AUDA-NEPAD
AFRICAN UNION DEVELOPMENT AGENCY

World Health Organization

African Medical Devices Forum

Specific Considerations for Regulating Maternal, Newborn, and Child Health Medical Devices — Market Authorization

FOREWORD

One of the key objectives of the African Medical Devices Forum (AMDF) is building the technical capacity of national regulatory agencies (NRAs) in medical devices and in-vitro diagnostics regulatory frameworks through the development of technical guidance documents. The AMDF has developed and published *Guidelines on regulatory requirements for issuance of market authorization of medical devices including in-vitro diagnostic medical devices; Guidelines for registration of medical devices establishments; Guidelines on import and export of medical devices including in-vitro diagnostic medical devices;* and *Guidelines for inspection of manufacturing site(s) for assessment of the quality management system of medical devices* based on ISO 13485:2016.

Advancements in health technologies call for continuous considerations to carry forward and strengthen regulatory systems, and it is important to remain cognizant of areas with specific considerations, such as medical devices for maternal, newborn, and child subpopulations. In view of that, the AMDF, with the support of the US Agency for International Development (USAID) Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program implemented by Management Sciences for Health, has developed this document entitled *Specific Considerations for Regulating Maternal, Newborn, and Child Health Medical Devices – Market Authorization.* It outlines specificities when assessing these medical devices at the market authorization phase. It is to be used with the other guidance documents that the AMDF has developed on market authorization for medical devices, including in-vitro diagnostic (IVD) medical devices.

The AMDF considers this document a key resource that will provide information to NRAs in advancing regulatory system strengthening in Africa.

Paulyne Wairimu – Chair, AMDF

ACKNOWLEDGMENTS

The African Medical Devices Forum (AMDF) acknowledges the US Agency for International Development (USAID) Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program for its support to develop this document, *Specific Considerations for Regulating Maternal, Newborn, and Child Health Medical Devices – Market Authorization*.

The AMDF also acknowledges the support and review during development and finalization of this reference document by Jane Briggs, Senior Principal Technical Advisor, Lead on MNCH and FP, MTaPS; Kate Kikule, Principal Technical Advisor - Pharmaceutical Regulatory Systems, MTaPS; and Nereah Kisera, Senior Technical Advisor – Pharmaceutical Regulatory Systems, MTaPS.

The technical support of the World Health Organization (WHO) team—Agnes Sitta Kijo, Technical Officer; Sunday Kisoma, Consultant; and Josée Hansen, Consultant—is specifically acknowledged in the development of the document.

We also gratefully acknowledge the contributions of Alex Juma, Program Officer, Regulatory Systems Strengthening; Nancy Ngum, Program Officer, Public Health, AUDA-NEPAD; Sandra Ligia González, Leticia Fonseca, and Steven Bipes, USAID COVID-19 Medical Device Regulatory Convergence Project; Rebecca Richards Kortum, Jackie Foss, Kara Palamountain, and Elizabeth Asma, NEST; Melody Scott, USAID PQM Plus; and Leah Greenspan and Deborah Armbruster, USAID, in the technical review of the document.

The International Medical Device Regulators Forum (IMDRF), US Food and Drug Administration, and WHO are also acknowledged for making their guidelines available for reference.

Dimakatso Mathibe, vice-chair AMDF

JUNE 2023

EXECUTIVE SUMMARY

A national regulatory authority (NRA) assesses information/evidence submitted by the manufacturers of medical devices, including in-vitro diagnostic devices (IVDs), to verify safety and performance. Compliance with NRAs is expected to develop and align assessment requirements based on internationally recognized guidelines and standards as defined by the African Medical Devices Forum (AMDF), World Health Organization (WHO), International Medical Device Regulators Forum (IMDRF), International Organization for Standardization (ISO) standards, and Clinical Laboratory Standards International guidelines, among others.

The regulation of medical devices for maternal, newborn, and child health (MNCH) has been considered a priority to ensure they are safe and effective for their intended use to the targeted group. The AMDF developed guidelines for registration of medical devices that outline the principles of safety, performance, and efficacy and covers all medical devices, including IVDs. Given the rapid technological advancement in recent decades and the increased attention to the development of special newborn care units, providing technical support to countries to strengthen their regulatory frameworks to include medical devices for newborns is an urgent requirement to ensure the safety and quality of those devices.

This MNCH guidance document includes specific considerations for this vulnerable subpopulation, such as unique host characteristics as pertaining to size, growth, and development; body physique; development milestones; pathophysiology; behavioral factors; psychosocial factors; surgical factors for implantable devices; and guidance for clinical considerations to be considered by manufacturers.

The general principles of medical device regulation are also discussed, including risk-based classification of medical devices and applicable risk classification rules, essential principles of safety and performance, and the quality management systems for these medical devices.

An assessment of the technical documentation reviews the assessment criteria to be followed and the specific information that assessors can use in reviewing peculiarities of MNCH medical devices. The use of a reliance model of information sharing and the information to be assessed are also highlighted.

Specific labeling and post-market surveillance requirements for MNCH medical devices provide information and specifics to be included in the instruction for use.

The use of this document together with other published guidelines will support regulators in making decisions during the review of technical files for MNCH medical devices.

AMDF TC

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ABBREVIATIONS AND ACRONYMS

AMDF	African Medical Devices Forum
CPAP	continuous positive airway pressure
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IVD	in-vitro diagnostic
LMICs	low- and middle-income countries
MNCH	maternal, newborn, and child health
MTaPS	Medicines, Technologies, and Pharmaceutical Services
NRA	national regulatory authority
QMS	quality management system
USAID	US Agency for International Development
WHO	World Health Organization

TERMS AND DEFINITIONS

For the purpose of this document, the following definitions apply:

Adverse event: Event associated with a medical device that led to death or serious injury of a patient, user, or other person or that might lead to death or serious injury of a patient, user, or other person if the event recurs. [1]

Applicant: The person who makes, or on whose behalf is made, an application for a new registration or an update or amendment to an existing registration. After the product is registered, the applicant shall be the marketing authorization holder.

Benefit: A positive or valued outcome of an action or event.

Declaration of conformity: A mandatory document that a manufacturer or authorized representative signs to declare that products comply with the regulatory requirements. *(amended from EU declaration of conformity).* [2]

Incident: Malfunction or deterioration in the safety, quality, or performance of a device made available on the market; any inadequacy in the information supplied by the manufacturer; or undesirable side effects. [3]

Falsified: Medical products that deliberately/fraudulently misrepresent their identity, composition, or source. [4]

Fee: The fee prescribed in a regulation related to regulatory services and fines.

Field safety corrective action: An action taken by a manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device. Such actions should be notified via a field safety notice. [5]

Field safety notice: A communication sent out by a manufacturer or its representative to the device users in relation to a field safety corrective action. [5]

Instructions for use: Information provided by the manufacturer to inform the device user of the medical device's intended purpose and proper use and of any precautions to be taken. [6]

Label: Written, printed, or graphic information appearing on the medical device itself, on the packaging of each unit, or on the packaging of multiple devices. [6]

Labeling: The label, instructions for use, and any other information related to identification, technical description, intended purpose, and proper use of the medical device, excluding shipping documents. Labeling can also be referred to as "information supplied by the manufacturer." Labeling can be in printed or electronic format and may either physically accompany the medical device or direct the user to where the labeling information can be accessed (e.g., a website) as permitted by regulatory jurisdiction. [6]

Manufacturer: Any natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under its name; whether or not such a medical device is designed and/or manufactured by that person himself or herself or on his or her behalf by another person(s) [7].

Market surveillance: The activities carried out and measures taken by competent authorities to check and ensure that devices comply with the requirements set out in relevant legislation and do not endanger health, safety, or any other aspect of public interest protection. [3]

Medical device: Any instrument, apparatus, implement, machine, appliance, implant, reagent for in-vitro use, software, material, or other similar or related article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific medical purposes of:

- Diagnosis, prevention, monitoring, treatment, or alleviation of disease
- Diagnosis, monitoring, treatment, or alleviation of or compensation for an injury
- Investigation, replacement, modification, or support of the anatomy or of a physiological process
- Supporting or sustaining life
- Control of conception
- Cleaning, disinfection, or sterilization of other medical devices
- Providing information by means of an in-vitro examination of specimens derived from the human body that does not achieve its primary intended action by pharmacological, immunological, or metabolic means, in or on the human body, but that may be assisted in its intended function by such means. [8]

Pediatrics: The health care of children, defined in these guidelines as those below 12 years of age.

Pediatric use: Any use of a medical device in a pediatric population in which there is a primary pediatric indication.

Post-market surveillance: All activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market, or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions. [3]

Premarket controls: All controls applied by the national regulatory authority (NRA) to the manufacturer and/or the authorized representative before the manufacturer's medical device may be placed on the market or put into service. [9]

Recognition: Acceptance of the regulatory decision of another regulator or other trusted institution. Recognition should be based on evidence that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of the relying authority. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement. [10]

Regulatory authority: A government body or other entity that exercises a legal right to control the use or sale of medical devices within its jurisdiction and that may take enforcement action to ensure that medical products marketed within its jurisdiction comply with legal requirements. [11]

Reliance: The act whereby a regulatory authority in one jurisdiction takes into account and gives significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information, in reaching its own decision. The relying authority remains independent, responsible, and accountable for the decisions made even when it relies on the decisions, assessments, and information of others. [10]

Substandard: Also called "out of specification", an authorized medical product that fails to meet quality standards, specifications, or both. [4]

Technical documentation: The documented evidence, normally an output of the quality management system (QMS), that demonstrates that the medical device complies with the relevant principles of safety, performance, and labeling specified through legislation. [11] [12]

1. INTRODUCTION

The availability, accessibility, and effective use of essential medical devices for diagnosis and treatment are crucial for the delivery of quality health services. In 2017, more than 30% of World Health Organization (WHO) member states did not have regulations on the control of medical devices, and WHO found that of low-income countries with data available, only 45% had a legal framework for medical devices. [13] In a recent mapping of nine Asian and African countries, [14] MTaPS found that while six of the nine had a legal framework for the regulation of medical devices, only three were regulating medical devices. Even if legal frameworks exist, guidelines for the regulation of medical devices are often not available. WHA Resolution 67.20 “Recognizes that effective regulatory systems are an essential component of health system strengthening and contribute to better public health outcomes, that regulators are an essential part of the health workforce, and that inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality medical product”. [15]

2. MATERNAL, NEWBORN, AND CHILD HEALTH

It is estimated that up to 70% of the medical devices in health care centers in low- and middle-income countries (LMICs) are partially or completely nonfunctional. [16] [17]

Medical devices are a key part of services for maternal, newborn, and child health (MNCH), and the quality, safety, and reliability of those devices need to be assured. Maternal health refers to the health of women during pregnancy, childbirth, and the postnatal period; newborn health refers to the health and well-being of neonates under 28 days of age and newborns up to 2 months; and child health refers to the health and well-being of children 2 months to 12 years.

Pneumonia accounts for 14% of all deaths of children under 5 years old, killing 740,180 children in 2019. [18] It is estimated that 13% of all severe pneumonia cases in children under 5, which totaled 14 million in 2010, have hypoxemia and should be treated with oxygen. [19] Neonatal deaths represent 47% of all under 5 deaths, [20] with most deaths resulting from preterm birth complications, intrapartum-related complications, or infections. Medical devices that are essential to provide care to children under 5 and newborns in these conditions include newborn resuscitation equipment; hypoxemia diagnostics (pulse oximeters and other multimodal devices); and medical devices for oxygen therapy, including concentrators and continuous positive airway pressure (CPAP) devices. With pre-eclampsia affecting 5% to 7% of all pregnant women and responsible for more than 70,000 maternal deaths annually, [21] diagnostic devices such as glucometers and blood pressure meters are an essential part of the care package to address maternal conditions that can be managed at a district hospital or the nearest health facility for the mother and baby. The use of point of care devices in rural and small-town centers in LMICs is critical to offer health services to pregnant women, newborns, and children who are not able to reach hospitals in urban centers. Diagnostic devices, such as those mentioned above, are critical, and their safety and effective performance is essential for improved health outcomes.

The regulation of medical devices for MNCH is of great importance to ensure they are safe and effective for their intended use. The lack of regulatory systems in LMICs means that medical devices are frequently not assessed or that there are no standards to assess for compliance before market authorization, increasing the risk of a supply of medical devices that do not meet performance, quality, and safety standards.

Given the rapid technological advancement in recent decades and the increased attention given to the development of special newborn care units, providing technical support to countries to strengthen their regulatory frameworks to include medical devices for newborns is an urgent requirement to ensure the safety and quality of those devices.

While rules and guidelines based on intentional reference documents are applicable to all medical devices and the use of reliance and recognition mechanisms should be evaluated, this document pays specific attention to an important vulnerable user group and highlights specific considerations that regulators should be aware of when regulating MNCH medical devices.

3. INTENDED AUDIENCE

The intended audience of this guidance document is the national regulatory authorities (NRAs) responsible for regulating medical devices.

4. SCOPE

The objective of this document is to provide specific information on considerations that regulators should take into account when assessing technical documentation for MNCH medical devices. It is intended as a complement to the set of AMDF guidelines on the regulation of medical devices as a resource to support regulators when regulating MNCH medical devices.

As considerations for the MNCH technical file assessment, this document:

- Defines the priority medical devices used by the MNCH population
- Identifies the types of information needed to provide assurance of the quality, safety, and performance of medical devices intended for use in pregnant women, newborns, and children
- Outlines key considerations for all stages of regulation of MNCH devices

5. MATERNAL, NEWBORN, AND CHILD HEALTH POPULATION AND USE

This document uses the following categories of the MNCH population groups and their unique characteristics for considerations for the regulation of MNCH medical devices.

Pediatric Population Subgroups

Table 1 provides the lower and upper age limits of the pediatric subgroups.

Table 1: Pediatric subgroups

Pediatric Subgroup	Age Range
Neonate	Birth–28 days
Infant	29 days to less than 2 years
Child	2 years to less than 12 years

https://www.fda.gov/medical-devices/products-and-medical-procedures/pediatric-medical-devices

Considering the scope of medical devices for use by neonates, newborns, infants, and children who are still in their growth phase, factoring in weight, body size, and physiological development may be more relevant than age, particularly for low-birthweight babies:

- Low birthweight: less than 2.5 Kg
- Very low birthweight: less than 1.5 Kg
- Extremely low birthweight: less than 1 Kg [22]

The characteristics of the pediatric population should be used by manufacturers in the development, design, and device target product profiling and referred to in device labeling and clinical studies.

Maternal Population

Maternal health includes pregnancy, childbirth, and postnatal health. This population suffers from a variety of medical conditions that may require the use of medical devices. The most common medical conditions include maternal injury, excessive blood loss, infection, pre-eclampsia and eclampsia, unsafe abortion, miscarriage, and obstructed labor. This demographic is complex because of consideration for both maternal and fetal well-being, and anyone dealing with the population needs to take into consideration the risks and benefits of a medical device to both the mother and fetus.

5.1 Specific Considerations for MNCH Medical Devices

Medical devices should be reviewed based on their intended purpose and for the populations that a device is intended for. However, some medical devices need customization to suit the needs of pregnant women, newborns, and children. For these medical devices, there are specific considerations that are unique to those populations that manufacturers, regulators, and users should be aware of.

The considerations can be divided into two groups:

- Unique characteristics of the maternal, newborn, and child populations or host characteristics
- Clinical studies considerations

Since pregnant women, newborns, and children are more vulnerable, specific measures need to be undertaken or put in place to protect the safety of study subjects. Adult devices may be inappropriate for use in pediatric subjects for a variety of reasons or may require specific design changes and/or labeling to accommodate their use in pediatric subjects. To ensure the safe use of MNCH devices, some additional parameters may need to be assessed as part of the clinical evidence data or information submitted by the manufacturer for devices intended for use in MNCH.

Considerations include:

- Height and weight
- Growth and development
- Disease or condition
- Hormonal influences
- Anatomical and physiological differences from the adult population
- Activity and maturity level
- Immune status

Some characteristics are unique to women, such as breastfeeding, postpartum health status, weight, and history of postpartum hemorrhage, or to both women and children, such as age (in the case of a preterm baby); size; organ development (e.g., among adolescent girls, breast development can affect the placement of medical devices); hormones; and level of comfort to afford the user a quality service.

When choosing medical devices for MNCH, consider:

The age of the pediatric population: Some medical devices may not be appropriate for use in certain pediatric subgroups, such as cochlear implants, which may not be advisable for use due to the size of the implant or may be inappropriate due to the stage of neurological development of the child.

- The size of the medical device: This is an important consideration for pregnant women, as the changing body weight and size may require the use of medical devices that can be adjusted to different sizes.
- The impact of the medical device on the growth of the newborn or child: Consider whether the child will outgrow the device and the procedure to remove or replace it, if there are adjustments to the device that may be necessary, what further interventions may be needed, and any impact of technological advances such as a new series of the device.

Surgical factors for implantable devices in a pediatric subgroup: These factors include the surgical site, anatomical landmarks, short- and long-term effects of the surgery and device, and special considerations pertaining to combination products with a drug/device interaction.

- Other human factors to address the invasiveness of the medical device to the newborn and child, including portability and ease of use.

5.2 Unique Host Characteristics

The factors listed below should be considered by regulators with respect to device design, clinical study design, and labeling for each segment of the population. Relevant subsets of the population of interest must be specified by the manufacturer in the intended use and indications rather than pooling them all into a single population.

Characteristics such as the subject’s weight, body size, physiological and neurological development, and neuromuscular coordination may be more appropriate when assessing the appropriate subpopulation for a device. In the design of the clinical trial or labeling for the device, age may be used as a preliminary approximator, but other factors should be considered to better define the appropriate population. [23]

Size

When reviewing clinical data, determine whether design modifications are appropriate based on subject size (e.g., weight, height, body mass, surface area). For example, pulse oximeters with wrap sensors and finger clips should be tested in different age groups but may be more dependent on size in premature newborns or small, malnourished children than on age.

Growth and Development

Manufacturers should have taken the following factors into account:

- The effect of the subject's growth on the device (e.g., will the child outgrow the device and, if so, at what rate?)
- Whether adjustments to the device are necessary to adapt to the child's growth
- The impact of technological advances on the device

This is relevant for assessing a CPAP and the compatibility of mask sizes and/or prong sizes for neonates using a CPAP, for example.

Body Physique

The following should have been considered in the design of the device:

- Normal and abnormal variations in the targeted group
- Normal anatomic landmarks for each subgroup and anticipated deviations based on the targeted population
- The impact of anomalies, particularly congenital anomalies

This could apply particularly to a nonpneumatic shock garment, which must fit each body type. If this has not been considered sufficiently in the design, there may be patients for whom it does not fit in application. Similarly, if transcutaneous bilirubinometers and pulse oximeters have not been tested on different skin colors, there may be problems in their use and reliability.

Developmental Milestones

The child's developmental milestones should be considered in the design of the device, including the impact of the device on the child's:

- Activity level
- Ambulatory status
- Maturity level
- Stage of puberty (e.g., breast development in preadolescents and adolescents may influence device placement)

These considerations are especially important for machines that are fitted to a child, such as an ambulatory blood pressure meter or ECG monitor. Not fully testing such devices on children with different levels of activity and maturity could result in unsatisfactory performance.

Pathophysiology

Regulators should check that manufacturers have considered the impact of the disease or condition on the pediatric patient and biocompatibility, including:

- Maturity or immaturity of various organ systems, including the immune system
- Impact of materials (e.g., latex allergies), chemicals, electromagnetic radiation, electrical stimulation, and other agents
- Hormonal influences (e.g., effects of puberty in the preadolescent and adolescent population)
- Short- and long-term effects of device use

Behavioral Factors

During trials, the expected behavior in the targeted pediatric subgroup and its potential impact on the device should have been considered. For example, an adolescent with a learning disorder may struggle to interact with certain devices, such as digital devices, and may require additional help or alternative therapy. This may be relevant for glucometers, for example, if they are too complex for young children to use.

Psychosocial Factors

For some devices used with the maternal, newborn, and child population groups, manufacturers should have considered psychosocial factors such as the family structure and environment, including how supportive family members are and who the primary caregiver will be, especially if the device is to be used at home.

Information for use of the device, with language translations to fit the population the device is to be used by, is key as is considering any cultural factors affecting use of the device.

Human Factors

Each subgroup will have different needs that should have been considered in the design and use of the device. Regulators should check that the applicable factors have been considered for newborn and child populations, including:

- Invasiveness of the device
- Optimal size of the device
- Manual dexterity and strength required
- Resistance to damage from wear and tear (durability). This is important to have tested under various conditions and with different age groups of children. For example, plaster of paris used in a cast may be resistant enough for an adult but may not withstand the wear and tear of a child’s use.
- Portability
- Clarity of the labeling and instruction for use
- Ease of use
- Level of interaction required for the proper functioning and use of the device
- Age-appropriate usability of the user, including age and maturity level needed to operate the device safely and effectively, particularly in adolescents, and with regard to placement, compliance, and use of the device.

Surgical Factors for Implantable Devices

Particularly for newborns and children, regulators should determine if the following have been studied and assess for:

- Surgical site and anatomical landmarks
- Surgical technique and level of expertise needed
- Short- and long-term effects of the surgery and the effect of the device on immune status, with a recommendation to update immunizations if indicated
- Special issues pertaining to combination products, such as the possibility of drug/device interactions
- The need for antibiotic prophylaxis

5.3 Guidance from the Manufacturer: Clinical Considerations

Evaluators should check that the manufacturer has applied risk management and provided adequate data. [24] Where possible, any clinical indication of a medical device to the maternal, pediatric, and/or newborn population requires clinical data to support its use in those populations. In some instances, the expected benefit and safety can be determined without carrying out separate studies in each subgroup; data obtained from one age group may be extrapolated to another age group. In other pediatric age group populations, such as neonates, clinical data gathered specifically in that subgroup will likely be needed. It is therefore recommended that a manufacturer provides proof that the necessary clinical trials have been undertaken and be prepared to provide data for each targeted subpopulation indication or a justification as to why data are either not needed or can be extrapolated.

Where these factors exist, conducting clinical trials will help ensure that manufacturers:

- Design the device properly for the intended population
- Perform accurate risk assessments
- Provide clear instructions for use

If the manufacturer has carried out clinical studies on the MNCH device, the labeling should present such information in a very clear, objective, and meaningful manner, and study results should be reported in a format that allows the user to easily recognize substantive differences in performance between children and adults and between various pediatric and maternal subgroups. Labeling should summarize these data using appropriate qualitative or quantitative analyses, recognizing that subgroups may be too small to show statistical significance using standard tests.

Where clinical studies are not available in consideration of the fact that legal and ethical challenges may exist for medical devices to be used by the MNCH population, a plan for post-marketing surveillance studies should be provided by the manufacturer, who should make the results available to the regulator within a specified time after release on the market.

Not all MNCH medical devices require clinical data to demonstrate safety, performance, and quality. There are different factors that come into play in the type of evidence required, such as the nature of the device, existing information about the product in the adult population, whether

these data can be extrapolated to the pediatric population, and the condition being treated or underlying disease.

In LMICs, the use of studies conducted in another population may be considered for presentation by the manufacturer for regulatory considerations.

In cases where a device has already been approved and indicated for the adult population and modified for pediatric use, the manufacturer should provide evidence that supports the modifications by conducting a risk analysis of the changes made and addressing any concerns to mitigate identified risks.

Another important factor to consider is that weight, body size, and physiological development all vary among the newborn and pediatric population and subpopulations and change as the child grows. Clinical data may be needed in the different groups to assess quality, safety, and performance. If appropriate, clinical data can be extrapolated between subpopulations.

Unlike medicines, medical devices present additional challenges due to the technology incorporated and their varying applications. For this reason, risk assessment and mitigation strategies should be put in place to determine the types of risks for each targeted pediatric subgroup. Consider the newborn's and child's age and degree of physiological maturity, the nature and natural history of the clinical condition to be treated, the presence of other conditions that may present complications, and the safety and effectiveness of the device that may have been demonstrated in adult population or other clinical investigations. [23] [24]

6. GENERAL PRINCIPLES OF MEDICAL DEVICE REGULATION

6.1 Risk Classes of Medical Devices and Classification Rules

Risk-based classification of medical devices is based on classification rules. [25] The rules depend on the features of the device, such as whether it:

- Is life supporting or sustaining
- Is invasive and, if so, to what extent and for how long
- Incorporates medicinal products
- Incorporates human or animal tissues or cells
- Is an active medical device
- Delivers medicinal products, energy, or radiation
- Could modify blood or other body fluids
- Is used in combination with another medical device

This informs the categorization of the device into one of four groups (table 2).

Table 2: Classification for MNCH medical devices

Class	Risk level and example
A	Low risk: pediatric nasal oxygen cannula
B	Low-moderate risk: electronic thermometer, pulse oximeter
C	Moderate risk: bilirubinometer
D	High risk for intensive care: ventilator with CPAP and accessories

Class A medical devices carry the lowest risk, while class D medical devices pose the highest risk to patient health and/or treatment according to the International Medical Devices Regulators Forum (IMDRF) classification.

The manufacturer determines the risk class of a medical device. Its decision may be reviewed and challenged by the regulator. In determining the device risk classification of an MNCH medical device, the manufacturer:

- Decides whether the product being considered is a medical device using the definition provided and provides evidence
- Documents the intended use of the medical device for the population of pregnant women, newborns, and children

Takes into consideration all rules to establish the proper classification for the device, noting that where a medical device has features that place it in more than one class, classification and conformity assessment should be based on the higher risk class indicated

- Determines whether the device is subject to national rules that apply within a particular jurisdiction for use in MNCH

Annex 1 provides an illustrative list of priority medical devices for use in maternal, newborn, and child populations to orient regulators on the devices for which registration should be prioritized.

6.2 Assessment According to Risk Class

Risk-based classification of medical devices focuses on the devices with the highest risk, and regulatory requirements get more stringent as the risk presented by the class of medical devices increases. The regulatory process for pre-market approval, market placement, and post-marketing surveillance for medical devices is different than that for medicines: where medicines are individually assessed for their efficacy and benefit/risk, medical devices are grouped into risk classes. For class A and B medical devices, the regulatory authority usually does not assess the technical documentation. [11] The regulatory authority relies on documentation provided by the manufacturer (i.e., the declaration of conformity). The challenge for NRAs is to establish, maintain, and enforce clear written guidelines on the risk-based classification and respective risk-based regulation of medical devices, including for MNCH, to manufacturers and importers.

6.3 Essential Principles of Safety and Performance

The regulation of medical devices encompasses principles of safety and performance that are in accordance with the standards of the IMDRF guidance documents [8] and the WHO Global Model Regulatory Framework for medical devices, including in-vitro diagnostics (IVDs) [9]. The Global Model Regulatory Framework provides guidance and support for the development and deployment of medical device regulatory controls.

Manufacturers of all classes of medical devices are expected to demonstrate conformity to the essential principles of safety and performance [8] through the preparation and holding of technical documentation that shows how each medical device is developed, designed, and manufactured together with the descriptions and explanations necessary to understand the manufacturer's determination with respect to such conformity. These technical documents are used to create summary technical documentation for submission to register the device for marketing.

The principles of safety and performance for medical devices used for newborns and children should be adjusted to accommodate the size, weight, and other requirements for design changes and/or specific labeling to accommodate their use in pediatric subjects. Where data have been extrapolated from the adult population, or where these data are not available, manufacturers should clearly indicate this in the technical documentation for regulatory assessment.

Not all essential principles may apply to MNCH medical devices. Table 3 summarizes essential principles of safety and performance that manufacturers of MNCH medical devices are expected to demonstrate in their marketing authorization application files. It is important that reviewers verify the manufacturer's declaration of conformity and evidence provided to demonstrate conformance to these requirements. Study reports or references from published studies may be used depending on the type of device and its intended use. Note that other rules may be applicable based on intended use declared by the manufacturer.

Table 3. Applicable essential principles for illustrative medical devices for use in common MNCH conditions

	Applicable essential principles								
MNCH Device	General	General Chemical, Physical, and Biological Properties	Considerations of Environment and Conditions of Use	Protection against Electrical, Mechanical, and Thermal Risks	Active Medical Devices and IVD Medical Devices and Medical Devices Connected to Them	Medical Devices and IVD Medical Devices that Incorporate Software or are Software as a Medical Device	Medical Devices and IVD Medical Devices with a Diagnostic or Measuring Function	Labelling	Protection against Radiation
Respiratory support for newborns and children									
Pulse oximeter	√	-	√	√	-	√	√	√	-
CPAP ventilator	√	√	√	√	-	√	√	√	-
Oxygen blender	√	√	√	√	-	-	√	√	-
Oxygen concentrator	√	√	√	√	-	√	√	√	-
Humidifier	√	√	√	√	-	-	√	√	-
Flow splitter	√	√	-	-	-	-	√	√	-
Suction pump	√	√	-	-	-	-	√	√	-
Devices unique to newborns									
Bilirubinometer	√	-	-	-	-	√	√	√	-
Phototherapy lights	√	-	√	√	-	-	√	√	-
Radiant warmer	√	-	√	√	-	-	√	√	-
Infant incubator	√	-	√	√	-	-	√	√	-
Mobile diagnostic ultrasound scanner	√	-	√	√	-	-	√	√	√
Devices unique to mothers									
Fetal doppler solar powered	√	-	√	√	-	-	√	√	√
Non-pneumatic anti-shock garment	√	√	-	-	-	-	-	√	-
Vacuum extractor	√	√	-	-	-	-	√	√	-
Cross-cutting diagnostic devices for mother, newborns, and children									
Blood pressure machine	√	-	-	√	-	-	√	√	-
Hemoglobinometer	√	-	-	-	-	√	√	√	-

6.4 Quality Management System

A QMS ensures that medical devices are designed and manufactured to meet safety, performance, and quality requirements during their lifetime. A globally used standard for a QMS for medical devices is ISO 13485. [26] The QMS should be appropriate to the specific characteristics of the manufacturer's processes and MNCH medical devices. The QMS is also important for controlling the collections of technical evidence used by the manufacturer in preparing the declaration of conformity. [9]

7. ASSESSING THE TECHNICAL DOCUMENTATION

To ensure the quality and performance of the medical device the NRA may opt for a full assessment of the technical documentation or using the reliance mechanism to issue a market authorization. [10]

7.1 Full Assessment for Compliance with the Essential Principles of Safety and Performance

When assessing the technical dossier of a medical device WHO recommends regulatory authorities around the world adopt international standards as the basis for national regulations and pre-market regulatory controls. The AMDF has developed a set of guidance documents to orient regulatory authorities on the requirements for an applicant when submitting a technical file for registration and market authorization and be in compliance with QMS requirements in accordance with ISO 13485, including a post-market surveillance plan, among others. The regulatory authority decides on the level of scrutiny in assessing the technical documentation based on the risk class of the medical device. [9]

These AMDF guidelines on regulatory requirements for medical devices are:

- Guidelines on regulatory requirements for issuance of marketing authorization of medical devices
- Guidelines for registration of medical device establishments
- Guidelines for importation and exportation of medical devices
- Guidelines for inspection of manufacturing sites for assessment of the quality management system of medical devices [28]

The AMDF guidelines enable NRAs to effectively assess the quality, safety, and performance of medical devices, including those for MNCH. [27]

Specific elements to be considered in the assessment of MNCH medical devices include:

- The design of the clinical investigation, including population characteristics (e.g., skin color for pulse oximeters)
- The adaptation of a medical device to the newborn and child population
- The different age groups in the newborn and child population
- Clinical evidence specific for the newborn and child population
- Supporting information from performance studies, clinical experiences, and post-market surveillance data specifically from use in the newborn and child population

Information to be Assessed: Specificities of MNCH Medical Devices

The following documents are submitted by the manufacturer [29] and assessed by the regulatory authority. This information does not differ from the evidence provided for medical devices in general but requires confirmation on specificities of the target population.

- Device description and features, including summary information about the product
- Device details (intended use, instruction for use, precautions, contra-indications) [30]
- Risk class of the medical device, with the technical file if applicable [11] [12] [31]
- Device specifications
- Essential principles checklist (table 3)
- Label and labeling information (see below)

7.2 Reliance for Medical Devices

WHO urges regulatory authorities around the world to economize their limited public health resources by relying on the conformity assessment results of other jurisdictions. Reliance facilitates timely access to safe, effective, quality-assured medical products and can support regulatory preparedness and response, particularly during public health emergencies. [10] Reliance and recognition are mechanisms for benefitting from the regulatory work of other jurisdictions. Reliance may take many forms and reflect varying degrees of application in recognizing or taking into account the assessments, decisions, or other authoritative information available from other authorities and institutions. Reliance and recognition include accepting regulatory decisions on pre-market assessments, inspections/QMS audits, and regulatory decisions made by authorities in other jurisdictions.

Information to be Assessed

- Device description and features, including summary information about the product.
- Device details (intended use, instruction for use, precautions, contra-indications) [30]
- Device description and intended use
- Device specifications
- Label and labeling information (see below)

8. SPECIFIC REQUIREMENTS FOR MEDICAL DEVICES FOR MNCH

8.1 Labeling

Basic Elements of Labeling

MNCH device labeling should follow the requirements laid out the IMDRF's *Principles of Labelling for Medical Devices and IVD Medical Devices* [6] and ISO 15223-1:2021, *Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements.* [32]

Device Description

Many devices and device accessories come in different models, sizes, shapes, and materials as well as different modes of operation and different levels of sophistication, all of which require varying degrees of user interface. The labeling should describe various options recommended for use in MNCH subgroups and, where feasible, present these options in tabular form by age, weight, or other appropriate criteria. For a device's description, the use of simple artwork in the demonstration for use of the device by the parent or caregiver serves as a valuable tool for information and proper guidance. [29]

Intended Use

If a medical device is intended for use in pregnant women, newborns, or children, the manufacturer should clearly define the indication(s) for use as well as the target population in the labeling. The indication may be in the form of general statements (e.g., cut, coagulate, ablate) or be very specific (e.g., determination of fetal heart rate). The target population who can use the device may be broad (e.g., children and adults of all ages) or narrowed to a specific population (e.g., infants between the ages of 6 and 9 months). The manufacturer should give adequate information and, when necessary, support the indication and targeted population(s) with appropriate data.

Contraindications, Warnings, and Precautions

Due to the vulnerability of the users of MNCH devices and other specific concerns, it is important that the labeling include contraindications, warnings, and precautions to provide clear descriptions and well-defined actions and consequences. Contraindications, warnings, and precautions should clearly address the risks associated with the age, size, and maturity of the pediatric subject or maternal population and alert the user to specific hazards associated with the use of the device in the target population.

Instructions for Use

Labeling information should include written instructions for the use of an MNCH medical device for the health care practitioner or caregiver to ensure safe and effective use. [6] This includes addressing anatomical, developmental, educational, and other age-related factors to help ensure proper use of the device and prevent avoidable device-related adverse events. Instructions for use directed to the parent or guardian or a health practitioner who acts as the immediate contact person should be labeled clearly, with pictorial illustrations where possible for less literate individuals.

Any instructions provided specifically for use by young children should be age-appropriate with respect to written language and other visual and auditory tools.

Labeling symbols should conform to IMDRF, ISO, and EN medical device standards:

- *Principles of Labelling for Medical Devices and IVD Medical Devices* [6]
- ISO 15223-1 Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements [32]

8.2 Post-Marketing Surveillance

Post-marketing surveillance for medical devices for MNCH follows the same guidelines and procedures as those developed by the NRA, with the manufacturer playing a key role. To act pro-actively, the manufacturer should develop a post-market surveillance plan, In the case of an MNCH medical device adverse event or incident, the manufacturer should investigate the adverse event or incident fully and, where necessary, consider the outcome of adverse event reporting in other jurisdictions and involve relevant public health departments responsible for MNCH. Similarly, any adverse event or incident reported for a medical device used in MNCH, from either a device malfunction or improper use, in addition to being reported to the regulatory authority should if appropriate undergo a field safety corrective action, and users should be informed through a field safety notice. The regulatory authority should consider including MNCH medical devices in its risk-based market surveillance plan. [33]

The manufacturer needs to establish whether reporting to the regulatory authority is required. Initial, follow-up, and final investigation reports should contain all details of any investigation conducted. [33]

Depending on the seriousness of the adverse event or incident, the manufacturer should submit the following within the indicated timeline. [33]

Table 4. What should be reported and the time to report to the NRA

What to report	Time to report to the regulatory authority
Serious public health threat	Immediately but no later than 48 hours
Death or serious deterioration in health of patient, user, or other person occurred	As soon as possible but no later than 10 calendar days
Death or serious deterioration in health of patient, user, or other person might have occurred	As soon as possible but no later than 30 calendar days

Further information to support the NRA in post-marketing surveillance and market surveillance can be found in the WHO reference guidance for medical devices.

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ANNEX 1: ILLUSTRATIVE ESSENTIAL MEDICAL DEVICE FOR USE IN COMMON MNCH CONDITIONS

While many devices are listed for use in MNCH,[1] this table lists the essential medical devices used for the majority of commonly encountered MNCH conditions and that should be accessible in health facilities. This is an illustrative list of prioritised devices to guide regulators but should not be considered an exhaustive list.

MNCH Medical Device	Risk Classification for Regulatory Use
Respiratory support for newborns and children	
Pulse oximeter (with wrap sensor for newborns)	B
CPAP ventilator	D
Oxygen blender	C
Oxygen concentrator	C
Humidifier	B
Flow splitter	B
Suction pump	B
Devices unique to newborns	
Bilirubinometer	C
Phototherapy lights (treatment of neonatal jaundice)	A
Radiant warmer	B
Infant incubator	B
Mobile diagnostic ultrasound scanner	B
Devices unique to mothers	
Fetal doppler solar powered	B
Nonpneumatic antishock garment	A
Vacuum extractor	B
Cross-cutting diagnostic devices for mothers, newborns, and children	
Blood pressure machine	B
Hemoglobinometer	B
Nasal tubes for oxygen administration	B

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