WHO GLOBAL BENCHMARKING TOOL PLUS MEDICAL DEVICES (GBT+Medical Devices) FOR EVALUATION OF NATIONAL REGULATORY SYSTEM OF MEDICAL PRODUCTS

REGISTRATION AND MARKETING AUTHORIZATION (MA): INDICATORS AND FACT SHEETS

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World Health Organization

Function:	**02- REGISTRATION AND MARKETING AUTHORIZATION (MA)**
Description:	The issuance of marketing authorizations (also referred to as product licensing or registration) is critical to any National Regulatory Authority (NRA). Marketing authorization (MA) refers to a procedure for approval of a medical product for marketing after it has undergone a process of evaluation to determine the safety, efficacy/performance and quality of the product and the appropriateness of the product information. The objective of this regulatory function is to provide a system which ensures that only medical products which have been duly authorized by the NRA are allowed to be manufactured, imported, distributed, sold or supplied to end-users. The process of assessment for MA includes the review of data on quality, safety and efficacy/performance submitted by the applicant. The same standards should be applied to imported and locally manufactured medical products. Nevertheless, the evaluation of the complex data used to support marketing authorization of new or novel medical products may require specialized resources and experience not available in the NRA; therefore, countries with limited resources may wish to give priority to well-established products. In the evaluation of products, evidence of Good Manufacturing Practices (GMP) inspections or Quality Management System (QMS) audits or certifications should be part of the MA requirements. For IVDs, an independent performance evaluation may also be part of the MA requirements. The NRA may elect to prepare its own report, rely on evaluation reports prepared by other national authorities, recognize decisions made by another NRA, or use a combination of these approaches. A legal provision should exist that allows the NRA to grant MA of either unlimited or limited duration. In the earlier case, measures should be in place to ensure continued adherence of the medical product to quality, safety, and efficacy/performance standards (e.g. through a vigilance system). The MA should be renewed at a predefined time interval. For MA of limited duration, a vigilance system should also be in place. Mechanisms should exist to ensure that information on MA applications, including authorized, suspended, rejected or completed applications, is published, according to applicable laws and regulations, to promote transparency and information sharing among stakeholders. Regular publication of MA decisions is helpful to procurement and distribution networks and to other NRAs. Mechanisms and procedures should be in place to monitor and ensure that all activities within the MA function are checked to reduce errors and to reasonably ensure that the processes are consistent and will provide assurance of high quality outputs. Such approaches would lead to consistency in the performance of the MA regulatory function and to reliability of the regulatory outputs. For medical devices, including in-vitro diagnostics, notification or listing of low risk products is also covered by this function. If Conformity Assessment Bodies (CABs) are involved in registration and marketing authorization, NRAs need to establish clear and transparent regulations/procedure on selection and designation of CABs. In this case the assessor should assess and evaluate the NRA's oversight of the CABs, not the CABs themselves.

Indicator:	**MA01 Legal provisions, regulations and guidelines required to define regulatory framework of registration and/or marketing authorization.**
Objective:	The objective of this indicator is to ensure the existence of the legal provisions, regulations and guidelines which form the backbone of the regulatory framework. Such mandates will support the MA function by ensuring that medical products for human use in a particular jurisdiction have been assessed by an NRA and found to be of adequate quality, safety and efficacy/performance before being registered or granted MA and placed in the market. The legal provisions empower the NRA with the legal mandate to register and grant MA and also to penalize those who market medical products without the proper health registration or MA. For medical devices including in-vitro diagnostics, the legal provisions, regulations and guidelines should also support notification or listing of low risk products.
Category:	Legal provisions, regulations and guidelines
Sub Indicator:	**MA01.01: There are legal provisions that require the receipt of a registration or marketing authorization (MA) before placing the product on the market.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines 3. Plasma Derived Medicinal Products (PDMPs) 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that legal provisions requiring registration or MA before placing a medical product on the market exist and are enacted and implemented. Listing of marketed products could be an option for some medical products namely MD including IVDs . The legal provision s should clearly mandate that all medical products require registration or MA before they are placed on the market. These provisions should provide a list of medical product classes that require registration or MA before they are marketed or sold and also those medical devices including IVDs that require listing by the NRA. The legal provisions should specify the applicable fines, charges, penalties, or sanctions in the event of non-compliance. The assessor should note that some medical products may be imported and marketed before registration or MA in special circumstances such as during an emergency or in response to an urgent public health concern. The National Regulatory Authority

	(NRA) should have systems in place for the active monitoring of such medical products. The assessor may refer to the legal provisions related to emergency situations before applying the scoring.
Objective:	The objective of this sub-indicator is to ensure legal provisions, that require that a medical product must have been registered or granted MA or listed by the NRA before it is marketed or placed on the market, are in place and have been implemented.
Requirement:	Legal provisions for medical product registration, MA or listing.
Evidence to review:	The assessor should ask for and review: 1) Legal provisions that mandate that all medical products require registration, MA, listing or notification before they are placed on the market. 2) Evidence that the applicable fines, charges, penalties, and sanctions in the event of non-compliance are specified. 3) Evidence that the legal provisions have been published and implemented; 4) Evidence that registrations, MA, listing or notification have been issued. Note that this evidence may be the registration or MA numbers or the registration or MA certificates or listing databases.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 6. Principles of Conformity Assessment for Medical Devices, GHTF/SG1/N78:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical-devices-121102.pdf#search=%22declaration%20of%20conformity%22 8. Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices, Global Harmonization Task Force, GHTF/SG1/N046:2008 , (http://www.imdrf.org/docs/ghtf/final/sg1/procedural-docs/ghtf-sg1-n046-2008-principles-of-ca-for-ivd-medical-devices-080731.pdf#search=%22conformity%20assessment%22) 9. Registration of Manufacturers and other Parties and Listing of Medical Devices. GHTF/SG1/N065:2010 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n065-listing-of-medical-devices-100827.pdf

Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of legal provisions to hold a registration, MA, listing or notification before placing the product on the market. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted legal provisions to hold a registration, MA, listing or notification but it has not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions to hold a registration, MA, listing or notification and has been applying it for less than two years. ⇒ IMPLEMENTED (I): The NRA has legal provisions to hold a registration, MA, listing or notification before placing a product on the market and can demonstrate a proven track record of applying them.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.02: There are legal provisions that require the NRA to withhold, suspend, withdraw or cancel an MA if there are concerns regarding quality, safety or efficacy issues.**
ML	1
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that legal provisions are in place that address the withholding, suspending, withdrawing or cancelling of a registration or MA or de-listing in the event that quality, safety or efficacy/performance issues are uncovered. Such legal provisions should be enacted and implemented. The legal provisions should also specify requirements on when and how to withhold, suspend, withdraw or cancel a registration or MA or listing.

Objective:	The objective of this sub-indicator is to ensure that legal provisions exist mandating the NRA to withhold, suspend, withdraw or cancel registration or MA or listing in the event of adverse findings related to the quality, safety or efficacy/performance of medical products. The NRA is empowered by legal provisions to withhold, suspend, withdraw or cancel a registration or MA if the requirements set forth for registration or MA or de-listing are no longer being met. Details on reasons for these decisions should be notified to MA holders. These legal provisions should provide for the sanctioning of those who market medical products without the proper registration, MA, listing or notification.
Requirement:	Legal provisions on withholding, suspending, withdrawing or cancelling an MA or listing
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that mandate the NRA to withhold, suspend, withdraw or cancel a registration or MA or listing in the event of adverse findings related to the quality, safety and efficacy/performance of the medical products. 2. Regulations and guidelines presenting details on when and how to withhold, suspend, withdraw or cancel registration or MA or listing, 3. Evidence that the legal provisions have been implemented, and if possible, examples of implementation. 4. Evidence that stakeholders (e.g., applicants, wholesalers, and retailers) are aware of the legal provisions.
References:	1. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. Geneva. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822) (2) (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 2. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 6. Principles of Conformity Assessment for Medical Devices, GHTF/SG1/N78:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical-devices-121102.pdf#search=%22declaration%20of%20conformity%22 7. Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices, Global Harmonization Task Force, GHTF/SG1/N046:2008 , (http://www.imdrf.org/docs/ghtf/final/sg1/procedural-docs/ghtf-sg1-n046-2008-principles-of-ca-for-ivd-medical-devices-080731.pdf#search=%22conformity%20assessment%22)9. Registration of Manufacturers and other Parties and Listing of Medical Devices. GHTF/SG1/N065:2010 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n065-listing-of-medical-devices-100827.pdf

Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of legal provisions to withhold, suspend, withdraw or cancel a MA or listing in case there are concerns on quality, safety or efficacy/performance issues. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted the legal provisions to withhold, suspend, withdraw or cancel a MA or listing in case there are concerns on quality, safety or efficacy/performance issues, but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions to withhold, suspend, withdraw or cancel a MA or listing in case there are concerns on quality, safety or efficacy/performance issues and has been applying them for less than two years. ⇒ IMPLEMENTED (I): The NRA has legal provisions to withhold, suspend, withdraw or cancel a MA or listing in case there are concerns on quality, safety or efficacy/performance issues and can demonstrate proven track record of applying them
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.03: There are legal provisions that require a medical device, including in-vitro diagnostics to comply with essential principles of safety and performance for their intended purpose prior to marketing authorization.**
Maturity Level:	1
Scope:	Medical devices including in-vitro diagnostics (IVDs)
Description:	Legal provisions or Legislation should define the Essential Principles of Safety and Performance (EPSPs) for medical devices including IVDs for all risk classes. The EPSPs are general requirements that are applicable for all medical devices including IVDs, covering all applicable aspects for medical devices including IVDs.
Objective:	The objective of this sub-indicator is to ensure legal provisions are in place that require that medical devices including IVDs must comply with essential principles of safety and performance for their intended purpose prior to marketing authorization.
Requirement:	Legal provisions for medical devices including IVDs to comply with essential principles of safety and performance for their intended purpose prior to marketing authorization

Evidence to review:	The assessor should request for and review: 1. Legal provisions that mandate that all medical devices including IVDs comply with essential principles of safety and performance for their intended purpose prior to marketing authorization; 2. Evidence that the legal provisions have been published and implemented; 3. Evidence that the legal provisions are applicable to all risk classes of medical devices including IVDs; 4. Evidence that marketing authorizations have been issued (e.g., Number or certificates of the issued MA).
References:	1. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 2. Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices, IMDRF/GRRP WG/N47 FINAL 2018 http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grrp-essential-principles-n47.pdf 3. Principles of Medical Devices Classification. GHTF/SN77:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n77-2012-principles-medical-devices-classification-121102.pdf 4. Principles of Conformity Assessment for Medical Devices, GHTF/SG1/N78:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical-devices-121102.pdf#search=%22declaration%20of%20conformity%22 5. Principles of In Vitro Diagnostic (IVD) Medical Devices Classification, International Medical Device Regulators Forum, IMDRF/IVD WG/N64FINAL:2021, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-wng64.pdf) 6. Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices, Global Harmonization Task Force, GHTF/SG1/N046:2008 , (http://www.imdrf.org/docs/ghtf/final/sg1/procedural-docs/ghtf-sg1-n046-2008-principles-of-ca-for-ivd-medical-devices-080731.pdf#search=%22conformity%20assessment%22) 7. Registration of Manufacturers and other Parties and Listing of Medical Devices. GHTF/SG1/N065:2010 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n065-listing-of-medical-devices-100827.pdf
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of legal provisions for all medical devices including IVDs to comply with essential principles of safety and performance for their intended purpose prior to marketing authorization ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted legal provisions to for all medical devices including IVDs comply with essential principles of safety and performance for their intended purpose prior to marketing authorization. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions for all medical devices including IVDs comply with essential principles of safety and performance for their intended purpose prior to marketing authorization

	⇒ IMPLEMENTED (I): The NRA has legal provisions for all medical devices including IVDS comply with essential principles of safety and performance for their intended purpose prior to marketing authorization and can demonstrate a proven track record of applying them.
Limitations and remarks:	▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.04: There are legal provisions or regulations limiting the duration of the validity of the MA and requiring periodic reviews of MAs (i.e. renewals)**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that legal provisions or regulations specifying the validity period for registrations or MAs (and their renewals) exist and be enacted and implemented. The legal provisions or regulations should mandate the NRA to register or grant MA with limited validity and also require that the registration or MA be renewed before the medical product is re-introduced onto the market. The legal provisions and regulations should specify the appropriate validity periods of the initial registration or MA and subsequent renewals of registration or MA. The legal provisions also should provide information on the requirements for renewing the registrations or MAs. Ideally, the validity period for MA should not be more than five years.
Objective:	The objective of this sub-indicator is to ensure that legal provisions or regulations exist that mandate the NRA to list, register or grant MA with limited duration and that require the listing, registration or MA to be renewed for the medical product to remain on the market.
Requirement:	Listing, registration or MA validity period and listing, registration or MA renewal
Evidence to review:	The assessor should ask for and review: 1. Legal provisions or regulations that mandate the NRA to list, register or grant MA with limited validity and that require the listing, registration or MA to be renewed before the medical product is re-introduced onto the market 2. Legal provisions or regulations that specify the validity periods for the initial listing, registration or MA and subsequent registration or MA

	renewals. 3. Regulations and guidelines that provide the requirements for renewing listings, registrations or MAs.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 3. Principles of Conformity Assessment for Medical Devices, GHTF/SG1/N78:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical-devices-121102.pdf#search=%22declaration%20of%20conformity%22 4. Principles of In Vitro Diagnostic (IVD) Medical Devices Classification, International Medical Device Regulators Forum, IMDRF/IVD WG/N64FINAL:2021, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-wng64.pdf) 5. Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices, Global Harmonization Task Force, GHTF/SG1/N046:2008, (http://www.imdrf.org/docs/ghtf/final/sg1/procedural-docs/ghtf-sg1-n046-2008-principles-of-ca-for-ivd-medical-devices-080731.pdf#search=%22conformity%20assessment%22) 6. Registration of Manufacturers and other Parties and Listing of Medical Devices. GHTF/SG1/N065:2010 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n065-listing-of-medical-devices-100827.pdf
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no legal provisions or regulations regarding the limited duration of the validity of the MA and for periodic reviews to MAs ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted legal provisions or regulations regarding the limited duration of the validity of the MA and for periodic reviews to MAs, but they have not yet been implemented. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions or regulations regarding the limited duration of the validity of the MA and for periodic reviews to MAs and has been applying them for less than two years. ⇒ IMPLEMENTED (I): The NRA has legal provisions or regulations regarding the limited duration of the validity of the MA and for periodic reviews to MAs and can demonstrate a proven track record of applying them.

Limitations and remarks:	The assessor should note that some NRAs have regulations that mandate them to grant a "One Time" registration to a medical product. In this case, the assessor should review alternative approaches replacing renewal (e.g., continuous monitoring of the product risk benefit balance through vigilance and marketing surveillance activities). This review should be performed in coordination with assessors of other regulatory functions (e.g., vigilance [VL] function, market control and surveillance [MC] and regulatory inspection [RI] functions). If the aforementioned review is satisfactory, the scoring of this sub-indicator should be "Not Applicable".
Sub Indicator:	**MA01.05: There are regulations or guidelines for the definitions, types and the scope of variations along with the required documentation for these variations**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that the regulations or guidelines with respect to the definitions, types and the scope of variations/changes as well as the documentation requirements and procedures for these variations/changes exist and be enacted and implemented. The regulations or guidelines should provide details of the corresponding documentation requirements for each type or class of variation/changes as well as guidance on the scope of evaluation required. Ideally, these guidelines should follow international best practices such as those from World Health Organization (WHO) or International Council on Harmonization (ICH).
Objective:	The objective of this sub-indicator is to ensure that regulations or guidelines exist to provide definitions, types and the scope of variations/changes , as well as documentation requirements and procedures for each variation/change. Scientific and technological advancements or new developments and approaches that may affect the requirements that permitted the original product registration or MA should be communicated to the NRA in support to the variation or post-approval changes application.
Requirement:	Regulations/ guidelines on variations/changes
Evidence to review:	The assessor should ask for and review: 1. Regulations or guidelines that document the definitions, types and scope of variations/changes, as well as the corresponding documentation requirements and procedures.

	2. Evidence that the regulations or guidelines are published, easily accessible, implemented and known to the applicant, and that these regulations and guidelines effectively communicate requirements and procedures. 3. Examples of the types of variations/changes documented and the scope of evaluations required. 4. Documentation supporting the appropriateness of the corresponding fees (if any). 5. Processes, procedures and applicable timelines for submitting variations/changes to the NRA for review and for receiving feedback
References:	1. Procedure for Assessing the Acceptability, in Principle, of Vaccines for Purchase by United Nations Agencies, (77), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 2. Collaborative procedure between the World Health Organization (WHO) Prequalification Team and interested national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines, (56), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 3. Guidelines on procedures and data requirements for changes to approved vaccines, (50), (http://apps.who.int/medicinedocs/en and https://www.who.int/biologicals/vaccines/en/) 4. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 5. Regulation (EU) 2017/745 on medical devices https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02017R0745-20200424&qid=1598541546872&from=EN6. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 6. INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE, ICH HARMONISED GUIDELINE TECHNICAL AND REGULATORY CONSIDERATIONS FOR PHARMACEUTICAL PRODUCT LIFECYCLE MANAGEMENT Q12, 20 November 2019 7. REPORTABLE CHANGES TO A WHO PREQUALIFIED IN VITRO DIAGNOSTIC MEDICAL DEVICE, WHO 2016, https://apps.who.int/iris/bitstream/handle/10665/251915/WHO-EMP-RHT-PQT-2016.01-eng.pdf;jsessionid=830C82950055325AF37A0A8302BE4623?sequence=1
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no regulations or guidelines for the definitions, types and the scope of variations/changes along with the required documentation and procedures.

	⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted regulations or guidelines for the definitions, types and the scope of variations/changes along with the required documentation and procedures but they have not yet been implemented. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has regulations or guidelines for the definitions, types and the scope of variations/changes along with the required documentation and procedures and has been applying them for less than two years. ⇒ IMPLEMENTED (I): The NRA has regulations or guidelines for the definitions, types and the scope of variations/changes along with the required documentation and procedures and required evidence of implementation.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.06: There are legal provisions to cover circumstances under which the routine MA procedures may not be followed (e.g., for public health interest)**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that legal provisions, which describe the circumstances under which the routine medical product registration, MA or listing procedures may not be followed, exist and be enacted and implemented. The legal provisions should clearly describe the instances or situations when the normal or routine procedures should not be applied. The legal provisions also should provide guidance on the scope of evaluation and on the documentation required in the event that the non- routine approach is used for registration, MA or listing. In addition, if the conditional authorization is time limited, the assessor should verify that the duration of validity is defined in this regulation.
Objective:	The objective of this sub-indicator is to ensure that legal provisions exist to allow the NRA to use a non-routine approach or procedure for registration or MA of medical products under exceptional circumstances in the interest of public health (e.g. emergencies or epidemics).
Requirement:	Exemptions to routine MA or listing procedures

Evidence to review:	The assessor should ask for and review: 1. Legal provisions that define circumstances or instances under which derogation of the routine MA or listing procedures may be applied. 2. Regulations or guidelines that give clarity on the regulatory requirements for granting MA or listing to medical products through a route other than the routine MA or listing procedure. 3. Records of medical products, if any, that have been authorized by this route.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. WHO Emergency response framework, second edition. Geneva. World Health Organization, 2017 (140) (http://apps.who.int/iris/bitstream/handle/10665/258604/9789241512299-eng.pdf?sequence=1) 3. Emergency Use Assessment and Listing Procedure (EUAL) for Candidate Medicines for Use in the Context of a Public Health Emergency, (121), (http://apps.who.int/medicinedocs/en/) 4. Emergency Use Assessment and Listing Procedure (EUAL) for Candidate Vaccines for Use in the Context of a Public Health Emergency, (122), (http://apps.who.int/medicinedocs/en/) 5. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 6. WHO Emergency use listing. https://www.who.int/teams/regulation-prequalification/eul/
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no legal provisions to cover circumstances in which routine MA or listing procedures are exempted ⇒ ONGOING IMPLEMENTATION (OI): There are draft legal provisions to cover circumstances in which routine MA or listing procedures are exempted ⇒ PARTIALLY IMPLEMENTED (PI): There are recently established legal provisions (less than two years) to cover circumstances in which routine MA or listing procedures are exempted. ⇒ IMPLEMENTED (I): There are well-established (for more than two years) legal provisions to cover circumstances in which routine MA or listing procedures are exempted
Limitations and remarks:	▪ It is proposed that the NRA should establish a provision to clarify the role and responsibilities of all involved stakeholders who are involved in the emergency. The establishment of an advisory committee is suggested to make decisions and to share the responsibilities during an emergency situation.

	▪ Non-routine MA or listing procedures are those applicable only under specific circumstances (e.g., emergencies with public health impact) and aimed at reducing the time needed for registration or granting MA or listing. The terminology may vary according to the national legislation. Examples of such procedures include different types of collaborative and facilitated registration and MA procedures (e.g., WHO collaborative procedure or stringent regulatory authority facilitated registration procedure). The collaborative procedure is a procedure for collaboration between the WHO Prequalification Team and interested national regulatory authorities for the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.07: There are legal provisions or regulations that define regulatory requirements to approve donation of medical products.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that legal provisions or regulations, which define the circumstances under which medical products can be received through donation, exist and are implemented. The legal provisions should provide guidance regarding required information and documentation that should be reviewed before approval of donated medical products. The provisions should also provide guidance on the scope of evaluation as well as the documentation required to show quality, safety and efficacy/performance of donated medical products.
Objective:	The objective of this sub-indicator is to ensure that legal provisions or regulations exist and are implemented to mandate the NRA to have adequate regulatory oversight on medical products received through donation.
Requirement:	MA procedures for donated medical products
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that mandate the NRA to have adequate regulatory oversight on medical products received through donation. 2. Regulations or guidelines giving clarity on the regulatory requirements for use of medical products that are received through donation. 3. Supporting records for any application of these provisions.

References:	1. GPV Policy statement. Vaccine donations. Geneva. World Health Organization (WHO/VSQ/97.03), (111), (https://www.who.int/immunization/hpv/plan/who_unicef_joint_statement_on_vaccine_donations_who_unicef_2011.pdf) 2. Guidelines for Medicine Donations - Revised 2010. (First Edition 1996, Second Edition 1999, Third Edition 2011), (141), (http://apps.who.int/medicinedocs/en/) 3. Improvements for International Medicine Donations: a Review of the World Health Organization Guidelines for Medicine Donations, 3rd Edition, (142), (http://apps.who.int/medicinedocs/en/) 4. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 5. Medical device donations: considerations for solicitation and provision; https://apps.who.int/iris/bitstream/handle/10665/44568/9789241501408_eng.pdf;jsessionid=25B2AC9145E4EEF29BA106992E2550D5?sequence=1
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence for existence of legal provisions or regulations that define regulatory requirements for use of donated medical products ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these legal provisions or regulations but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has these legal provisions and has been applying them for less than two years. ⇒ IMPLEMENTED (I): The NRA has legal provisions or regulations that define the regulatory requirements for use of donated medical products and these have been applied for all medical products received through donation.
Limitations and remarks:	In exceptional cases in the interest of public health (e.g., emergencies or epidemics), use of a non-routine approach or procedure should be considered to permit use of a donated medical product or to grant MA to a donated medical product. If the NRA uses the same regulatory approach for review of donated products as it uses for review of other medical products , this sub indicator can score as not applicable.
Sub Indicator:	**MA01.08: Legal provisions or regulations allow the NRA to recognize and/or rely on MA-relevant decisions, reports or information from other NRAs or regional and international bodies**

Maturity Level:	1
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that the legal provisions or regulations allowing the NRAs to recognize and/or use relevant MA or listing decisions, reports or information from other NRAs or regional and international bodies should exist and be enacted and implemented. The legal provisions or regulations should provide clarity on the modalities, processes and procedures to employ to recognize and/or use relevant MA or listing decisions, reports or information from other NRAs or regional and international bodies. The legal provisions also should provide clarity on the conditions (i.e., when and how) under which it is acceptable to recognize and/or use relevant MA or listing decisions, reports or information from other NRAs, or regional and international bodies. The legal provisions or regulations should also provide clear directives on the scope or extent of recognition and/or use of MA or listing decisions, reports or information from other NRAs, or regional and international bodies (e.g., WHO prequalification).
Objective:	The objective of this sub-indicator is to verify that legal provisions or regulations exist to allow the NRA to establish a systematic framework to recognize and/or use relevant MA decisions, reports or information from other NRAs, or regional and international bodies.
Requirement:	Recognition of and/or reliance on MA application decisions and information from other NRAs, or regional and international bodies
Evidence to review:	The assessor should ask for and review: 1. Legal provisions including guidelines that permit the NRA to recognize and/or use relevant MA or listing decisions, reports or information from other NRAs or regional and international bodies 2. Documentation defining the scope and extent of recognition and /or use of relevant MA or listing decisions, reports or information from other NRAs, or regional and international bodies. 3. Documentation providing examples of instances or situations that have permitted recognition and/or use of relevant MA or listing decisions, reports or information from other NRAs or regional and international bodies 4. List of NRAs or regional and international bodies whose relevant decisions, reports or information may be used to influence a MA or listing application decision. 5. Evidence that the listed NRAs or regional and international bodies are aware that their relevant MA or listing decisions, reports or information may be used (i.e., aware of the legal provision).

References:	1. Good regulatory practices: guidelines for national regulatory authorities for medical products, (112), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO general guidance on variations to multisource pharmaceutical products, (143), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Guidelines on procedures and data requirements for changes to approved vaccines, (50), (http://apps.who.int/medicinedocs/en and https://www.who.int/biologicals/vaccines/en/) 4. Guidelines on procedures and data requirements for changes to approved biotherapeutic products, (144), (http://apps.who.int/medicinedocs/en/) 5. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 6. Good reliance practices in the regulation of medical products: high level principles and considerations. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 10 (WHO Technical Report Series, No. 1033), (https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations) 7. Regulatory collaboration. WHO Drug Information Vol. 30, No.4, 2016 https://www.who.int/medicines/publications/druginformation/WHO-DI_30-4_RegCollaboration.pdf
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence for existence of legal provisions or regulations that allow the NRA to recognize and/or use MA-relevant decisions, listings, reports or information from other NRAs or regional and international bodies ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these legal provisions or regulations but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has these legal provisions or regulations and has been applying them to some supported resources for less than two years. ⇒ IMPLEMENTED (I): The NRA has legal provisions or regulations allowing the NRA to recognize and/or use MA-relevant decisions, listings, reports or information from other NRAs or regional and international bodies and is able to provide evidence supporting implementation for a list of NRAs or regional and international bodies.

Limitations and remarks:	If the NRA has adequate resources, this sub indicator can be considered not applicable; however, the NRA should have the legal bases for any reliance that does exist.
Sub Indicator:	**MA01.09: Specific guidelines on the quality, nonclinical and clinical aspects are established and implemented**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that specific guidelines on quality, nonclinical, and clinical requirements (as well as guidelines for BE/BA studies in the case of multisource generic medicines) for registering or granting MA or listing should be established and implemented. The guidelines should be detailed and should provide the specific regulatory requirements for each section of the quality, nonclinical, and clinical dossier for medicines, vaccines and blood products. Similarly, for medical devices including IVDs detailed guidelines should be available on regulatory requirements for the technical documentation on safety and performance as well as benefit-risk evaluation using analytical, nonclinical and clinical data. The guidelines should be specific for the type of medical product. The specific guidelines may consist of documents that were not prepared by the NRA but instead were adopted in accordance with proper process (e.g., recognition of ISO standards for medical devices).
Objective:	The objective of this sub-indicator is to verify that specific guidelines exist on the quality, nonclinical and clinical/performance requirements for registering or granting MA, and to verify that they have been implemented.
Requirement:	Requirement on quality, nonclinical and clinical/performance aspects
Evidence to review:	The assessor should ask for and review: 1. Guidelines detailing the specific regulatory requirements for the quality, nonclinical and clinical aspects (as well as guidelines for bio-equivalence/bio availability studies in the case of multisource generic medicines) of the MA dossier. The requirements, including the content and format, should comply with updated international best practices such as those from WHO, ICH or IMDRF. 2. Evidence that the guidelines are specific for the quality, nonclinical, and clinical aspects of the MA or listing application dossier and for the type of application and medical product.

	3. For medical devices including IVDs detailed guidelines should be available on regulatory requirements for the technical documentation on safety and performance as well as benefit-risk evaluation using analytical, nonclinical and clinical data. 4. Evidence that the guidelines are published and implemented. 5. Examples of MA or listing application submissions that are in compliance with the published guidelines. 6. Evidence that documents submitted (see previous point) were appropriate for the type of product and type of application (e.g., new drug application, multisource drug, or product of biological origin or chemical synthesis). 7. Specific guidelines related to a. product labelling and packaging, b. package inserts, c. summary of product characteristics (SPC) information pamphlet for professionals or equivalent d. information pamphlet for patients. 8. Copies of all quality, safety, efficacy/performance reports for recently approved MA or listing applications to determine whether reviews were done thoroughly and based on guidelines requirements.
References:	1. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/) 2. Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology, (54), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 4. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 5. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. Geneva. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 6. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 7. Clinical Investigation, International Medical Device Regulators Forum, IMDRF MDCE WG/N56FINAL:2019 (formerly GHTF/SG5/N2R8:2007), http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-191010-mdce-n56.pdf 8. Clinical Evaluation, International Medical Device Regulators Forum, IMDRF MDCE WG/N57FINAL:2019 (formerly GHTF/SG5/N3:2010), http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-191010-mdce-n57.pdf

	9. Clinical Evidence - Key Definitions and Concepts, International Medical Device Regulators Forum, IMDRF MDCE WG/N55 FINAL:2019 (formerly GHTF/SG5/N1R8:2007), http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-191010-mdce-n55.pdf 10. Software as a Medical Device (SaMD): Clinical Evaluation, International Medical Device Regulators Forum, IMDRF/SaMD WG/N41FINAL:2017, http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170921-samd-n41-clinical-evaluation_1.pdf
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence for the existence of specific guidelines on the quality, nonclinical, and clinical/performance aspects. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these guidelines but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has these guidelines and has been applying them for less than two years. ⇒ IMPLEMENTED (I): The NRA has established and implemented specific guidelines on the quality, nonclinical, and clinical/performance aspects.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.10: There are guidelines on the format and content for submission of MA applications that are consistent with the WHO or other internationally accepted standards**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that guidelines on the format and content of a MA or listing submission exist and that they are consistent with international best practices, such as those proposed or recommended by WHO or other internationally established agencies such as ICH or

	IMDRF. The guidelines should provide clarity on the format and content on all sections of the MA or listing application submission and should provide specific guidance for each medical product stream. The guideline also should describe the processes and procedures for submitting the application to the NRA. Additionally, the guidelines should be established and implemented. For medical devices, the assessor should note that there is no such WHO guidelines on the format and content for submission of MA applications. Rather, other internationally accepted standard are available.
Objective:	The objective of this sub-indicator is to verify that guidelines exist for the format and content of a MA or listing application submitted to the NRA; these guidelines should consider the nature of products and the different medical product streams. The content and format of submitted applications should be consistent with the recommendations from the WHO (for medical devices, such WHO guidelines do not exist) or other internationally accepted agencies (such as IMDRF in the area of medical devices).
Requirement:	Format and content for MA or listing application
Evidence to review:	The assessor should ask for and review: 1. Guidelines providing clarity on the format and content of the MA or listing application submission, as well as the processes and procedures for submitting the application to the NRA or CAB. 2. Evidence that the guidelines are consistent with international best practices, such as those proposed by the WHO or other internationally accepted agencies. 3. Copies of the checklist used to ensure that MA or listing submissions actually comply with the content of the guidelines before a MA or listing application is acknowledged by the NRA.
References:	1. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology, (54), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 4. Open this document and view its content Guidelines on Submission of Documentation for a Multisource (Generic) Finished Product. General Format: Preparation of Product Dossiers in Common Technical Document Format, (65), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 5. Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part, (52), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 6. International Conference on Harmonization, ICH tripartite guidelines. The Common Technical document for registration of pharmaceuticals

for human use: quality. M4Q (R1). Quality overall summary of Module 2. Module 3: Quality; September 2002, (118), (https://www.ich.org/products/ctd/ctdsingle/article/m4qr1-quality.html)

7. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1

8. Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices, IMDRF/GRRP WG/N47 FINAL 2018 http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grrp-essential-principles-n47.pdf

9. Principles of Medical Devices Classification. GHTF/SN77:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n77-2012-principles-medical-devices-classification-121102.pdf

10. Principles of Conformity Assessment for Medical Devices, GHTF/SG1/N78:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical-devices-121102.pdf#search=%22declaration%20of%20conformity%22

11. Principles of In Vitro Diagnostic (IVD) Medical Devices Classification, International Medical Device Regulators Forum, IMDRF/IVD WG/N64FINAL:2021, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-wng64.pdf).

12. Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices, Global Harmonization Task Force, GHTF/SG1/N046:2008, (http://www.imdrf.org/docs/ghtf/final/sg1/procedural-docs/ghtf-sg1-n046-2008-principles-of-ca-for-ivd-medical-devices-080731.pdf#search=%22conformity%20assessment%22)

13. IMDRF/RPS WG/N13(Edition 3) FINAL:2019 In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC)

14. IMDRF/RPS WG/N9(Edition 3) FINAL:2019 Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVD MA ToC)

15. GHTF/SG1/N063:2011 Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices

16. Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVDMAToC), International Medical Device Regulators Forum, IMDRF/RPS WG/N9(Edition 3) FINAL:2019, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-190321-nivd-dma-toc-n9.pdf)

17. In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC), International Medical Device Regulators Forum, IMDRF/RPS WG/N13(Edition 2) FINAL:2019, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-190321-ivd-mdma-toc-n13.pdf)

18. Assembly and Technical Guide for IMDRF Table of Contents Submissions, International Medical Device Regulators Forum, IMDRF/RPS WG/N27 FINAL:2019, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-190124-assembly-technical-guide-toc-submissions-n27.pdf)

Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no guidelines for the format and content of submitted MA or listing applications. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently developed or drafted these guidelines, but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted these guidelines and has been applying them for less than two years, or these guidelines have not been applied for all marketed medical products. ⇒ IMPLEMENTED (I): The NRA has guidelines for the format and content of submitted MA or listing applications that are consistent with WHO or other internationally accepted standards and that specify required documentation. This process is implemented and followed for all marketed medical products.
Limitations and remarks:	▪ In case of benchmarking for more than one medical product stream, the assessor should consider and review different guidelines, as applicable. In some cases, instructions for dossier compilation may be part of the main (technical) guideline. ▪ For medical devices, the assessor should note that there is no such WHO guidelines on the format and content for submission of MA applications. Rather, other internationally accepted standard are available (please refer to the references section for examples including table of content TOC). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.11: There are guidelines for MA holders that define the types and scope of variations, the format and content to be used for documenting the variations, and the identification of those variations that require prior approval or notification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify the existence, enactment and implementation of guidelines for MA holders that provide guidance on the types and scope of variations/changes , the format and content to be used for documenting the variations/changes , and the identification of the

	variations/changes that require prior approval or notification. The guidelines should include directives on changes made to leaflets, package inserts, labelling (i.e., container and package), and SPCs. They should also clearly communicate to the MA holder the variations/changes that require NRA approval before implementation, those that require only notifying the NRA before or during implementation, and those that do not require notifying the NRA.
Objective:	The objective of this sub-indicator is to ensure that guidelines exist that provide information to MA holders on the types and scope of variations/changes , the format and the content to be used for documenting the variations/changes , and the identification of those variations/changes that require prior approval or notification.
Requirement:	Variation/changes documents for MA holders
Evidence to review:	The assessor should ask for and review: 1. Guidelines that provide guidance to MA holders on the types and scope of variations/changes, the format and content to be used for documenting the variations/changes, and the identification of those variations/changes that require prior approval or notification. The assessor should note that the guidelines should include changes to information contained in leaflets, package inserts, labelling (i.e., package and containers), and SPCs that have been previously approved. 2. Guidelines that communicate to the MA holder the variations/changes that require approval before implementation, those that require only notifying the NRA before or during implementation, and those that do not require notifying the NRA. The assessor should review examples of submitted and processed variation/changes applications and evaluate them for conformance to the guidelines.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. Guidelines on procedures and data requirements for changes to approved biotherapeutic products, (144), (http://apps.who.int/medicinedocs/en/) 4. WHO guidelines on variations to a prequalified product, (145), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 5. Guidelines on procedures and data requirements for changes to approved vaccines, (50), (http://apps.who.int/medicinedocs/en and https://www.who.int/biologicals/vaccines/en/)

	6. Regulation (EU) 2017/745 on medical devices https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02017R0745-20200424&qid=1598541546872&from=EN 7. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence for existence and implementation of guidelines for MA holders that define the types and scope of variations/changes, the format and the documentation required for each variation/changes, and the identification of the variations/changes that require prior approval. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently developed or drafted these guidelines, but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted these guidelines and has been applying them for less than two years or they have not been applied to all marketed medical products. ⇒ IMPLEMENTED (I): The NRA has guidelines for MA holders that define the types and scope of variations/changes, the format and the documentation required for each variation/change, and the identification of the variations/changes that require prior approval, and they have been implemented and documented for all marketed medical products
Limitations and remarks:	▪ In case of benchmarking of more than one medical product stream, the assessor should consider and review different guidelines as applicable. ▪ Variations may be referred to as “changes” or “post approval changes”. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.12: There are established guidelines that cover circumstances under which the routine MA procedures may not be followed (e.g., for public- health interest)**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines

	3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that guidelines that provide guidance to the NRA on how to manage MA or listing applications using a non-routine MA or listing application procedure during public health emergencies are established and implemented. The guidelines should provide guidance on the critical requirements that need to be reviewed by the NRA (e.g. label indication, mode of usage or application, storage conditions, and Good Manufacturing Practice (GMP) or Quality Management System (QMS) certificates and reports), and on the information that should be documented and monitored (e.g., location of deployment, quantities to be deployed, and identity of persons to receive and manage deployment) by the NRA before registration of the medical products. The guidelines should be supported with Standard Operating Procedures (SOPs) that provide guidance on the assessment and evaluation process and on the scope of evaluation needed. The assessor should verify that the NRA will have access to experts (e.g., advisory committees) to support the NRA during the decision-making process. Guidance on the application processing flow and corresponding timelines should be available.
Objective:	The objective of this sub-indicator is to ensure that guidelines exist to provide guidance to the NRA on how to process MA or listing applications using a non-routine MA or listing approach or procedure in exceptional cases and in the interest of public health (e.g. emergencies or epidemics).
Requirement:	Non-routine MA or listing procedures
Evidence to review:	The assessor should ask for and review: 1. Guidelines that provide guidance to the NRA on the application of a non-routine MA or listing procedure in emergency situations, as well as the corresponding SOPs or supporting documents. 2. A sample application that was processed using the guidelines. The assessor should verify that the information required by the guidelines was submitted and duly evaluated, and that the evaluation process flow and timelines were respected. 3. Evidence of access to experts or advisory committee in case of emergency
References:	1. Guidance on development and implementation of a national deployment and vaccination plan for pandemic influenza vaccines. Geneva: World Health Organization; 2012, (76), (http://apps.who.int/iris/bitstream/handle/10665/75246/9789241503990_eng.pdf?sequence=1) 2. WHO Emergency response framework, second edition. Geneva. World Health Organization, 2017, (140), (http://apps.who.int/iris/bitstream/handle/10665/258604/9789241512299-eng.pdf?sequence=1) 3. WHO Emergency use listing. https://www.who.int/teams/regulation-prequalification/eul/

	4. FDA Emergency Use Authorization of Medical Products and Related Authorities; Guidance for Industry and Other Stakeholders, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities 5. EUROPEAN COMMISSION COMMUNICATION FROM THE COMMISSION Guidelines on the adoption of Union-wide derogations for medical devices in accordance with Article 59 of Regulation (EU) 2017/745, 19-05-2020, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52020XC0519(01)&qid=1634549947867&from=EN
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no guidelines that cover circumstances under which the routine MA or listing procedures may not be followed. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently developed or drafted these guidelines but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or officially adopted these guidelines but has not been applied them to all medical products that were approved by non-routine regulatory procedures. ⇒ IMPLEMENTED (I): The NRA has guidelines that cover circumstances under which the routine MA or listing procedures may not be followed and has applied them for all medical products that have been approved under this condition.
Limitations and remarks:	• There is need to verify that these guidelines have been applied in emergency situations and that all relevant records are available. If there were not any emergency situations after development of the guidelines, the assessor should verify that all required resources are available. • Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.13: There are legal provisions that require a manufacturer to establish and maintain a quality management system**
Maturity Level:	1
Scope:	Medical devices including IVDs
Description:	A mandate represented by well-established and enforced legal provisions should require manufacturers to implement and maintain a quality management system for their operations in order to ensure that medical devices comply with the principles of safety and performance

	throughout the lifecycle of the device. In addition, the responsibilities and arrangements for the management of adverse events, recalls, the retention of records and the requirements for dealing with an initial assessment and subsequent surveillance assessment, and the assessment of variations or changes to the product design and the QMS are to be set out in legislation to clarify responsibility and to provide for enforcement actions. Manufacturers should also prepare all necessary documentation, including declaration of conformity, for their medical products, to fulfill the legal requirements.
Objective:	The objective of this sub-indicator is to ensure legal provisions are in place that require the manufacturer to produce and maintain evidence to a formally documented Quality Management System.
Requirement:	Legal provisions that require manufacturers of all classes of medical devices including IVDs to establish and maintain a Quality Management System including the requirements for all required legal documentation to be prepared.
Evidence to review:	The assessor should request for and review: 1. Legal provisions that mandate that all medical devices including IVDs require manufactures to establish and maintain a Quality Management System including the requirements for a declaration of conformity. The legal provisions should also specify the applicable fines, charges, penalties and sanctions in the event of non-compliance; 2. Evidence that the legal provisions have been published and implemented; 3. Evidence that the legal provisions are applicable to all risk classes of medical devices including IVDs; 4. Evidence that manufacturers submit proof of their Quality Management System (e.g. Declarations of Conformity, QMS certificates).
References:	1. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 2. Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices, IMDRF/GRRP WG/N47 FINAL 2018 http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grrp-essential-principles-n47.pdf 3. Medical devices Quality management systems. Requirements for regulatory purposes. ISO 13485:2016 https://www.iso.org/standard/59752.html 4. Medical devices Application of risk management to medical devices. ISO 14971:2019 https://www.iso.org/standard/72704.html 5. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Structure/Foundation/Input

Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of legal provisions defining and requiring the Quality Management System of the manufacturer and the Declaration of Conformity. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted legal provisions although they do not exist, demonstrable steps have been taken towards developing them. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions defining and requiring the Quality Management System of the manufacturer and the Declaration of Conformity but has not yet promulgated and enforced. ⇒ IMPLEMENTED (I): The NRA has legal provisions to defining and requiring the Quality Management System of the manufacturer and the Declaration of Conformity promulgated and enforced.
Limitations and remarks:	▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.14: A list of standards recognized by the NRA as a means to demonstrate compliance with the principles of safety and performance of medical devices is established.**
Maturity Level:	2
Scope:	Medical devices including IVDs
Description:	The NRA should establish a procedure to identify national versions of international standards which are recognized in their country and which manufacturers and economic operators (agents, representatives, importers) can use as proof to comply with requirements in the regulations.. The preferred, but optional, way by which the NRA may establish the in-country recognized standards is to apply voluntary international standards that are appropriate and relevant. The law shall include provisions allowing the regulatory authority to formally recognize such standards for that purpose. The other option, which may be too challenging, is for the NRA to establish its recognized standards by itself. In the latter case, the national standards should be aligned with the international ones. Preference for the recognition of standards shall be given to international standards, e.g. those of the International Organization for Standardization (ISO) and the International Electro-Technical Commission (IEC), regional standards and the national versions of international standards. It is also important that national standards correspond to the current version of international standards. As international standards are periodically revised, national standards will have to be revised accordingly and the authority shall establish a transition period for manufacturers to adopt the new versions. To maintain the necessary flexibility in utilizing standards, it is better to adopt a system of

	recognizing standards through guidance documents or guidelines than placing the standards into legislation; they can then be updated to stay current and can be revised much faster than legislation can be updated. The list of in-country recognized standards should be published and readily accessible to the relevant stakeholders including the public and should be regularly updated whenever needed.
Objective:	The objective of this sub-indicator is to provide for a documented mechanism to determining the suitability of international standards to demonstrate compliance with regulatory requirements. The list of recognized standards is regularly updated.
Requirement:	Legal provisions allowing the regulatory authority to formally recognize standards by which the manufacturer may demonstrate conformity with the principles of safety and performance.
Evidence to review:	The assessor should request for and review: 1. Legal provisions for a mechanism to formally recognize standards. The legal provisions include allowing the manufacturer to demonstrate conformity with the Essential Principles of safety and performance by means of these standards. 2. Evidence that the legal provisions have been published and implemented; 3. Evidence that the legal provisions are applicable to all risk classes of medical devices including IVDs; 4. Evidence that the list of recognized standards is updated and published.
References:	1. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 2. ISO. Geneva. International Organization for Standardization. https://www.iso.org/home.html 3. IMDRF Optimizing Standards for Regulatory Use. IMDRF/Standards WG/N51 Final:2018. http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181105-optimizing-standards-n51.pdfIMDRF/GRRP WG/N47 FINAL:2018 4. Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices, Proposed document: Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices (imdrf.org)
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of legal provisions allowing the regulatory authority to formally recognize standards by which the manufacturer may demonstrate conformity with the principles of safety and performance.

	⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted legal provisions although they do not exist, demonstrable steps have been taken towards developing them. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions and regulations that were recently developed as draft but not yet promulgated and implemented. ⇒ IMPLEMENTED (I): The NRA has legal provisions and regulations defining the use of recognized standards are promulgated and implemented.
Limitations and remarks:	▪ In a short time, it may not be possible for the assessor to review all aspects that this indicator includes. Preferably the country profile or other documents that provide a good description of the regulatory landscape in the country should be studied beforehand.
Sub Indicator:	**MA01.15: There are guidelines on labelling and instructions for use (IFU) of medical devices and in vitro diagnostics as part of MA application requirements.**
Maturity Level:	3
Scope:	Medical devices including IVDs
Description:	The assessor should verify the existence and implementation of guidelines that provide guidance on the MA application requirements with respect to the content of the labelling and instructions for use (IFU) of medical devices and IVDs.
Objective:	The objective of the sub-indicator is to establish whether guidelines exist to provide clarity on the MA application requirements on labelling and instructions for use (IFU) of medical devices including IVDs.
Requirement:	Guidance on labelling information and instructions for use (IFU) of medical device including in vitro diagnostics.
Evidence to review:	The assessor should request for and review the guidelines and /or regulations that provide guidance on the MA application requirements on labelling and instructions for use (IFU) of medical devices including in vitro diagnostics.
References:	• WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 • IMDRF/GRRP WG/N52 FINAL:2019 Principles of Labelling for Medical Devices and IVD Medical Devices , http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-190321-pl-md-ivd.pdf

	• Overview of the WHO prequalification of in vitro diagnostics assessment; https://apps.who.int/iris/bitstream/handle/10665/259403/WHO-EMP-RHT-PQT-2017.02-eng.pdf?sequence=1&isAllowed=y • IMDRF/GRRP WG/N47 FINAL:2018 Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grrp-essential-principles-n47.pdf
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no guidelines on the content of labelling information or instructions for use (IFU) of medical devices including IVDs ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these guidelines but they have not yet been followed ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted these guidelines and has been applying them for less than two years or has not fully followed them for all marketed medical devices including IVDs. ⇒ IMPLEMENTED (I): The NRA has guidelines on the labelling information and instructions for use (IFU) of medical devices including IVDs and they are followed for all marketed products.
Limitations and remarks:	▪ According to IMDRF, Labelling is defined as follows: The label, instructions for use, and any other information that is related to identification, technical description, intended purpose and proper use of the medical device, but excluding shipping documents. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure that there is a legal basis and relevant administrative process supporting the organization and governance of the authority that is responsible for registration and MA or listing. These provisions should be documented and should provide for the smooth coordination, collaboration and exchange of information inside and outside the regulatory authority. The arrangement should establish and define the roles and responsibilities inside and outside the NRA for registration and MA or listing activities. Provisions should ensure that the NRA responsible for registration and MA or listing has complete control or access to all relevant submitted information related to produced, procured or received medical products. Relevant information includes, for example, GMP or QMS inspection reports, analyses of laboratory data, collected vigilance data, applications for registration and MA or listing, the number and identity of medical products

	registered and granted MA or being listed, activities of ongoing registrations and MAs, new directives, registrations for newly registered products, withdrawn or suspended registrations and MAs or listings, and rejected applications. The objective of this indicator is to establish that structures are in place at the organizational and governance levels to promote effective intra- and inter-NRA relationships and efficient management of information traffic.
Category:	Organization and governance
Sub Indicator:	**MA02.01: There is a defined structure with clear responsibilities to conduct registration or MA activities**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that defined structures with clear responsibilities to conduct registration or MA or listing activities have been established and implemented. The organizational structure should identify the entities within the NRA that have the mandate for registration or MA or listing activities. The structure should be supported with regulations or guidelines mandating such entities to conduct registration or MA or listing activities and defining the scope and extent of their roles and responsibilities within the NRA in relation to registration or MA or listing activities. The guidance should also clarify lines of reporting in these structures. The organizational structure of the entities should be defined with respect to relationships and ranks, as well as information exchange and flow both inside and outside (e.g., officers at the port of entry or officers in the PMS unit) of the entities.
Objective:	The objective of this sub-indicator is to ensure that there are structures in place, with clearly defined roles and responsibilities for each structural and governance level, to carry out registration or MA or listing activities that ensure effectiveness, efficiency and consistency.
Requirement:	Structure and responsibilities to conduct registration or MA or listing activities
Evidence to review:	The assessor should ask for and review: 1. Documents that define the roles and responsibilities of the entities responsible for registration or MA or listing activities, and that describe the placement of the entities on the organizational chart in relation to other entities involved in registration or MA or listing –related activities.

	2. Regulations or guidelines empowering such entities or authorities with the responsibility to conduct registration or MA or listing activities. 3. Documentation of the organizational structure of the entities
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html). 5. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve)
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence for a defined structure with clear responsibilities to conduct registration or MA or listing activities. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted a defined structure with clear responsibilities to conduct registration or MA or listing activities, but it has not yet been implemented. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has a defined and established structure with clear responsibilities to conduct registration or MA or listing activities; however there is the need to improve this function by providing the additional resources and support needed for effective implementation and coordination with other entities. ⇒ IMPLEMENTED (I): The NRA has a defined structure with clear responsibilities to conduct registration or MA or listing activities that is fully supported with the required resources.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA02.02: Documented and implemented procedures exist to ensure involvement and communication with all relevant regulatory entities as necessary**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify the existence and implementation of documented procedures describing involvement and communication between all relevant entities inside the NRA. These procedures should be supported with adequate documentation. The procedures should provide clear directives on the regulatory divisions and provide guidance on how to implement the operational procedures to ensure the involvement and communication between relevant entities within the NRA (e.g., the dossier assessment entity, quality control laboratory, vigilance and market surveillance entities, and inspectorate). The procedures should be clear on the scope and extent of the roles and responsibilities of each relevant entity. In addition, the procedures should be supported by an information and documentation transfer policy that ensures that directives, information, and other documentation reach the intended recipients and that feedback is received. The procedures should be captured in the form of SOPs and guidelines which are approved and authorized to be implemented. In case of exchange of confidential information, appropriate measures should be considered; such measures may include confidentiality agreements.
Objective:	The objective of this sub-indicator is to ensure there are documented procedures, mechanisms, and structures in place to ensure proper relationships between and within entities within the NRA (e.g., dossier assessment entity, quality control laboratory, vigilance and PMS entities and inspectorate) and to ensure effective and efficient exchange of information among these entities.
Requirement:	Procedures for involvement and communication with all relevant regulatory entities
Evidence to review:	The assessor should ask for and review: 1. The registration or marketing application or listing guidelines that capture the duties, roles and responsibilities of those entities inside the NRA that are involved in registration or marketing activities.

	2. Evidence that the guidelines and related documents are known to the relevant organizations, divisions, institutions, and/or departments. 3. Evidence that the documented procedures have been implemented, and that the impact of the implementation has been evaluated. 4. SOPs that guide and inform effective communication and collaboration within and among relevant entities inside the NRA (e.g., dossier assessment entity, quality control laboratory, vigilance entity, and inspectorate). 5. Documentation for the feedback mechanism in the information and documentation transfer policy that covers information exchange among all relevant regulatory divisions.
References:	1. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 2. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html). 5. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve)
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of documented procedures to ensure involvement and communication with all relevant regulatory entities as necessary. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted procedures to ensure involvement and communication, but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The relevant entities inside the NRA established the procedures to ensure involvement and communication, but these either have not been fully incorporated or they are not consistent with relevant SOPs.

	⇒ IMPLEMENTED (I): The NRA has procedures to ensure involvement and communication with all relevant regulatory entities as necessary, including required documentation and records and these are being followed.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA03 Human resources to perform registration and marketing authorization activities.**
Objective:	The objective of this indicator is to ensure that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce, and are empowered to fully perform the function of registering and granting MA or listing for medical products. This will ensure that medical products registration and MA or listing processes or activities are performed in accordance with international best practices. The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition of the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform the registration and MA or listing function.
Category:	Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**MA03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform MA or registration activities**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that the human resources assigned to perform MA or registration or listing activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for MA or registration or listing activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform the MA or registration or

	listing function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for MA or registration or listing is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire MA or registration or listing chain.
Requirement:	Sufficient number of competent human resources in charge of MA or registration or listing activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire MA or registration or listing process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in MA or registration or listing activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the MA or registration or listing chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html). 5. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11

	(https://apps.who.int/iris/rest/bitstreams/1337931/retrieve) 6. Competence, Training, and Conduct Requirements for Regulatory Reviewers, International Medical Device Regulators Forum, IMDRF/GRRP WG/N40FINAL:2017, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform MA or registration or listing activities ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ⇒ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform MA or registration or listing activities.
Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA03.02: Duties, functions, and responsibilities of the staff in charge of MA or registration activities are established and updated in the respective job descriptions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)

Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in MA or registration or listing activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in MA or registration or listing activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.
Requirement:	Up-to-date duties, roles and responsibilities of the staff relevant to MA or registration or listing activities.
Evidence to review:	The assessor should ask for and review: 1. Procedure and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)

	4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 6. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html). 7. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve)
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ⇒ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	▪ The issue of overlapping responsibilities among members of the MA assessment teams is very common in some NRAs. Assessor should recognize the arrangement and assess on the basis of the adequacy of competencies of the official for each of the different functions to which they have been assigned. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA03.03: Training plan developed, implemented and reviewed at least once a year and updated if needed for staff in charge of marketing authorization activities.**

MATURITY LEVEL:	3
Scope:	Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that training plans are developed, implemented and reviewed at least once every year to reflect the current situation by considering education and experience of the staff. Based on the outcomes of the annual review, the training plan may need to be updated. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and reviewed at least once every year and updated if needed. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts. The aforementioned requirements apply to entities and organization which may perform marketing authorization activities on behalf of the NRA (i.e., NRA designated auditing organization(s).
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and reviewed annually and also if it is updated when needed. Through the training plan, NRA can be sure that competency of staff in charge of marketing authorization activities is maintained and enhanced.
Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual review (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. Furthermore, update of the plan is performed when needed. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan.

	5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 2. Competence, Training, and Conduct Requirements for Regulatory Reviewers, International Medical Device Regulators Forum (IMDRF), IMDRF/GRRP WG/N40FINAL:2017, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf)
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planed training or has been applying the plan for less than two years. ⇒ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans should be reviewed regularly; ideally on an annual basis, but not less frequently that once every two years. Based on the outcomes of the review, the training plan may be updated when needed. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine MA-relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.
Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1

	4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 5. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve) 6. Competence, Training, and Conduct Requirements for Regulatory Reviewers, International Medical Device Regulators Forum (IMDRF), IMDRF/GRRP WG/N40FINAL:2017, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf)
Framework:	Output
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ⇒ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities.
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA04 Procedures established and implemented to perform registration and/or marketing authorization**
Objective:	The objective of this indicator is to ensure that procedures have been established and implemented to effectively perform registration and MA or listing activities. The NRA should have documented procedures for registration and MA or listing activities and these procedures should be implemented. The documented procedures should be efficiently designed to assist in the preparation of the registration and MA or listing application dossier and in the documentation of the receipt and evaluation of the dossier. The procedures should present an overview of the activities to be carried out, the steps to be followed, the resources

	required, and the processes to be implemented. These activities include, but are not limited to, receipt of registration applications, acknowledgement of registration applications, assessment of the various components of the applications, generation of recommendations following the assessment process, issuance of a decision (i.e., approval, deferral, or rejection) for registration applications, issuance of registration and MA numbers or certificates or lists, and publication and public sharing of Summary of Product Characteristics-like information and technical evaluation summary reports. The established procedures will give guidance on how registration and MA or listing applications should be handled to ensure efficiency and effectiveness of the process.
Category:	Regulatory process
Sub Indicator:	**MA04.01: Documented procedures and tools are implemented for the assessment of the different parts of the application (i.e., quality, and efficacy) and for the assessment of specific requirements applicable to specific classes of medical products**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that documented procedures and tools are developed, made available and implemented for the assessment of the different parts of the registration or MA applications and for assessment of particular requirements applicable to a specific class of medical products. The benefit-risk balance of the medical product under review for registration or MA is the core consideration for regulatory authorities. The assessment procedures should be designed to be adaptable to all applications regardless of the source and product class. The procedures should provide guidance on the different parts of the MA application processing flow, including receipt, screening, review, and decision-making. The procedures for the assessment of registration or MA should be supported by adequate SOPs or similar documents. The scope and extent of the screening and review processes should be clearly documented for routine and non- routine MA applications. The assessor should note that there may be other registration or MA routes in special cases, e.g., for prequalified products or during emergencies when the normal procedures and tools may not apply.
Objective:	The objective of this sub-indicator is to ensure that documented procedures and tools exist for the assessment of the different parts of the registration or MA application and for the assessment of particular requirements applicable to a specific class of medical products. These procedures and tools should be implemented during the assessment process to avoid discrimination or bias.

Requirement:	Documented procedures and tool implemented for the assessment of applications
Evidence to review:	The assessor should ask for and review: 1. Documented procedures and tools, including SOPs, that are developed and used in the assessment of different parts of registration or MA applications or in the assessment of particular requirements applicable to a specific class of medical products 2. SOPs used for different parts of MA applications, such as receipt, screening, review and decision-making. 3. Evidence of use these SOPs, for example, by checking whether major milestones and decision points are recorded for a selected recent MA. 4. Documents addressing the scope and extent of the assessment process with respect to MA applications received and processed through the routine and non-routine routes. 5. Documents addressing the registration application backlog and that relate the backlog to the timelines for the review process and to the number of competent officers involved in the review process
References:	1. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (WHO/V&B/99.10), (6), (http://apps.who.int/iris/bitstream/handle/10665/65968/WHO_V-B_99.10_eng.pdf?sequence=1) 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/) 4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 5. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no documented procedures or tools for the assessment of the different parts of the application (i.e., quality, safety & efficacy/performance) and for the assessment of particular requirements applicable to specific classes of medical products.

	⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted the documented procedures and tools for the assessment of MA but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted documented procedures and tools for the assessment of MA and has been applying it for less than two years, or has not considered them for all marketed products. ⇒ IMPLEMENTED (I): The NRA has documented procedures and tools for the assessment of different parts of the application (i.e., quality, safety & efficacy/performance) and for the assessment of particular requirements applicable to specific classes of medical products and has applied them for all reviewed and marketed medical products.
Limitations and remarks:	▪ There may not be adequate time during the on-site assessment to review and compare the scope, extent, and consistency of the assessment processes for two or more MAs. This may be done off site though review of point 4 (scope and extent of the assessment process) and will likely require expert assessors (e.g., dossier reviewers) from stringent regulatory authority or pre-qualification assigned reviewers. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). ▪ For PDMPs, a comprehensive science-based assessment of risks and benefits should be performed as part of the registration or MA. Specific requirements include effective inactivation and removal of transmissible infectious agents potentially present in plasma. ▪ For medical devices including IVDs, the conformity assessment process taken by conformity assessment bodies (CAB) should be addressed by this sub-indicator.
Sub Indicator:	**MA04.02: Documented procedures have been implemented to renew and/or to periodically review the MAs granted**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that documented procedures and tools to renew and /or periodic review medical product registrations or MAs have been established and implemented. Similar to the initial registration and MA, the benefit-risk balance of the medical product is the core consideration for marketing re-authorization by regulatory authorities. The procedures should be supported with guidance on the requirements to be reviewed, and on the SOPs to be implemented at the various stages of the renewal or periodic review process. Guidance

	should be available for each stage of the renewal process, including, for example, receipt of application, screening, reviewing, and decision-making. The process flow should be documented and implemented.
Objective:	The objective of this sub-indicator is to ensure that documented procedures and tools exist and are implemented for the renewal and /or periodical review of registrations or MAs previously granted. These procedures will ensure consistency and effectiveness of the renewal process.
Requirement:	Procedures for registration or MA renewal
Evidence to review:	The assessor should ask for and review: 1. Document listing legally-approved validity periods for authorized products. 2. Documented procedures and tools, including SOPs and other technical documents covering the stages of the renewal process, e.g., receiving, screening, reviewing, decision-making, and issuing of registration numbers or certificates. 3. Procedures describing process flow with responsible divisions and timelines
References:	1. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of documented procedures to renew and/or to periodically review the MAs granted. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted documented procedures to renew and/or to periodically review the MAs granted, but they have not yet been applied. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted documented procedures to renew and/or to periodically review the MAs granted and has been applying them for less than five years or has not developed them yet for all marketed medical products.

	⇒ IMPLEMENTED (I): The NRA has documented procedures to renew and/or periodically review the MAs granted and has applied them for all marketed products.
Limitations and remarks:	The assessor should note that not all NRAs apply the registration and/ or MA renewal or periodic review system. Some NRAs maintain a stringent and functional vigilance and market surveillance system or structure with a demonstrated ability to perform its functions. In this case, the assessor should score this sub indicator as not applicable.
Sub Indicator:	**MA04.03: Documented procedures are implemented for assessing applications for variations of MAs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that documented procedures and SOPs that will guide the assessment of the various classes and types of variations/changes for the various product classes are established and implemented. These documents should contain procedures for receiving and processing the various classes and types of variation/changes applications.
Objective:	The objective of this sub-indicator is to ensure that documented procedures to assess variations/changes to registrations or MAs or listings exist and are implemented.
Requirement:	Documented and implemented variations/changes assessment procedures
Evidence to review:	The assessor should ask for and review. 1. Procedures and SOPs that guide the assessment of the various classes of variations/changes. The documented procedures should be medical product class specific. 2. Procedures for receiving and processing variation/changes applications, and evidence that the prescribed procedures been implemented. 3. A sample application that was received and reviewed by the NRA. The assessor should review for compliance with documented procedures.
References:	1. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/)

	2. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence of documented procedures for assessing the applications for variations of MAs. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted documented procedures for assessing the applications for variations/changes of MAs, but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted documented procedures for assessing the applications for variations/changes of MAs and has been applying them for less than two years or all submitted variations were not reviewed based on these procedures. ⇒ IMPLEMENTED (I): The NRA has documented procedures for assessing the applications for variations/changes of MAs and has implemented them for all marketed medical products.
Limitations and remarks:	▪ This review may also require an expert dossier reviewer. The assessor should note that NRA may have different requirements and guidelines for different medical product streams. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.04: The same criteria apply for assessing applications regardless of the origin of or destination for the medical products (e.g., domestic, foreign, public sector, or private sector)**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that the criteria applied to assess registration or MA applications are the same regardless of the origin or source of the medical product and the product application, and regardless of the location where the product will be used. A set of criteria for assessment

	should be documented and implemented for the various classes of medical product applications. The criteria should be documented in the form of SOPs. Guidance in the form of SOPs should be documented and implemented.
Objective:	The objective of this sub-indicator is to ensure the criteria used for assessing registration or MA applications for medical products is the same, regardless of the source or origin of the product or the destination for use of the product.
Requirement:	Same criteria for assessing registration or MA applications regardless of applicant
Evidence to review:	The assessor should ask for and review: 1. Evidence that SOPs or similar documents are in place to ensure that the same set of criteria is used to assess registration or MA applications regardless of source, origin or destination of the medical product. 2. Evidence that the staff members are aware of the single set of criteria and know how to apply the criteria in their assessment activities. 3. Evidence that the criteria are documented, published and implemented. 4. Sample registration or MA applications from different sources. The assessor should review these for the purpose of verifying consistent compliance with specified procedures. The assessor also should compare the procedures and determine whether there are any discrepancies in terms of scientific review and assessment. Sample MA applications of medical products coming from different sources (e.g. domestic, imported, public, or private,) along with their assessment reports, should be checked by the assessor.
References:	1. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 4. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve)
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): The NRA does not apply the same criteria for assessing all applications (e.g., domestic, foreign, public sector, or private sector)

	⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently defined or drafted the same criteria or policy for assessing all applications but they have not yet been applied. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has defined the same criteria or policy for assessing all applications and has been applying them for assessing applications for less than two years or has not applied them for all currently market medical products. ⇒ IMPLEMENTED (I): The NRA has the same criteria or policy for assessing applications regardless of the origin or destination of the medical products (e.g. domestic, foreign, public sector, or private sector) and has applied them for all marketed medical products.
Limitations and remarks:	▪ There may not be adequate time during the on-site assessment to review and compare the scope, extent, and consistency of the assessment processes for two or more MAs. This may be done off site though review of the evidence gathered for this sub-indicator. ▪ The assessor should consider that in non-producing countries, there would be no records for a domestic product that could be used when evaluating the implementation of this requirement. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.05: An advisory or scientific committee, including external experts is involved in the review of MA applications (as needed)**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that the use of advisory or scientific committees, including external experts, in the review of registration or MA applications is documented and supported by adequate regulations. The objectives and functions of the committee, as well as the professional profile of the committee members, should be available. The composition of the committee should be guided by appropriate regulations. For each member of the committee, there should be clearly defined roles and responsibilities in the review of registrations or MAs. Terms of reference and DOI for each member of the committee and each external expert should be prepared and documented.

Objective:	The objective of this sub-indicator is to ensure that an advisory or scientific committee, including external experts, is involved in the review of the registration or MA applications.
Requirement:	Advisory or scientific committee, including external experts
Evidence to review:	The assessor should ask for and review: 1. Documents defining the composition of the advisory or scientific committee, and evidence that the composition is in line with the directives prescribed in the regulations. 2. Documents defining the objectives and functions of the committee and its individual members, as well as that of the external experts. 3. The terms of reference for committee and its members as well as that of the external experts. 4. Documents defining the scope and extent of the advisory or scientific contributions to the registration or MA activities of the NRA 5. SOPs defining the review activities of the advisory or scientific committee and its programme of work. 6. Meeting minutes and related documents that provide evidence for the activities that result in registration or granting MA.
References:	1. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 2. Principles of Conformity Assessment for Medical Devices, GHTF/SG1/N78:2012 http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical-devices-121102.pdf#search=%22declaration%20of%20conformity%22 3. Principles of In Vitro Diagnostic (IVD) Medical Devices Classification, International Medical Device Regulators Forum, IMDRF/IVD WG/N64FINAL:2021, (http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-wng64.pdf)
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): The NRA does not have access to an advisory or scientific committee, including external experts, for assisting in review of MA applications or providing scientific advice as necessary. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently defined the criteria and composition of the advisory or scientific committee, but the advisory or scientific committee has not yet been established. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has established the advisory or scientific committee, but less than two years ago.

	⇒ IMPLEMENTED (I): The NRA has access to an advisory or scientific committee, including external experts, in the review of MA applications; this is supported by adequate documentation and records.
Limitations and remarks:	The assessor should note that some NRAs may not involve an advisory or scientific committee, including external experts, in the review of the submitted registration or MA applications, due to the availability of internal experts with the requisite competencies. Some NRAs may refer to the committee or external experts only certain applications that require their specialist attention and expert advice. In this case the scoring is not applicable.
Sub Indicator:	**MA04.06: Timelines for the assessment of the applications are defined and an internal tracking system has been established to monitor adherence to the targeted time frames**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that documented timelines and internal timeline tracking systems that guide the registration or MA or listing application process exist and are implemented. These should be supported by guidelines that stipulate that MA or listing applications should be processed and assessed per a published timeline and that the published timeline should be monitored internally for compliance. The guidelines should be supported by SOPs that provide guidance on how to establish the timelines and how to monitor the established timelines. The guidelines should be designed to adapt to the various classes of medical products registration or MA or listing applications (e.g., innovative medicines, generic medicines, new molecular entities, in vitro devices, and vaccines). Timelines should be designed to address each stage of the registration or MA or listing application process flow. The system should be developed to monitor the various timelines for the various registration or MA or listing application assessment procedures (i.e., the routine and non-routine procedures). The assessor should note that some NRAs will have varied timelines for the different registration or MA or listing assessment routes, as well as varied internal tracking systems to ensure adherence to the timelines. In this case, the assessor should review the timelines for each route and their corresponding tracking systems.
Objective:	The objective of this sub-indicator is to ensure that timelines for the assessment of registration or MA or listing applications exist, and that the timelines are monitored by internal tracking systems to ensure compliance.

Requirement:	Assessment timelines and internal control mechanisms for timelines
Evidence to review:	The assessor to ask for and review: 1. The documented registration application process flow and corresponding timelines for the various registration or MA or listing application routes and product classes. 2. Documentation for the internal tracking systems used for monitoring adherence to the assessment timelines. 3. Evidence that the timelines are published, easily accessible and known to all stakeholders, including the applicants and reviewers. 4. Evidence that these timelines have been implemented and are being adhered to during the assessment process. 5. Evidence that a dedicated unit or office is responsible for instituting, implementing and monitoring the assessment timelines tracking system for the purposes for compliance. 6. Evidence that corrective measures are available in the event of non-compliance.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 3. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve) 4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Structure/Foundation/Input & Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no timelines for the assessment of the applications and no internal tracking system to monitor the targeted time frames ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently defined timelines for the assessment of the applications but an internal tracking system to monitor the targeted time frames has not been implemented.

	⇒ PARTIALLY IMPLEMENTED (PI): The NRA has defined the timelines for the assessment of the applications and it has been applying an internal tracking system to monitor the targeted time frames for less than two years. ⇒ IMPLEMENTED (I): The NRA has timelines for the assessment of the applications and an internal tracking system to monitor the targeted time frames has been implemented
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.07: There are documented mechanisms to handle non-routine registration or MA requirements in special situations (e.g., public-health interest)**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify the existence and implementation of regulations and guidelines allowing the use of a non-routine mechanism that is supported with specific registration requirements. The regulation also should be supported with guidelines and SOPs that clearly specify the registration requirements and the instances (e.g., products for use in public health emergencies, or orphan medicines) in which an application would be considered for a specific pathway in the interest of public health. In addition, the registration or MA application process flow and their corresponding specific timelines should be provided, published and implemented. SOPs for the assessment process should be developed to reflect the process flow and the specific requirements.
Objective:	The objective of this sub-indicator is to ensure that documented mechanisms for specific registration requirements exist and are implemented when necessary in special situations (e.g., public-health interest).
Requirement:	Non-routine registration or MA applications

Evidence to review:	The assessor should ask for and review: 1. Regulations related to the establishment and implementation of a mechanism, with specific registration requirements, that can be used, in special situations, for assessing MA applications and for granting MA. 2. Guidelines on the instances and special situations in which this system applies, and guidelines on the specific registration requirements that should be applied. These requirements should be based on the nature of the products (e.g., new, biological, or generic products). 3. An example of an application that was processed through this route. The documents should be reviewed to determine if content and format is consistent with the prescribed requirements and if the process adhered to published timelines. 4. Documents describing the registration or MA application process flow and the corresponding timelines. The timelines should demonstrate timely review relative to the normal route or process. 5. SOPs that provide guidance for the assessment process.
References:	1. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (WHO/V&B/99.10), (6), (http://apps.who.int/iris/bitstream/handle/10665/65968/WHO_V-B_99.10_eng.pdf?sequence=1). 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. Guidelines on evaluation of similar biotherapeutic products (SBPs), (70), (http://apps.who.int/medicinedocs/en/q/) 4. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 5. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve) 6. WHO Emergency use listing https://www.who.int/teams/regulation-prequalification/eul/
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no documented mechanism, with specific registration requirements, for special situations (e.g., public-health interest)

	⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted a documented mechanism, with specific registration requirements, for special situations (e.g. public-health interest) but it has not yet been applied. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted a documented mechanism, with specific registration requirements, for special situations (e.g. public-health interest), and has been applying this for less than two years or in fewer than three cases. ⇒ IMPLEMENTED (I): The NRA has a documented and implemented non-routine mechanism, with specific registration requirements, for special situations (e.g. public-health interest)
Limitations and remarks:	In case that there has been no emergency that required the application of this mechanism, the assessor should verify the implementation of this sub-indicator by considering the availability of adequate resources and procedures for implementation of the non-routine mechanism.
Sub Indicator:	**MA04.08: Labelling information is reviewed and approved by the NRA as part of the MA procedure.**
Maturity Level:	3
Scope:	Medical devices including in vitro diagnostics
Description:	The assessor should note if the information on labelling comply with the existing regulations on labelling and if the information is reviewed as part of the registration /marketing authorization. During assessment process information must be found to be appropriate, satisfactory and implemented. The regulation should be supported by specific guidelines and /or SOPs for reviewing labelling information. See also MA01.15.
Objective:	The objective of the sub-indicator is to establish whether the information on labelling is reviewed and approved by the NRA as part of the registration /marketing authorization application process. The NRA should have clear requirements regarding labeling requirements.
Requirement:	labelling information
Evidence to review:	The assessor should request for and review: 1. Regulation and /or guidelines that state that the information on labelling should comply with the regulations provided to cover information on labelling of medical devices including IVDs, and the information should be assessed as part of the registration /marketing authorization, and must be found to be appropriate and satisfactory. 2. The guidelines and /or SOPs for assessing product information on labelling

	3. Registration / marketing authorization application assessment reports to verify whether recommendations are provided by the assessor on labelling information and how the information influenced the outcome of the application. 4. The registration / marketing authorization application processing flow for the stage or phase that require review of the product information on labelling, and whether the assessment process is conducted by trained staff with the requisite qualification.
References:	1. IMDRF/GRRP WG/N52 FINAL: 2019 Principles of labelling for medical devices and IVD medical devices. 2. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Process
Rating Scale:	⇒ **NOT IMPLEMENTED (NI):** There are no requirements for approving labelling information by the NRA as part of the MA procedure. ⇒ **ONGOING IMPLEMENTATION (OI):** The NRA has recently drafted or adopted the requirements to comply with the regulations provided to cover product labelling information but they have not yet been followed. ⇒ **PARTIALLY IMPLEMENTED (PI):** The NRA has defined the requirements to comply with the regulations provided to cover product labelling information and has been applying them for less than two year or they have not been considered for all marketed medical products. ⇒ **IMPLEMENTED (I):** The NRA is approving labelling information as part of the MA procedure for all reviewed medical products.
Limitations and remarks:	▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.09: GMP inspection report and/or certification is considered as part of the MA process.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs

	4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that regulations or guidelines are established and implemented that specify the type, content and format of GMP documentation or QMS certification that should be submitted to the NRA by another NRA (i.e., in case of imported medical products), or that describes the processes and procedures through which an on-site inspection or verification will be conducted by the NRA. The guidelines should be supported by supplementary guidelines or SOPs that provide guidance for use during the on-site inspection or verification visits or during assessment of the submitted GMP documentation or QMS certification. The assessor should verify the existence and implementation of procedures and SOPs that ensure that the GMP inspections or GMP documentation or QMS certification verifications are part of the medical products registration or MA process and that ensure that GMP or QMS requirements are established, implemented, published, and easily accessible as part of the registration or MA application process. The assessor should note that, in some NRAs, the GMP on-site visits and inspections may be carried out by consultants hired by the NRA to perform the task rather that by NRA staff. Similarly, for medical devices, QMS audits may be performed by other organizations on behalf of the NRA. In such instances, if the competencies of the hired consultants are appropriate, the scoring will apply.
Objective:	The objective of this sub-indicator is to ensure that GMP or QMS inspections or certifications are part of the registration or MA requirements, and that the NRA has a legal provision to request the manufacturer to demonstrate adherence to GMP and QMS in the manufacture of the medical products. This can be done either through on-site verification or inspection/audits by the NRA or through a satisfactory assessment of GMP or QMS documentation issued by other NRAs or other designated auditing organizations (e.g., CAB).
Requirement:	GMP inspection or QMS audit report or certificate as part of MA process
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that clearly state that compliance with the principles of GMP or QMS is part of the medical products registration or MA application requirements. 2. Legal provisions that clearly describe the format and content of the GMP or QMS requirements, i.e., either through a satisfactory on-site verification or inspection by the NRA or through a satisfactory assessment of GMP or QMS documentation issued by another NRA or designated auditing organizations. 3. Guidelines and SOPs that provide guidance to be used during the on-site inspection/audits or verification visits or during assessment of the submitted GMP or QMS documentation. These should be reviewed for completeness. 4. Guidelines or regulations that specify the type, content and format of GMP or QMS documentation that should be submitted to the NRA by another NRA (i.e., for the purpose of GMP or QMS verification), or that describes the processes and procedure through which an on-site inspection or verification will be conducted by the NRA. 5. Procedures that ensure that the GMP inspections, QMS audits or the verifications of submitted GMP or QMS documentation are part of the

	authorization process, as well as procedures that ensure that GMP or QMS requirements are implemented as part of the MA application process. 6. Evidence that a GMP or QMS report or certification is a requirement for all registration or MA applications and that a risk-based routine inspection is required periodically. 7. A record of registration and MA application submissions. These should be evaluated for the purposes of verification and compliance with the guidelines.
References:	1. Guidance on Good Manufacturing Practices (GMP): inspection report, (32), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Medical Devices – Quality Management Systems – Requirements for regulatory purposes. ISO 13485:2016. https://www.iso.org/files/live/sites/isoorg/files/store/en/PUB100422_preview.pdf 4. Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy; https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg4/technical-docs/ghtf-sg4-n30r20-guidance-regulatory-auditing-060628.pdf 5. Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 4: Multiple Site Auditing; http://www.imdrf.org/docs/ghtf/final/sg4/technical-docs/ghtf-sg4-n83-2010-guidelines-for-auditing-qms-part-4-multiple-sites-100827.pdf 6. Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers Part 5: Audits of Manufacturer Control of Suppliers; http://www.imdrf.org/docs/ghtf/final/sg4/technical-docs/ghtf-sg4-n84-2010-guidelines-for-auditing-qms-part-5-control-of-suppliers-100827.pdf 7. Requirements for Medical Device Auditing Organizations for Regulatory Authority Recognition IMDRF/MDSAP WG/N3 FINAL:2016- https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-160324-requirements-auditing-orar.pdf 8. Competence and Training Requirements for Auditing Organizations; IMDRF/MDSAP WG/N4 FINAL:2013 https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-131209-competence-and-training-requirements-140901.pdf 9. MDSAP Overview of Auditing Organization Assessment and Recognition Decision Related Processes; IMDRF/MDSAP WG/N22 FINAL:2014 - https://www.imdrf.org/sites/default/files/docs/imdrf/final/procedural/imdrf-proc-140918-decision-related-processes.pdf

	10. Medical Device Regulatory Audit Reports; IMDRF/MDSAP WG/N24 FINAL:2015 https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-151002-mdra-audit-report.pdf 11. Quality Management System“ - Medical Devices“ - Nonconformity Grading System for Regulatory Purposes and Information Exchange GHTF/SG3/N19:2012 – https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n19-2012-nonconformity-grading-121102.pdf 12. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 13. IMDRF Medical Device Single Audit Program (MDSAP) https://www.fda.gov/medical-devices/medical-device-single-audit-program-mdsap/imdrfmdsap-wg-and-gthf-documents
Framework:	Structure/Foundation/Input & Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): A GMP inspection report, QMS audit report or certification is not required as part of the MA process ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently defined GMP inspection report, QMS audit report or certification as a requirement for MA authorization, but it has not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has required a GMP inspection report, QMS audit report or certification as a requirement for MA authorization and has been applying this for less than two years. ⇒ IMPLEMENTED (I): GMP inspection report, QMS audit report or certification is required by the NRA as part of the MA process, and has been considered in all received MA applications.
Limitations and remarks:	▪ The assessor should verify that all requirements are same regardless of the source of products. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.10: The regulations and guidelines for good review practices (GRevPs) are developed or recognized and implemented.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that procedures and documentation on GRevPs are established and implemented. The procedures should be supported by an operation manual (i.e., with documented and approved SOPs for the screening and review of the various classes of medical products and their corresponding routine or non-routine application routes) that guides the screening and review of registration or MA applications. The procedures should include quality control and quality assurance systems or structures that ensure that actual application assessment and review is conducted in accordance with approved SOPs. The procedures should provide guidance on how to handle medical product application non-conformities.
Objective:	The objective of this indicator is to ensure that regulations and guidelines exist for the NRA to review and evaluate the different components of registration or MA applications; to review and evaluate the specific requirements of each product class; and to register or grant MAs or to reject registrations following documented procedures for the assessment of different parts of the application. These procedures will provide consistency in the approval or rejection of applications through the application of defined requirements and criteria such that the resultant decision would be seen to be based on submitted documentation irrespective of the reviewer.
Requirement:	Guidelines and SOP for GRevPs
Evidence to review:	The assessor should ask for and review: 1. Regulations and guidelines that provide guidance on principles of GRevP. 2. SOPs for assessment of registration or MA applications that guide the reviewer during the screening and review of the different components of the various classes of medical products. 3. Evidence that the same set of principles is applied during the screening and review of MA applications submitted through the non-routine procedure. The assessor should request SOPs that provide guidance on how to handle actual review of applications through the non-routine procedure. 4. Evidence that procedures are in place to ensure that actual application assessments and reviews are conducted in accordance with the principles of GRevP and that the assessment reports are peer-reviewed. 5. An example of an assessment report for a particular product class. The assessor should evaluate this for compliance to the corresponding GRevP SOPs and related documents.

References:	1. Good review practices: guidelines for national and regional regulatory authorities, (49), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. Competence, Training, and Conduct Requirements for Regulatory Reviewers; http://www.imdrf.org/docs/imdrf/final/consultations/imdrf-cons-requirements-regulatory-reviewers-160502.pdf 3. Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews; http://www.imdrf.org/docs/imdrf/final/consultations/imdrf-cons-rrar-cabc-mdrr.pdf 4. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Process
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no regulations or guidelines for GRevPs ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted GRevPs but they have not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted GRevPs and has been applying them for less than two years or the principles are not yet reflected in other relevant SOPs and guideline for MA activities. ⇒ IMPLEMENTED (I): The NRA has regulations or guidelines for GRevPs and is following them in all relevant activities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA05 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place to ensure that information on registration and MA applications, including authorized, suspended, rejected and completed applications, are published to promote transparency and information sharing among stakeholders and potential stakeholder (e.g., retailers and patients). This approach will build trust among stakeholders. A mechanism for appeal of MA should be described.
Category:	Transparency, accountability and communication

Sub Indicator:	**MA05.01: Updated list of all medical products granted MA is regularly published and publicly available**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that a list of medical products registered or granted MA is in existence. This list should be regularly updated and published. The published information should be supported by SOPs that provide guidance on the procedure to enter information, the procedure to translate the information into the appropriate format, and the type of information to enter (e.g., may include, but is not limited to, the product brand name, International Nonproprietary Name, the registration or MA number, the registration or MA certificate number, the validity period of the registration or MA, the active ingredients, manufacturer, and potency or concentration). The host or website where the list is published should be documented and should be easily accessible to the general public.
Objective:	The objective of this sub-indicator is to ensure that guidelines and regulations exist to guide and advise the NRA to regularly update and publish the list of medical products that are registered or granted MA
Requirement:	List of all medical products registered or granted MA
Evidence to review:	The assessor should ask for and review: 1. The published list of medical products registered or granted MA. 2. Evidence that the information published for the registered medical products is in compliance with guidelines and SOPs. 3. Evidence that the list is regularly updated. The assessor should verify that the list is current. 4. SOPs or similar documents for updating the list. 5. Evidence that an internal register (i.e., paper or electronic version) for entering registered medical products exists. If the internal register exists, the assessor should review the guidelines and SOPs for completing and regularly updating the register. 6. Evidence that the published list is accessible. The assessor should also identify the host organization, e.g., NRA, MoH, or other organization.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)

	2. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 3. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve) 4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Output
Rating Scale:	⇒ NOT IMPLEMENTED (NI): The updated list of all medical products granted MA is not published. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently committed to publish the list of all medical products granted MA, but it has not yet been followed. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has initiated publication of the list of all medical products granted MA; however it is not updated regularly, or the list does not reflect of all medical products granted MA. ⇒ IMPLEMENTED (I): The NRA has publicly published the list of all medical products granted MA and it is regularly updated.
Limitations and remarks:	▪ For different products medical streams, some NRAs publish different lists. If so, each list should be easy to access. The assessor should consider that existence of the database of all granted MA medical products is not adequate to fulfill this requirement (unless the database is publicly available), since the purpose is transparency. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA05.02: A summary technical evaluation report for approved registration MA applications is published and available to the public**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines 3. PDMPs

	4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that the summary technical evaluation reports of those medical products registration/MA applications that have been approved, are published and made available to the public, and these actions are supported by a regulation or a guideline. The content and format of the report should be guided by an SOP to ensure uniformity. Procedures should be in place to monitor the generation of the reports to ensure that the content and format conforms to the approved standards, and that the reports are regularly published and made available to the public.
Objective:	The objective of this sub-indicator is to ensure that guidelines or regulations exist to allow the NRA to publish and make available to the public the summary technical evaluation reports of approved MA applications. The NRA should actually publish and make available to the public the summary technical evaluation reports.
Requirement:	Summary technical evaluation report (Public assessment report) available to stakeholders
Evidence to review:	The assessor should ask for and review: 1. Procedures in place to support and monitor the generation of the reports, to ensure that the content and format conforms to the approved standards, and to ensure that the reports are regularly published and made available to the public. 2. A sample of a report for the purpose of evaluating conformance to the published guidelines and or SOPs. The assessor should verify that the report is generated, published and made available to the public. 3. The website for hosting the reports, and the SOPs that provide guidance to staff on procedures for uploading new reports and updating existing reports.
References:	1. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (WHO/V&B/99.10), (6), (http://apps.who.int/iris/bitstream/handle/10665/65968/WHO_V-B_99.10_eng.pdf?sequence=1). 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1 4. EMA procedural advice for medicinal products intended exclusively for markets outside the European Union in the context of co-operation with the World Health Organisation (WHO) Procedure under Article 58 of Regulation (EC) No 726/2004, May 2021,

	https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-procedural-advice-medicinal-products-intended-exclusively-markets-outside-european-union-context_en.pdf
Framework:	Output
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no evidence for publication and public availability of a summary technical evaluation report for approved registration or MA applications. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently defined this requirement for publication and public availability of a summary technical evaluation report for approved registration or MA applications, but it has not yet been implemented. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has initiated publication of summary technical evaluation reports for approved registration or MA applications, but this has not been applied for all evaluated medical product applications. ⇒ IMPLEMENTED (I): The NRA has published and made available to the public summary technical evaluation reports for approved registration or MA applications for all evaluated medical product applications.
Limitations and remarks:	The assessor should note that some NRAs will not publish the summary of the technical evaluation report for medical product applications processed under special circumstances, for example, emergencies, WHO collaborative registration procedures, WHO prequalified products, Article 58 reviews (see references), or reviews by orphan drug route (i.e., abridged registration application processing route or pathway).
Indicator:	**MA06 Mechanism in place to monitor regulatory performance and output**
Objective:	The objective of this indicator is to ensure that mechanisms and procedures are in place to monitor and ensure that all activities within the MA functionality are subjected to quality control and other checks to reduce errors and to ensure that the processes and results of the registration application assessment are consistent and able to generate a reliable output. These monitoring mechanisms lead to consistency in the regulatory performance of the registration and MA function and to reliability of outputs.
Category:	Monitoring progress and assessing outcomes & impact
Sub Indicator:	**MA06.01: There is a database of all product applications received, approved, rejected, suspended or withdrawn along with their supporting documentation.**

Maturity Level:	3
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)
Description:	The assessor should verify that a database to keep all medical product registration applications received, approved, rejected, suspended or withdrawn, as well as their supporting documentation exists, and that the database is continually updated to reflect the current situation. The operation and management of the database should be supported by guidelines and SOPs that specify the types of information and documentation to keep and the format and duration of storage. Personnel with authorization to access information should be documented and the procedure to access the information should be defined. The location of the actual database should be documented. Information on the back-up database should be provided. Plans or efforts to secure a back-up system should be reviewed if a back-up system is not currently available.
Objective:	The objective of this sub-indicator is to ensure that regulations or guidelines exist to require the NRA to keep and manage a database of the supporting documentation for all medical products registration or MA applications received, approved, rejected, suspended or withdrawn. This database should continually be kept up to date. This database would significantly contribute to consistency in regulatory approach and to expansion of institutional memory.
Requirement:	Database of all medical products application
Evidence to review:	The assessor should ask for and review: 1. Evidence that a database exists for keeping an up to date list of supporting documentation and information (e.g., legal information and requirements, communications, application files, and bases of decision) for all medical products registration or MA applications received, approved, rejected, suspended or withdrawn. 2. Guidelines and SOPs that define the essential information to keep in the database and the timelines for retaining this information. 3. Evidence that the database is up to date and current and that it is supported by a back-up data base. 4. Documents defining the authorization needed to access or to update the information in the database. Procedures for monitoring, maintaining, and updating the database should also be reviewed.
References:	1. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1

	2. Good regulatory practices in the regulation of medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fifth report. Geneva: World Health Organization; 2021: Annex 11 (https://apps.who.int/iris/rest/bitstreams/1337931/retrieve) **3.** Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Output
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There is no database of all product applications received, approved, rejected, suspended or withdrawn, along with their supporting documentation. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated and drafted the requirement to create the database but it has not yet been established. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has established a database of all product applications received, approved, rejected, suspended or withdrawn along with their supporting documentation but not all applications have been included in the database or the database is not regularly updated or fully integrated. ⇒ IMPLEMENTED (I): The NRA has a database of all product applications received, approved, rejected, suspended or withdrawn along with their supporting documentation, and the database is kept up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA06.02: Performance indicators for registration and MA activities are established and implemented**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines 3. PDMPs 4. Medical devices including in-vitro diagnostics (IVDs)

Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the registration and MA functions. Specifically, the system should define key performance indicators (KPIs) along the entire registration and MA activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement. In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire registration and MA chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of registration and MA regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for registration and MA activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire registration and MA activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the registration and MA function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for registration and MA activities 4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. Quality management -- Quality of an organization -- Guidance to achieve sustained success, ISO 9004:2018, International Organization for Standardization (ISO), (115), (https://www.iso.org/standard/70397.html)

	2. WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. World Health Organization, 2017. https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1
Framework:	Structure/Foundation/Input
Rating Scale:	⇒ NOT IMPLEMENTED (NI): There are no KPIs for registration and MA activities. ⇒ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for registration and MA activities but they have not yet been reported. ⇒ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for registration and MA activities and has been applying them for less than two year or they have not covered all critical steps. ⇒ IMPLEMENTED (I): The NRA has established and implemented KPIs for registration and MA activities. The indicators are reviewed regularly, and appropriate actions are taken, and decisions made.
Limitations and remarks:	▪ When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. ▪ Different methodologies are used to measure the NRAs performance on registration and MA activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time- bound (i.e., “SMART”). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).