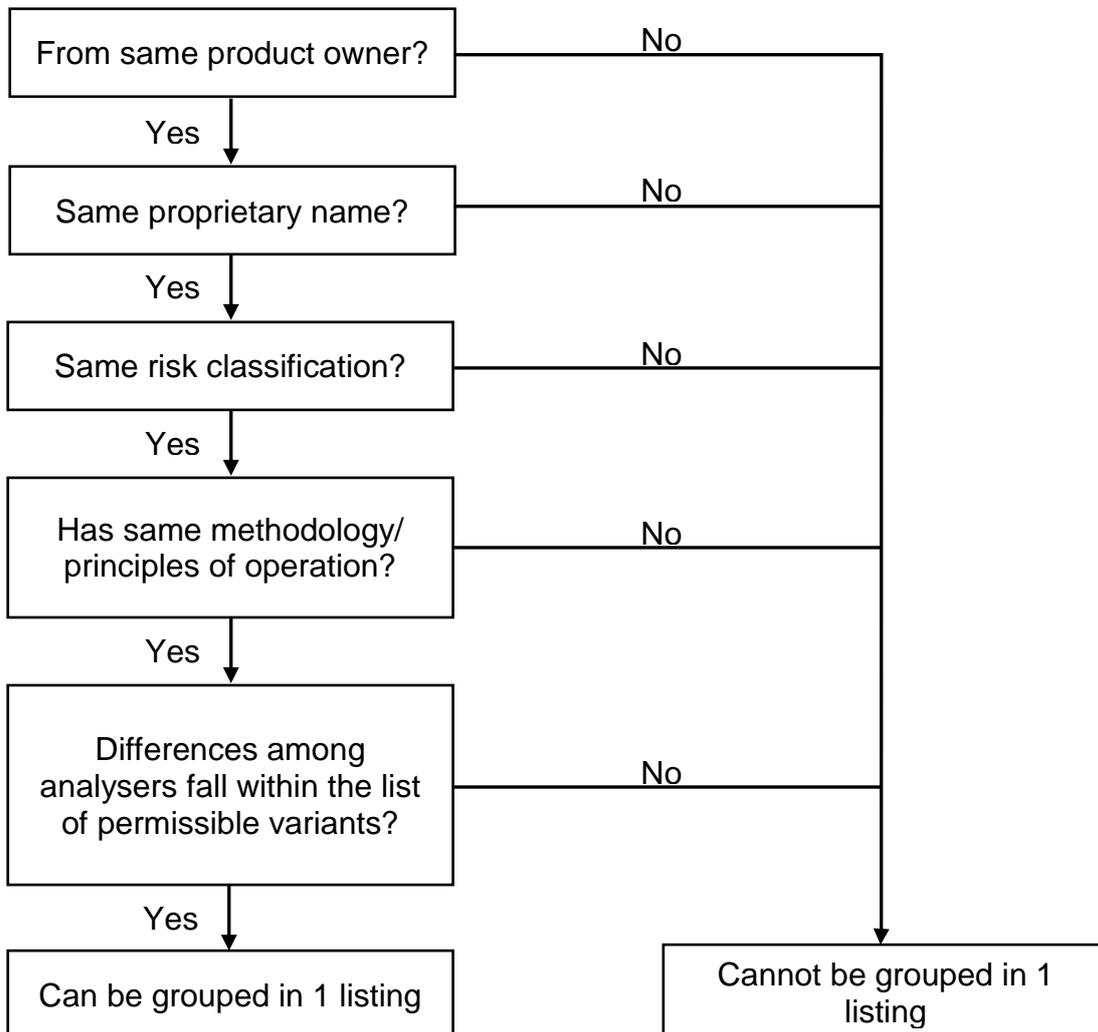
Table 2: List of Permissible and Non-permissible Variants for 'FAMILY'

Grouping of IVD Analysers

Permissible Variants	Non-Permissible Variants
<p>1. Features that do not impact the diagnostic function</p> <ul style="list-style-type: none"> • throughput • differences in user interface • printing function • wireless capability • software version • sample volume • onboard stability • calibration frequency 	<p>1. Features that impact the diagnostic function or lead to different performance characteristics for their compatible reagent kits, for example but not limited to:</p> <ul style="list-style-type: none"> • sensitivity • specificity • linearity • measuring range <p>2. Methodology/ principles of operation</p>

Refer to Flowchart 2 for the decision flowchart on 'FAMILY' grouping of IVD analysers under a single device listing.

Flowchart 2: Decision Flowchart on ‘FAMILY’ Grouping of IVD Analysers under one Device Listing on SMDR



4. SMDR LISTING OPTIONS FOR IVD SYSTEMS WITH CLOSED-SYSTEM IVD ANALYSERS

For relevant scenarios encountered for pre-market product registration applications, refer to the following sections below:

- Section 4.1: For listing options of new closed-system analyser(s).
- Section 4.2: For closed-system analyser(s) that are currently **NOT** listed on SMDR in **SPLIT** IVD analyser device listing(s)
- Section 4.3: For closed-system analyser(s) that are currently listed on SMDR in **SPLIT** IVD analyser device listing(s)

Note: Section 4.3 applies only to closed-system analysers that are already listed on SMDR in their own IVD analyser device listing and does not apply to analysers listed as part of another IVD system on the SMDR.

4.1. Singapore Medical Device Register (SMDR) Listing Options for New IVD SYSTEMS

Two SMDR listing options will be available for IVD systems comprising of test kits, reagents and analysers (and compatible analyser accessories) submitted in product registration applications WEF 01/12/2017. Applicants can opt for one of the following SMDR listing options for the analyser (and compatible analyser accessories) upon approval of the product registration application:

- **Option 1 (IVD SYSTEM LISTING):** Listing of analysers together with its compatible IVD reagents

Note: This is as per the existing SMDR listing option for closed-system IVD SYSTEMS.

- **Option 2 (SPLIT LISTING):** Listing of the IVD analysers separately from the compatible IVD reagents. The IVD analyser may be listed on its own or with other IVD analysers that meet the 'FAMILY' grouping criteria. (Refer to Section 3 of this guidance for more information.)

Note: Option 2 will incur additional annual (risk-class based) registration retention fee for the SPLIT LISTING of analysers. Analyser accessories such as cleaning solutions and bulk reagents may be listed with the analyser.

Upon selecting one of the two listing options, change to the other listing option is not permitted.

4.2. Product Registration Application with Closed-System IVD Analysers Not Listed on SMDR in their own Device Listing(s)

Product registration requirements remain unchanged but registrants are to inform the Branch of their selected listing option as indicated in Section 4.1 of this guidance. For applicants that opt for **SPLIT** Listing of the IVD analyser(s), they may list the analyser in:

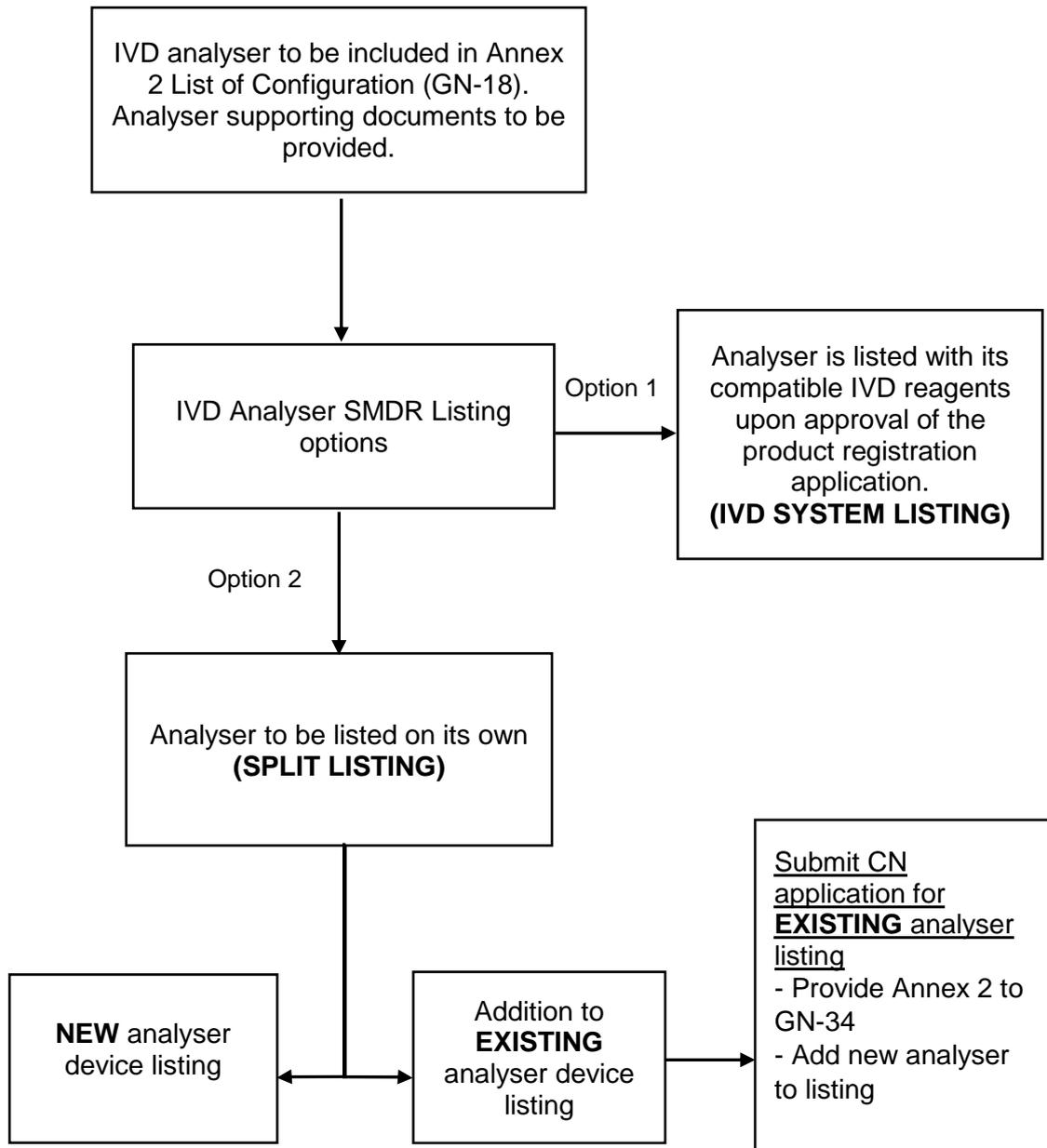
- A. A **NEW** IVD analyser listing; OR
- B. An **EXISTING** IVD analyser listing for which the FAMILY grouping criteria is fulfilled.

A Change Notification submission for the addition of the new analyser to the **EXISTING** IVD analyser listing will be required upon approval of the product registration application to update the list of registered reagents that are compatible and intended for use with the listed analyser.

The Change Notification category shall be 'Other Notification Changes (Verified by HSA prior to submission)' and tabulation of the list of compatible reagents with analysers in SPLIT IVD analyser device listings (Annex 2 to GN-34) is to be submitted. For other required submission documents, please refer to GN-21 Guidance on Change Notification for Registered Medical Devices and Section 5 of this guidance for more information.

Refer to Flowchart 3 for an overview on the workflow.

Flowchart 3: Workflow for Product Registration Applications Submitted for Closed-System IVD Analyser Not Listed on SMDR in a **SPLIT** IVD Analyser Device Listing.



4.3. Product Registration Applications with Closed-System IVD Analyser(s) Currently Listed on SMDR in their own Analyser Device Listing(s)

If the product registration application includes an analyser that is already listed in a **SPLIT** IVD analyser device listing,

- The analyser shall be excluded from Annex 2 List of Configurations
- The analyser's relevant supporting documents need not be submitted

(A) When there are no changes to analyser specifications (inclusive of analyser software), labels and user manual as compared to the registered IVD analyser:

- Registrants are to submit a declaration for registered IVD analysers in SPLIT IVD analyser device listings (Refer to Annex 1 for the declaration template)
- Registrants are to submit a Change Notification for the affected analyser device listing to update the list of registered reagents that are compatible and intended for use with the listed analyser (Refer to Annex 2 for tabulation of the list)

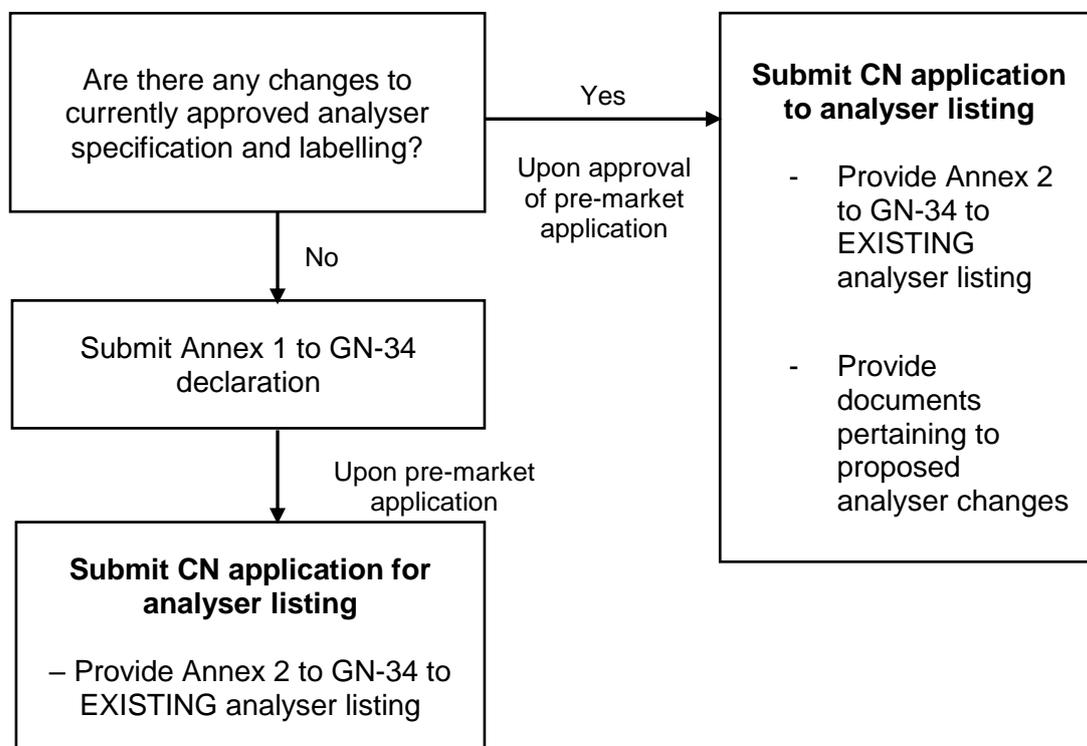
(B) When there are changes to the currently-approved analyser specifications (inclusive of analyser software), labels and user manual:

- Registrants are to submit a Change Notification for the affected analyser device listing to update the list of registered reagents that are compatible and intended for use with the listed analyser (Refer to Annex 2 for tabulation of the list)
- Registrants are to submit the proposed changes made to the registered analyser in the IVD analyser listing.

Please refer to Section 5 of this guidance and GN-21 Guidance on Change Notification for Registered Medical Devices for more information on Change Notification.

Refer to Flowchart 4 for an overview on the workflow.

Flowchart 4: Workflow for Product Registration Applications Submitted for Closed-System IVD Analysers Currently Listed on SMDR in their own Analyser Device Listing(s)



5. CHANGE NOTIFICATION APPLICATIONS

Changes described in this section are intended to complement change categories in GN-21 Guidance on Change Notification for Registered Medical Devices.

5.1. Addition of Analyser to a Device Listing

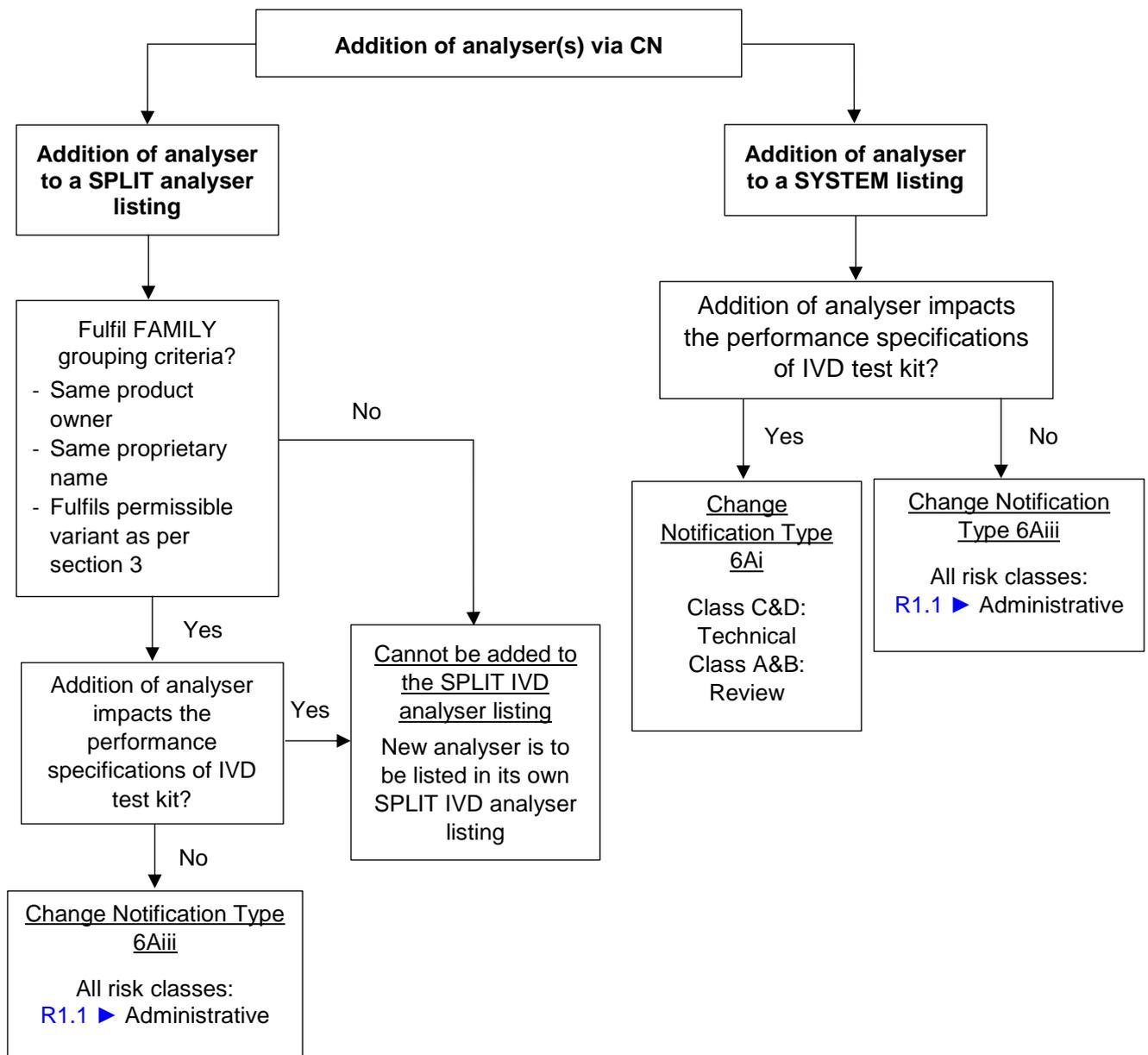
IVD analysers which are determined to be of risk class other than Class A, will no longer qualify under change type 6Aiv – ‘Unless changes only involve the addition of Class A medical device accessories that complement the registered medical device as a closed system’ for the addition of IVD analysers to either the **SYSTEM** or **SPLIT** IVD analyser listing.

For addition of analysers to an IVD **SYSTEM** listing and where the addition of the new IVD analyser does not impact the performance specifications of its compatible IVD reagents, change type 6Aiii [Unless change involves an addition of new device or software identifier with no change to the performance characteristics or specifications of the device] will be applicable. Otherwise, change type 6Ai – [Addition of new medical devices to device listing] will be applicable.

New analysers to be added to a **SPLIT** IVD analyser listing must fulfil the FAMILY grouping criteria highlighted in Section 3 of this guidance. Where the addition of the new IVD analyser does not impact the performance specifications of its compatible IVD reagents, change type 6Aiii [Unless change involves an addition of new device or software identifier with no change to the performance characteristics or specifications of the device] will be applicable. Otherwise, the analyser(s) will have to be listed separately.

Refer to Flowchart 5 for an overview workflow applicable to Change Notification types for the addition of analysers to a **SPLIT** IVD analyser device listing.

Flowchart 5: Workflow for Applicable Change Notification Types for the Addition of Analyser to **SPLIT** IVD Analyser or IVD SYSTEM Listing

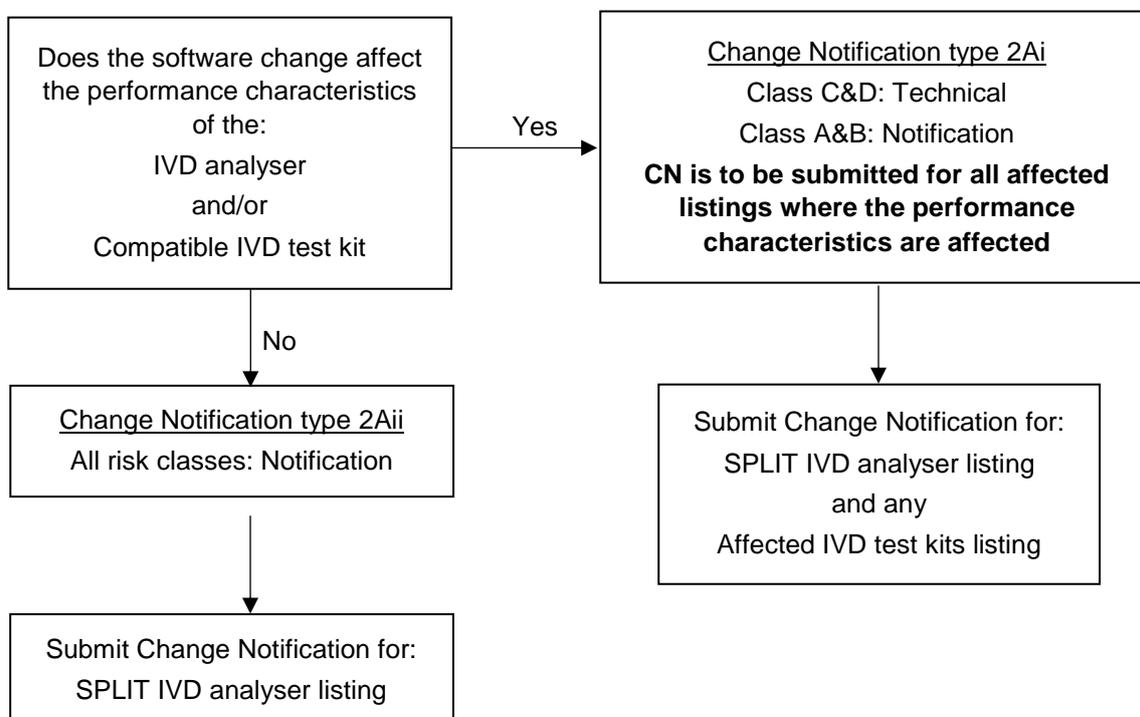


5.2. Changes to Software of IVD Analysers in **SPLIT** IVD Analyser Listings

Changes to the software of IVD analysers that are listed in a **SPLIT** IVD analyser listing will require a Change Notification application. The change category will depend on whether there are any changes to the performance specifications of the IVD analyser.

Where the changes to the software of the IVD analyser also impact the performance characteristics of the compatible IVD reagents that are listed separately from the analyser, Change Notification will have to be submitted for the affected IVD reagent listings as well. Refer to Flowchart 6 for the applicable change categories.

Flowchart 6: Workflow for Applicable Change Notification Categories for Changes to Software of IVD Analysers in **SPLIT** Analyser Listings



5.3. Changes to the List of Compatible IVD Reagent Kits for **SPLIT** IVD Analyser Device Listings

Change Notification submission for the **SPLIT** analyser listing is required when new IVD reagent kits compatible to the listed analyser are registered. The purpose of this Change Notification is to maintain the list of compatible IVD reagents to the IVD analyser listing. A Change Notification is to be submitted via change category 'Other Notification Changes (Verified by HSA prior to submission)'. Apart from required documents for Change Notification submission as indicated in GN-21 Guidance on Change Notification for Registered Medical Devices, Annex 2 to GN-34 is also to be submitted.

Where there are other changes to be made to the **SPLIT** analyser listing, other Change Notification categories as per GN-21 Guidance on Change Notification for Registered Medical Devices and Sections 5.1 and 5.2 of this guidance will apply.

6. SPLIT ANALYSER LISTING OPTION FOR REGISTERED IVD SYSTEMS ON THE SMDR

Note: *This section is only applicable to IVD systems registered on the SMDR before the **SPLIT** listing options for analysers and reagents were implemented (WEF 01/12/2017).*

Registrants that wish to opt for the **SPLIT** listing option for existing registered IVD systems, comprising of IVD analysers and their compatible reagents listed together on the SMDR, can do so via Change Notification.

When the proposed changes consist **solely** of filing for the SPLIT listing option, registrants may submit Change Notification under the Change Notification type of 'Other Notification Changes'. Where the changes are identical (i.e. the same analyser/ analysers to be removed from the IVD system listings), companies can group the affected device listings of the same risk class together in one application.

In the Change Notification application filed for the SPLIT listing option, registrants will need to update the model information of all affected device listings to remove the analysers and proceed to create new device listings for the analysers. Only analysers that meet the 'FAMILY' grouping criteria in GN-12-1 Guidance on Grouping of Medical Devices and contains permissible variants in Section 3 of this guidance will be permitted to be listed under one device listing. Analyser accessories such as consumables and bulk solutions may be listed together with their compatible analysers in the analyser device listings.

Registrants are to provide the following for Change Notification submission:

- Annex 2 to GN-34
- Confirmation of the software version and device labelling (inclusive of user manual) intended for import and supply
- Master copy of Annex 2 List of Configurations specifying the models to be removed from the affected device listings and which are to be added to the new **SPLIT** analyser device listings created.

Note: For the other applicable Change Notification documents, please refer to GN-21 Guidance on Change Notification for Registered Medical Devices for more information.

ANNEX 1**Declaration for Registered IVD Analysers in SPLIT IVD Analyser Device Listing(s) Template***[To be printed on Company Letterhead of Applicant]*

Medical Devices Branch
 Medical Devices Cluster
 Health Products Regulation Group
 Health Sciences Authority

[Date]

Dear Sir/Madam,

[Name of Company], the Applicant for registration of the medical device(s) stated below, hereby declare that:

The compatible analyser(s) for the medical device(s) in this application is as per indicated in Table 1: List of Compatible Analyser(s).

Table 1: List of Compatible Analyser(s)

Name of analyser (as per device labelling)	Software version	Device Registration Number

There are no changes to the currently approved compatible analyser(s) specifications, including the analyser software versions, labels and user manuals.

A change notification application shall be submitted for the affected analyser device listing(s) upon approval of this pre-market application to update the list of registered compatible reagents with the analyser.

This declaration shall apply to the following medical device(s):

[List containing product names of IVD reagents/ assays]

I, the Applicant, am aware that making a declaration which I know to be false is an offence under Section 30(10) of the Health Products Act (Cap. 122D) and may result in the cancellation of registration of the above medical devices under Section 37(1) of the Act.

Yours Sincerely,

[Signature]

[Full Name and Title of Senior Company Official]

[Name and address of company]

ANNEX 2

**List of Compatible Reagents with Analysers in SPLIT IVD Analyser
Device Listings Template****Compilation of Compatible Reagents with <Name of Analyser>**

Analyser identifier: <indicate identifier of analyser>

Software version(s): <indicate currently-approved software version i.e.
X.XX.XX>

Date of addition (DD/MM/YYYY)	Date of removal (DD/MM/YY) <if applicable>	Name of Reagents (as per device labelling)	Singapore Medical Device Registration (SMDR) number
<i>Example:</i>			
<i>07/05/2017</i>		<i>XYZ reagent</i>	<i>DE1234567</i>

HEALTH SCIENCES AUTHORITY

Health Products Regulation Group
Blood Services Group
Applied Sciences Group

www.hsa.gov.sg

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