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Injection systems for self-administration by paediatric patients — Requirements and guidelines for design

Systèmes d'injection pour auto-administration par des patients pédiatriques — Exigences et lignes directrices relatives à la conception

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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This document was prepared by Technical Committee ISO/TC 84, *Devices for administration of medicinal products and catheters*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

An increasing number of therapies for paediatric use rely upon a drug delivery system for administration. However, many existing drug delivery systems in widespread use incorporate design features that might not conform with current thinking on human factors/usability engineering principles for use by the paediatric population or include some significant differences from those applicable to the average adult user population and other demographic groups. In some cases, these design features can result in incorrect use of the drug delivery system and unacceptable risks.

Therefore, guidelines on the design input to the development of drug delivery systems specifically intended for administration of medicinal products by paediatric users are relevant. Especially, guidelines are relevant for development of those devices where the paediatric user is performing some or all use steps. The guidelines in this document are dedicated to those products. Guidelines in relation to the development of products intended for administration of medicinal products by caregivers only are not covered by this document as those devices are developed for the average adult population.

Due to the variation of design of drug delivery systems, this document does not specify requirements for developing, assessing and evaluating drug delivery systems.

Manufacturers should follow a risk-based approach during the design and development of drug delivery systems serving the paediatric population.

Figure 1 summarizes the applicability of this document.

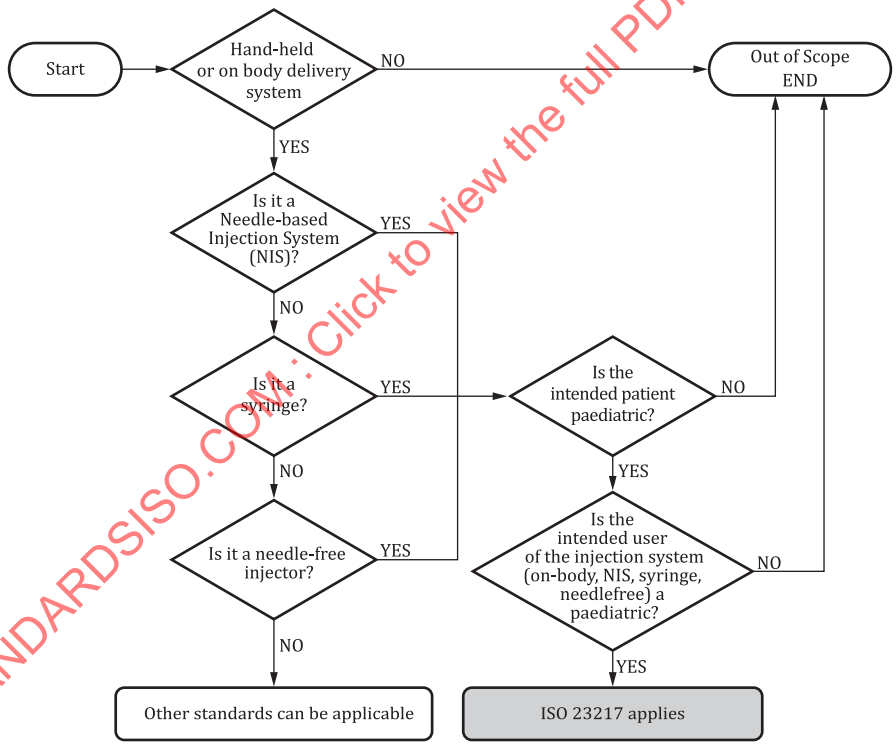

Figure 1 — Roadmap for the use of this document

Guidance on transition periods for implementing the content of this document is given in ISO/TR 19244.

Injection systems for self-administration by paediatric patients — Requirements and guidelines for design

1 Scope

This document provides requirements and guidelines on the development of drug delivery systems intended for self-administration of medicinal products by the specific demographic group of paediatric patients who are performing some or all use steps required for their intended use.

Use steps include any handling action performed after the patient has received the product; these can include but are not limited to:

— transport – carrying the product while travelling (e.g. by walking, train, airplane, automobile, bus);

— storage – storage by the patient in their home, school, office or in temporary storage cases before or between uses;

— preparation – steps necessary to place the product in a state where it is ready to be administered;

— operation – steps necessary to initiate, adjust, pause, stop, or otherwise manage the delivery of medication using the product;

— maintenance – steps necessary to keep the product in good working order;

— disposal – steps to ensure safe disposal of the product after use (e.g. placement of the product in a suitable receptacle).

This document is applicable to injectable drug delivery systems for administration of medicinal products. Furthermore, this document can be useful for the development of other drug delivery devices or systems if they are intended for use by the paediatric population. Devices not in the scope of this document include catheters, for example those in the scope of ISO 10555 series, and infusion pump systems, e.g. IEC 60601-2-24 and aerosol delivery devices (ISO 20072).

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

ISO 14971:2019, *Medical devices — Application of risk management to medical devices*

IEC 62366-1, *Medical devices — Part 1: Application of usability engineering to medical devices*

3 Terms and definitions

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

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
accompanying documentation
materials accompanying a medical device and containing information for the *user* (3.15) or those accountable for the installation, use and maintenance of the medical device, particularly regarding safe use

Note 1 to entry: The accompanying documentation can consist of the *instructions for use* (3.8), technical description, installation manual, quick reference guide, etc.

Note 2 to entry: Accompanying documentation is not necessarily a written or printed document but can involve auditory, visual, or tactile materials and multiple media types.

Note 3 to entry: Medical devices that can be used safely without instructions for use are exempted from having instructions for use by some authorities with jurisdiction.

[SOURCE: ISO 14971:2019, 3.1, modified — "decommissioning and disposal" have been deleted from the definition, and Note 3 to entry has been added.]

3.2
caregiver
non-professionals (e.g. family members, parents, guardians or friends) who provide care to the *patient* (3.11)

3.3
drug delivery system
medical device or system whose primary purpose is the administration of a medicinal product such as drugs and biologics

Note 1 to entry: This term applies to combination of components and subassemblies of the system that are intended to be integrated with the medicinal product with the purpose of providing a method of administration of the medicinal product.

[SOURCE: ISO 20069:2019, 3.1.2]

3.4
harm
injury or damage to the health of people, or damage to property or the environment

3.5
hazard
potential source of *harm* (3.4)

[SOURCE: ISO/IEC Guide 63:2019, 3.2]

3.6
health care provider
healthcare professional with proficient skills and experience with the use of a device so that they can aid or train patients and *caregivers* (3.2) to use and maintain the device

3.7
usability engineering
human factors engineering
UE/HFE
application of knowledge about human behaviour, abilities, limitations, and other characteristics to the design of medical devices (including software), systems and tasks to achieve adequate *usability* (3.13)

Note 1 to entry: Achieving adequate usability can result in acceptable *risk* (3.19) related to use.

[SOURCE: IEC 62366-1:2015, 3.17]

3.8
instructions for use
IFU
directions provided by the manufacturer for the correct handling and operation of the *drug delivery system* (3.3)

[SOURCE: ISO 11608-1:2022, 3.10, modified — “needle-based injection system” replaced with “drug delivery system”.]

3.9
intended use
use specification
intended purpose
use for which a product, process or service is intended according to the specifications, instructions and information provided by the manufacturer

Note 1 to entry: The intended medical indication, patient population, part of the body or type of tissue interacted with, *user profile* (3.17), use environment, and operating principle are typical elements of the intended use.

[SOURCE: ISO/IEC Guide 63:2019, 3.4, modified — the preferred terms "use specification" and "intended purpose" have been added.]

3.10
paediatric
relating to children and/or adolescents

Note 1 to entry: The definition of paediatric varies by region and organization. See Annex A for different organizations’ classifications of “child” and “adolescent”.

3.11
patient
person undergoing a medical, surgical, or dental procedure

3.12
self-administration
process by which the *patient* (3.11) enters medication into their own body

3.13
usability
characteristic of the *user interface* (3.16) that facilitates use and thereby establishes effectiveness, efficiency and user satisfaction in the intended use environment

Note 1 to entry: All aspects of usability, including effectiveness, efficiency, and user satisfaction, can either increase or decrease safety.

[SOURCE: IEC 62366-1:2015, 3.16]

3.14
use error
user (3.15) action or lack of user action while using the medical device that leads to a different result than intended by the manufacturer or expected by the user

Note 1 to entry: Use error includes the inability of the user to complete a task.

Note 2 to entry: Use errors can result from a mismatch between the characteristics of the user, *user interface* (3.16), task, or use environment.

Note 3 to entry: Users can be aware or unaware that a use error has occurred.

Note 4 to entry: An unexpected physiological response of the *patient* (3.11) is not by itself considered use error.

Note 5 to entry: A malfunction of a medical device that causes an unexpected result is not considered a use error.

[SOURCE: IEC 62366-1:2015, 3.21, modified — Note 6 to entry has been deleted.]

3.15
user
person interacting with (i.e. operating or handling) the medical device

Note 1 to entry: There can be more than one user of a medical device.

Note 2 to entry: Common users include clinicians, *health care providers* (3.6), *patients* (3.11), *caregivers* (3.2).

[SOURCE: IEC 62366-1:2015, 3.24, modified — Note 2 to entry has been changed.]

3.16
user interface
means by which the *user* (3.15) and the medical device interact

Note 1 to entry: User interface includes all the elements of the medical device with which the user interacts including *accompanying documentation* (3.1), packaging, and the physical aspects of the medical device as well as visual, auditory, tactile displays and is not limited to a software interface.

Note 2 to entry: A system of medical devices can be treated as a single user interface.

[SOURCE: IEC 62366-1:2015, 3.26, modified — Note 1 to entry has been deleted.]

3.17
user profile
summary of the mental, physical and demographic traits of a *user* (3.15) group, as well as characteristics, such as knowledge, skills and abilities, which can have a bearing on design decisions

[SOURCE: IEC 62366-1:2015/Amd 1:2020, 3.29]

3.18
residual risk
risk (3.19) remaining after *risk control* (3.21) measures have been implemented

[SOURCE: ISO/IEC Guide 63:2019, 3.9]

3.19
risk
combination of the probability of occurrence of *harm* (3.4) and the severity of that harm

[SOURCE: ISO/IEC Guide 63:2019, 3.10, modified — Note 1 to entry deleted.]

3.20
risk analysis
systematic use of available information to identify *hazards* (3.5) and to estimate the *risk* (3.19)

[SOURCE: ISO/IEC Guide 63:2019, 3.11]

3.21
risk control
process in which decisions are made and measures implemented by which *risks* (3.19) are reduced to, or maintained within, specified levels

[SOURCE: ISO/IEC Guide 63:2019, 3.12]

3.22
risk evaluation
process of comparing the estimated *risk* (3.19) against given risk criteria to determine the acceptability of the risk

[SOURCE: ISO/IEC Guide 63:2019, 3.14]

4 Considerations for design inputs

4.1 General

The specific requirements that shall be fulfilled for a specific demographic population can partly be developed by applying the risk approach (see 4.2.1) and usability engineering (see 4.2.2) specified in applicable standards.

4.2 Risk assessment and usability engineering

4.2.1 Risk assessment

The manufacturer shall perform risk analysis, risk evaluation, risk control and an evaluation of residual risk acceptability in accordance with ISO 14971.

4.2.2 Usability engineering

A usability engineering program in accordance with IEC 62366-1 shall be applied. It shall include addressing use risks and tests and/or assessments throughout the development and as part of the design verification and design validation.

4.3 Considerations for the determination of requirements for the design of medical devices specific to paediatric users

4.3.1 Considerations in relation to risk (risk-based approach to design)

The risk assessment in accordance with ISO 14971 shall take into account the characteristics of the paediatric users including use risks in accordance with IEC 62366-1. See Table A.4 for examples of potential use errors.

4.3.2 Considerations in relation to human factors

4.3.2.1 General

During the design and development of a drug delivery system intended for self-administration by paediatric users, the intended uses, intended user profiles, and use environments shall be identified and clearly defined.

Based on the human factors' considerations, the requirements for the medical device shall be documented.

NOTE 4.3.2 highlights aspects of the HFE/UE process defined and documented in IEC 62366-1 that require special attention when developing drug delivery systems for paediatric use.

4.3.2.2 Characterization of the intended use

4.3.2.2.1 Intended user profiles

The socio-economic environment, cognitive and physical development, age and aptitude of the intended user shall be defined. Within the population of paediatric users, variation can be expected in terms of size, strength, stamina, skeletal maturity, coordination (e.g. gross and fine motor skills), visual, tactile, auditory and perceptual capabilities, emotional maturity, motivation, decision-making abilities and the impact of their medical condition on their ability to use the drug delivery system safely and effectively. Furthermore, if it is anticipated that a paediatric user needs the support of a healthcare provider or caregiver to use the drug delivery system, the limitations and capabilities of adult users shall also be defined.

4.3.2.2.2 Intended use environment

The environment of intended use shall be characterized. Paediatric users tend to lead active lifestyles and so some medical products are used outside of the home (e.g. at school or on sports fields). During these use

scenarios they can be exposed to environmental factors (e.g. bright sunlight or excess temperatures) or used in a non-private setting.

4.3.2.3 Use-related risk

Manufacturers shall identify hazard-related use scenarios in accordance with IEC 62366-1, including potential use errors that can occur, identify known or foreseeable hazards and hazardous situations, and ensure that they are adequately controlled. When identifying and evaluating use-related risk, the content of the intended use shall be defined, and for drug delivery systems that are similar to the one under development with regard to use, the user interface or user interactions shall be analysed. The source of identification of potential use errors and risks can include human factors evaluations, literature research, and market experience.

4.3.2.4 User interface

4.3.2.4.1 General

When developing user interface requirements, the following aspects shall be evaluated.

It shall be evaluated how risks can be suitably controlled through the design of the drug delivery system including its associated materials. As covered in ISO 14971:2019, 6.2 the manufacturer shall use one or more of the following risk control options in the priority order listed:

a) inherent safety by design;

b) protective measures in the medical device itself or in the manufacturing process;

c) information for safety.

4.3.2.4.2 Design attributes

The characteristics of the paediatric user shall inform the design and development of a drug delivery system.

General drug delivery system design considerations are given in Table 1.

4.3.2.4.3 Training

While it is preferable to control risks through drug delivery system design, including associated materials, in some circumstances, mitigation by design alone can be insufficient for a paediatric population. In these situations, it can be appropriate to employ a training program. If training is a necessary component to mitigate risk of the drug delivery system, the manufacturer shall validate the effectiveness of the training program and justify how it is representative of the training that will be provided in commercial use of the drug delivery system.

The manner in which the training will be consistently implemented in the field shall be defined, however the risk of users not being trained shall also be assessed. For example, lay caregivers can learn how to use the system by observing a patient or another lay caregiver, and health care providers might not be directly trained.

4.3.2.4.4 Experience and knowledge of similar or other drug delivery systems

Paediatric users vary in their experience of managing their medication and of using similar drug delivery systems. Similarly, the knowledge and experience of their supporting health care provider or caregiver also vary. Therefore, the impact that both positive and negative knowledge transfer can have on safe and effective use of the drug delivery system shall be evaluated.

4.3.2.4.5 Dose regime

The medical condition and thus dosing regimen can influence the drug delivery system design and shall be evaluated in relation to managing complexity.

For example, whether:

— the medication is a fixed dose or requires the user to set the required dose;

— training information is retained (e.g. if the medication is administered infrequently);

— the medication shall be given very frequently and/or at a fixed time of day, in a home environment or elsewhere.

4.3.2.4.6 Transportation, storage, preparation, operation, maintenance and disposal by the user

Requirements for transportation, storage, preparation, operation, maintenance and disposal of the drug delivery system shall be defined. E.g. if the medication is stored under refrigerated conditions, the circumstances under which temperature excursions can occur shall be identified when describing potential use scenarios.

Table 1 — General drug delivery system design considerations

User interface interaction characteristics		Disease conditions impact	Paediatric design	
			Considerations	Illustrative examples
Perception (**sensory**)	— **Sight** (field of view, colour, contrast, acuity). — **Hearing** (sound detection, speech discrimination, localization). — **Touch** (including proprioception).	Certain disease conditions/disabilities can affect: — **visual capabilities** (e.g. low vision, myopia, etc.) and cause defective vision (e.g. colour blindness, etc.); — **hearing capabilities** and cause deafness; — **touch disorders** or cause other impairments that can affect the ability to use touch (e.g. affecting tactile pressure).	— Design (including instructions for use materials) shall be based on children's senses, limitations and preferences. — Design shall use appropriate senses for informing/feedback. — Design shall use simple and age appropriate language. — Design shall provide age appropriate affordance. NOTE Design affordance is an aspect of a device which directs how it is used. — Design shall consider familiarity with other model(s) of device(s) and build design on child's previous knowledge/ experiences.	— Children who have visual difficulties and language limitations can benefit from warnings they can hear. Avoid complex wording and ensure appropriate speed. — Identify which sense(s) can be used for informing when a dose is fully administered, or understand if speech-based warnings for potentially hazardous situations[35] are needed to alert children who do not read easily. — Avoid complexity or too distractive systems. — Children who have visual difficulties or touch disorders can benefit from design of appropriate protective measures for needle, etc. — Adjust font size(s) in screen(s) and instructions for use for legibility. When using colour to convey information to children with colour deficiencies, for example, locate important information in the same place each time it is presented[35].

Table 1 *(continued)*

User interface interaction characteristics		Disease conditions impact	Paediatric design	
			Considerations	**Illustrative examples**
Cognitive **(processing)**	— **Attention** (concentration). — **Recognition** (familiarity with technology, health literacy, training). — **Language and communication** (literacy, verbal, nonverbal). — **Problem solving**. — **Memory** (working, long term).	— Certain **disease conditions/disabilities that can cause hyperactivity, impulsive behaviour, attention spans** (e.g. Attention Deficit Hyperactivity Disorder) **or any cognitive development problem**. — **Complexity of treatment, dose regimen, frequency of use, use environment** (e.g. does the paediatric patient have to take different doses of a solution at different times during the day?).	— Design shall consider that children can have attention span limitations when using a device. — Design shall consider children's familiarity with other model(s) of device(s) and/or their previous knowledge/experiences that can influence their cognitive abilities when using the device. — Design shall avoid labelling characteristics that can lead children to believe that the product is safer than it really is. — Design shall consider that young children might not be able to understand the ramifications of an action taken when using a product (e.g. a warning) or can just explore a range of potential uses for an object[35] [41][42]. — Design shall consider that information or warnings can produce unintended effects if they are misunderstood. — Design shall use unambiguous and adapted language. — Design shall consider inter and intra age group differences: children can change rapidly.	— Present children with short, succinct tasks rather than long ones or make warnings "stand out" in order to capture children's attention. — Guide the child's steps to use the product such as providing adequate dose completion notification. — Avoid any abstract pictogram or symbol which can be misunderstood by children. Ensure that they are noticeable and comprehended by the children; e.g. the skull and crossbones pictogram can be interpreted as "pirate food" instead of "poison"[35]. — Children can be mistakenly attracted to dangerous products due to characteristics of the products packaging including colour, the container's shape and the presence of symbols or other characteristics[35]. — For older children or adolescents, warnings that include explicit language can be more effective and warnings can be especially valuable when combined with verbal warnings and instructions[35][41][42]. — What is intuitive for an 8-year-old might not be intuitive for a 6-year-old or even for another 8-year-old with a different background or maturity level[35].

Table 1 *(continued)*

User interface interaction characteristics		Disease conditions impact	Paediatric design	
			Considerations	**Illustrative examples**
Emotional and psychological **(Attitude)**	— **Attitude**: positive, neutral, or negative feeling toward the system. — **Motivation**: low, moderate or high due to interest, fear (injection, pain, etc.), adherence or compliance to the system. — **Patience**: patience or impatience expected in accomplishing goal. — **Expectations**: kindness and reasonableness. — **Stress level**: high, some, or no stress generally resulting from task performance. — **Socio-economic and cultural influence** (family context, country, community, etc.).	— **Patient education and training** (e.g. asthma care requires a partnership between the child, their parents and the health care professional. Patients need to know about the causes of their disease, causes of exacerbations and, perhaps most importantly, how to use the prescribed medication and device reliably)[33]. — **Severity of the disease conditions** (e.g. does the child see a direct impact from taking the medicine? How tolerable it is for the child?). — **Chronic vs. periodic disease**; chronic diseases (e.g. asthma, diabetes, etc.) or periodic/intermittent diseases. This can influence the ability to comply with a therapy. — **Complexity of dose regimen, frequency of use, use environment** [e.g. does the child have to take the medicine at lunch time (e.g. at school)?].	— Design shall consider that the socio-economic and cultural environment can be favourable or unfavourable to the use of the device. — Design shall consider children attitude/preferences towards the treatment and his disease. — Design shall consider children's familiarity with other model of device(s) and/or their previous knowledge/experiences that can influence their attitude towards the proposed system. — The drug delivery system shall be designed in a way that children can use them safely and fearlessly.	— How do parents/legal guardian care for the paediatrics? Are they involved in the treatment? Does their environment distract them and how does that affect the use of the device? — The treatment compliance is known to be an issue for some children with chronic disorders, particularly those that do not result in immediate discomfort when scheduled doses are missed or delayed. — Engage the child by opting for an appropriate, appealing, personalized design. — Children can fear needles or pain, therefore consider using a system that hides the needle, needle shielding, etc.

Table 1 *(continued)*

User interface interaction characteristics		Disease conditions impact	Paediatric design	
			Considerations	**Illustrative examples**
Physical **(action)**	— **Anthropometrics** (body size, hand size, skin thickness, etc.). — **Strength** (grip, push, pull, etc.). — **Flexibility** (achievable and comfortable postures). — **Dexterity** (acceptable forms and operations). — **Reach** (acceptable heights and offsets).	— Certain **disease conditions/disabilities can affect children's hand skills** which affects their engagement in manipulative activities (e.g. arthritis, musculoskeletal disorders). — **Severity of the disease conditions** (e.g. does the disease impact hand strength? How does that impact the daily life? Is it physically tolerable?). — **Chronic vs. periodic disease**; chronic diseases (e.g. asthma, diabetes, etc.) or periodic/intermittent diseases. This can influence physical capabilities. — **Dosing regimen, formulation and accuracy** (e.g. does the child have a fixed dose or variable dose? The dose regimen/volume is often based on weight and development).	— Design shall consider children's body anthropometrics to ensure safe and effective delivery. — Design shall consider disabilities or pre-existing musculoskeletal disorders, age, gender, stature, and physical activity levels. Consider what is "physically tolerable" for the paediatric patient when designing a drug delivery system. — Design shall consider children's familiarity with other model of device(s) and/or their previous knowledge/experiences that can influence their actions/physical abilities when using the device. — Design shall consider cultural differences and differences within and among age groups.	— Children's injection sites and skin thickness input help to ensure the dose can be administered effectively and safely; also consider the injection depth, the adequate needle length and whether there is a specific injection angle to apply. — Are there required physical capabilities that child has to have to maintain a precise posture while injecting?[35] — Is the child physically able to manipulate the system and to which extent is the child able to grip the drug delivery system? — How much strength does the child need to remove a needle cap? How is the child expected to open the packaging and use the drug delivery system?

Based on the attribute considerations noted in Table 1, the requirements for the medical device specific for the population shall be documented as described in ISO 13485.

4.3.3 Considerations for accompanying documentation

Drug delivery system markings and instructions for use (IFU) text and illustrations shall be understandable by the paediatric user. It can be necessary to include additional documentation intended for the caregiver, e.g. a medication guide, to supplement the IFU. A lowest common denominator of literacy level shall be assessed and used. It should be recognized that there can be 'subpopulations' within the population (see Annex A) and that, based on the paediatric user's physical development, self-administration, no matter how simple the instructions are, may not be appropriate. Consider use of additional electronic labelling, e.g. animation with demographically-relevant simulation.

Different complexities for IFU and markings shall be age appropriate and developmentally appropriate, e.g. instructions, explanations, drug delivery system accessories that use age appropriate language and visual aids/graphics. This includes:

— marking on the drug delivery system (e.g. accuracy of graduations) in accordance with relevant product standards;

— marking on the user packaging and/or unit packaging;

— legibility;

— IFU;

— information provided in electronic format that matches the validated labelling.

5 Development of the design

The manufacturer shall plan and control the design and development of the device based on:

— the requirements specified in ISO 13485;

— continuation of a risk-based approach in accordance with ISO 14971, which shall be performed in relation to risks that can arise given the application specifically to the intended user population;

— continuation of usability engineering in accordance with IEC 62366-1.

The manufacturer shall establish appropriate design and engineering specifications (e.g. assembly and component drawings, test and inspection criteria), such that the device exhibits the necessary form, fit and function design attributes to suit the intended patient demographic population. Examples of such attributes are provided in Table A.2. The chosen specification shall be justified and documented in the technical file. Additional engineering specifications can be required based on the device design.

Design and development and risk approach documentation shall be maintained and updated as the design and development progresses.

Preference shall be given to mitigating risks by design or process rather than by providing training alone, marking, warnings, labelling and IFU, since the risk mitigation by these tools can be less effective.

It shall be recognized that there can be 'populations' or 'subpopulations' where the risks associated with self-administration are not acceptable no matter how simple the instructions and design are.

NOTE ISO 13485 specifies requirements for design and development planning and execution. The risk approach can be derived from ISO 14971, which specifies requirements for risk management in relation to medical devices.

6 Design verification and validation

6.1 General

The manufacturer shall plan and execute the design verification and validation of the product based on:

— the requirements specified in ISO 13485;

— completion of a risk-based approach including risk analysis, risk evaluation, risk control, evaluation of residual risk acceptability in accordance with ISO 14971:2019, Clauses 4 to 8, which shall be performed in relation to risks that can arise given the application specifically to the intended users;

— completion of usability engineering in accordance with IEC 62366-1.

6.2 Design verification

The final design shall be fully verified including those specifications developed for the intended users.

NOTE If considering a specific demographic as part of a change to an existing design, then verification data for the existing design can be supplemented with justifications, risk assessments and/or by new verification testing for the new attributes/specifications alone.

6.3 Design validation

6.3.1 General

The final design of the drug delivery system shall be validated to ensure that the product can meet the requirements for the specified application or intended use.

If considering a change to an existing design to enable use by intended paediatric users, then validation data for the existing design shall be supplemented with justifications, risk assessments, and/or by new validation testing.

The drug delivery system labelling shall be validated for safe and effective use by simulated use testing that involves users of the intended population.

NOTE Validation can include data from other sources than usability and clinical studies such as clinical evaluations, market experience, literature, etc.

6.3.2 Usability evaluations (also known as usability tests or user studies)

Formative and/or summative evaluations shall be conducted as part of a drug delivery system development in accordance with IEC 62366-1 to demonstrate the safe and effective use of the drug delivery system and associated materials. When conducting such evaluations with paediatric users, the following aspects shall be assessed:

a) Informed consent
Paediatric patients are largely unable to legally provide informed consent and are dependent on their parent/legal guardian to consent to participation in a usability evaluation.

b) User groups
Users can vary considerably in terms of aspects that can influence the use of a drug delivery system. It can therefore be necessary to identify separate user groups differentiated by characteristics as noted in Table 1; e.g. for paediatric users, consider use of the drug delivery system by the user as well as by lay caregivers (e.g. the user's parent/legal guardian).

c) Support involvement
Depending on the nature of the usability evaluation and the user profile (e.g. age, disease conditions), it can be necessary to involve both paediatric users and lay caregivers (e.g. the user's parent/legal guardian) in the evaluation session. It is acceptable for paediatric users to be accompanied and/

or assisted by e.g. their parent/legal guardian if this is representative of the drug delivery system's intended use environment and end users. Observing the representative users operating the drug delivery system realistically will help understand the safety and effectiveness of use. The evaluation shall be designed to ensure a simulation as realistic as possible, and to enable feedback from both the lay caregiver and the paediatric user.

d) Recruitment
The recruitment of paediatric users can be conducted through parents or legal guardians rather than directly, depending on the age of the paediatric user and local laws/regulations. The recruitment of paediatric users can take longer than recruiting adults, users can be less likely to attend their scheduled interview (e.g. due to a change in circumstances) and evaluation sessions can be conducted from late afternoon (i.e. after school and school activities).

e) Simulated use environment
The environment simulated during the usability evaluation shall be representative of the intended use environment and be accommodating for the specific population being evaluated. The parent/legal guardian can bring along paediatric users' siblings to the evaluation session as well; therefore, consider hosting the nonparticipants in a separate room for the duration of the evaluation session.

f) Evaluation session
Paediatric users can quickly get tired and be less focused on directed tasks than adults are. They can also act more impulsively and say things they do not really mean. Therefore, consider adapting the evaluation session duration, administration style and vocabulary to be suitable to the specific user.

6.3.3 Clinical evaluation

Clinical evaluations for drug delivery systems are typically fulfilled through drug clinical studies along with evidence from literature searches and post-market information. It is generally expected that for most products, human factors simulated-use evaluations will be sufficient to assess the adequacy of the user interface and actual use (i.e. clinical studies) are not necessary.

The applicability of existing clinical data (i.e. previously conducted clinical data and/or clinical literature) to the intended population shall be evaluated. When conducting new clinical studies, special attention is required to protect the rights of the study participants and shield them from undue risk.

NOTE When new clinical studies will be conducted for a paediatric drug delivery system, they will likely be conducted under drug clinical requirements. In such cases, the guidance in ICH E11(R1)[26]: Clinical Investigation of Medicinal Products in the Paediatric Population can be applied as well.

a) Informed consent
Paediatric patients are largely unable to legally provide informed consent and are dependent on their parent/legal guardian to consent to participation in a clinical study.

b) Support involvement
Depending on the nature of the study and the intended user profile (e.g. age, disease conditions), it can be necessary to involve both paediatric users and lay caregivers (e.g. parent/legal guardian). Depending on the situation, paediatric users may be assisted by their parent/legal guardian if this is representative of the use environment and end users. If it is expected during the clinical study that the paediatric user will use the drug delivery system at home, consider the intended population user profile (e.g. age, disease conditions), what training to provide, and whether the user requires support from a lay caregiver to use the device safely and effectively.

c) Feasibility and recruitment
Paediatric clinical studies often face significant challenges to their feasibility, including limited patient pool for recruitment and limited centres with the experience and/or interest to conduct paediatric research. To enhance the participation, acceptability, and recruitment of a paediatric clinical study, consider the anticipated experience of paediatric patients and their parent(s)/legal guardians, such as

the emotional, physical, and convenience burden of study participation, and, where possible, solicit the input of paediatric patients and their caregivers.

Recruitment of paediatric users from specific populations can be done through parents or legal guardians rather than directly, depending on the age of the paediatric user and local laws/regulations. An attempt shall be made to include individuals representing the demographic of the disease unless there is valid reason to the contrary as justified by risk assessment. The recruitment of paediatric participants can take longer than recruiting adults.

d) Minimizing risk
As paediatric populations represent vulnerable study populations, every effort shall be made to minimize study risks. This includes making every effort to anticipate and reduce known risks, training users on how to use the drug delivery system, ensuring study personnel are aware of potential side effects prior to the study, and using study personnel that are experienced in studying paediatric populations.

e) Minimizing distress
Many procedures can be intimidating or painful to paediatric populations. Distress can be minimized by designing and conducting studies by personnel experienced in the treatment of paediatric patients. Practical steps shall be arranged to ensure a positive patient experience and to minimize discomfort and distress, such as using study personnel experienced in working with paediatric patients, using a physical setting appropriate for the age group, using study procedures that minimize the opportunity for pain or distress (e.g. collection of protocol specific measurements with routine clinical samples).

f) Extrapolation
When extrapolating clinical data for the purposes of validation, the factors that can result in different responses that can impact the applicability of the data from one population to another shall be evaluated. These factors shall include both intrinsic (e.g. developmental) and extrinsic (e.g. educational, regional) aspects. These considerations are applicable when extrapolating from adult to paediatric groups or from one paediatric subgroup to another paediatric subgroup.

g) Long-term studies
When clinical studies are conducted over a significant time span (e.g. over a year or multi-year), the possible change in maturity and competence of the paediatric patient as they advance in age, including impacts with regards to product administration and labelling, shall be evaluated.

Annex A
(informative)

Additional considerations for the “paediatric population”

A.1 General

This annex provides guidance specifically for the development of drug delivery systems intended for administration of medicinal products to paediatric patients who are performing some or all use steps required for its intended use.

Guidance for the development of products intended for administration of medicinal products to the paediatric group by caregivers only are not covered by this annex as those devices are developed on the premises of the average adult population. However, the guidance in this annex is useful to consider when developing products for a broader user group as well.

A.2 Paediatric population

A.2.1 Overview of different definitions of paediatric population

The organization should define the relevant paediatric population. Different classifications of the paediatric population exist. Table A.1 and Figure A.1 give an overview of classifications established by some organizations.

The paediatric population has different sub-classifications and different organizations have determined such classifications, primarily by age categories.

The aspect of self-injection excludes the youngest groups of the paediatric population (neonates, infants, and toddlers). Classification by age groups alone might be insufficient due to the variation in child development.

Table A.1 — Overview of definitions of the paediatric population

Organization	Paediatric classification
Centers for Disease Control and Prevention (CDC)[25]	Infants: 0 years to 1 year Toddlers: 1 year to 3 years Preschoolers: 3 years to 5 years Middle childhood: 6 years to 11 years Young teens: 12 years to 14 years Teenagers: 15 years to 17 years
US Food and Drug Administration (FDA)[22]	Neonates: birth to 28 days of life Infants: 29 days to 2 years Children: 2 years to less than 12 years Adolescents: 12 years to 21 years (not including 22nd birthday)
World Health Organization (WHO)[23]	Neonates: 0 days to 30 days Infant: 1 month to 2 years Young child: 2 years to < 6 years Child: 6 years to < 12 years Adolescent: 12 years to 18 years
Paediatric Regulation (EMA)[24]	Children: 0 years to17 years
ICH E11 (R1)[26]	Preterm infant: < 0 days Term newborn infant: 0 days to 27 days Infant and toddler: 28 days to 23 months Children: 2 years to 11 years Adolescents: 12 years to 16–18 years
American Academy of Paediatrics (AAP)[27]	Infancy: birth to 2 years Childhood: 2 years to 11 years Early adolescents: 12 years to 14 years Middle adolescents: 15 years to 17 years Late adolescents: 18 years to 21 years

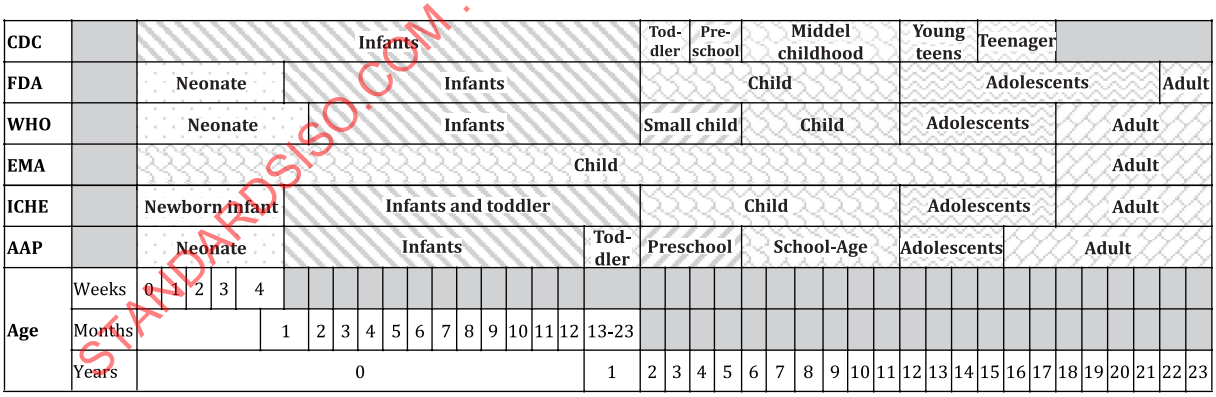

Figure A.1 — Graphical representation of classifications of paediatric population

A.3 Development milestones

A.3.1 General

Developmental milestones are approximate indicators of growth and developmental progress in children and adolescents. However, when a child experiences acute or chronic illness, developmental milestones can be altered, delayed, or missed altogether. Therefore, when considering the developmental milestones described

below, it is recommended to keep in mind that both the child's chronological age and development along with the specific disease can impact the physical and psychosocial trajectory as well as the achievement of these milestones. Consequently, the design and development of a drug delivery system should consider the individual child, the child's age group, and any disease-specific issues that can impact the stage of development and the patients' ability to successfully use the drug delivery system.

Table A.2 lists design attributes of drug delivery systems that should be addressed for the specific patient demographic population for which a design specification should be created. These attributes, while applicable to all demographic populations, are particularly important to the paediatric one.

NOTE 1 There are instances where relevant requirements related to the age group(s) are not specified in the appropriate International Standards, e.g. in the ISO 11608 series.

NOTE 2 Content in A.3.2 – A.3.6 was sourced from the Centers for Disease Control and Prevention (CDC). Reference to materials does not constitute the endorsement or recommendation by the US Government, Department of Health and Human Services, or the CDC. Material is otherwise available on the CDC website at no charge.

Table A.2 — Design attributes to consider for a drug delivery system for paediatric patients

Classification	Design attribute	Examples
Form/fit	Size/shape/ volume	— Consider if the device size is appropriate for handling based on the anthropometric needs and range of motion of the intended user population, including but not limited to; device circumference, total length, plunger rod reach for manual device, available surface area for injection site selection or application of device. — Consider if design utilizes small parts that can be unintentionally swallowed. — Consider if dose volume is appropriate for intended user population and delivery location.
	Markings/ aesthetics	— Consider whether markings and warnings are appropriate for the intended users, taking into account choice of language, vocabulary and symbols based on expected literacy levels. — Consider how aesthetic design elements can be perceived by the intended users, to ensure the device is unthreatening while not being perceived as a toy.
	Material selection	— Consider whether the materials selected for the device are appropriate for the intended patient population. Specifically, consider skin sensitivity, adhesive strength, material toxicity pertaining to ingestion. — Consider if alternative or more durable materials are necessary based on intended use environment, storage or transport.
	Dimensions	— Consider if the injection depth and other needle attributes of the device have been appropriately specified based on the target delivery location. — Consider if access to sharps in safety mode has been appropriately specified for the intended user population in accordance with ISO 23908:2011, Annex B.
	Time	— Consider if time to inject dose (Injection time) has been appropriately specified, taking into account both injection tolerability as well as feasibility of hold times throughout duration of delivery. — For injections that occur over longer timespans and can involve On Body Delivery Systems (OBDS), consider if design needs to accommodate for increased movement of the patient throughout the delivery.
NOTE Design attributes and associated examples in table are not comprehensive. The inclusion of specific examples into the table does not necessarily mandate changes to the associated Design Requirements or Specifications due to use with a paediatric population.		

Table A.2 *(continued)*

Classification	Design attribute	Examples
Function	Force	— Consider if the pull force to remove the cap is appropriate for the intended users. — Consider if the push and/or holding force to activate and deliver the device is appropriate for the intended users. — Consider if the peel force to remove adhesive patch or open device packaging is appropriate for intended users.
	Feedback	— Consider if visual, audible and/or tactile feedback mechanisms are appropriate for intended users based on existing mental models and interpretations, including but not limited to; tone or type of audible cues, speed of cues, expected reaction time to visual, audible and/or tactile cues.
	Device complexity	— Consider if complexity of device preparation and use steps are appropriate for the intended users, taking into consideration factors such as age, dosing frequency, intended training or oversight. — Consider if accessories required to support therapy are appropriate or if new accessories are necessary to mitigate risks specific to intended user population.
NOTE Design attributes and associated examples in table are not comprehensive. The inclusion of specific examples into the table does not necessarily mandate changes to the associated Design Requirements or Specifications due to use with a paediatric population.		

A.3.2 Ages 5 years to 8 years — Early childhood

Children of this age can dress themselves, catch a ball more easily using only their hands, and tie their shoes. Having independence from family becomes more important now. Events such as starting school bring children this age into regular contact with the larger world. Friendships become more and more important. Physical, social, and cognitive skills develop quickly at this time. Emotional and social changes include displaying more independence from parents and family, beginning to think about the future, understanding more about his or her place in the world, paying more attention to friendships and teamwork and wanting to be liked and accepted by friends. Children in this group show rapid development of cognitive skills, learn better ways to describe experiences and talk about thoughts and feelings, and have less focus on oneself and more concern for others. This age group can be exposed to and navigate mobile technology including games, videos, and other media (e.g. TV, videos, online streaming sources). If technology informs the therapy, there should be health care practitioner or parental controls that mitigate any modification of the therapy (e.g. activation code, parental lock/mode). Provide a disabling feature on multi-use devices to mitigate risk of overdose.

A.3.3 Ages 9 years to 11 years — Middle childhood

Children of this age are showing growing independence from the family and interest in friends can be obvious by now. Specifically, children start to form stronger, more complex friendships and peer relationships. It becomes more emotionally important to have friends, especially of the same sex. Also, physical changes of pre-puberty or puberty can be showing, especially for girls. Children experience more peer pressure and become more aware of their body as puberty approaches. Finally, body image and eating problems sometimes start around this age. Children who feel good about themselves are more able to resist negative peer pressure and make better choices for themselves. This is an important time for children to gain a sense of responsibility along with their growing independence. Children of this age also face more academic challenges at school, begin to see the point of view of others more clearly, and have an increased attention span. There continues to be increased use with mobile technology, including mobile technology. Continuation of software parental controls and other software mitigations implemented in the ages 5 years to 8 years group is advised.

A.3.4 Ages 12 years to 14 years — Early adolescence

Children of this age experience changes in hormones as puberty begins. This age group experiences the most dramatic physical changes of puberty. Most boys grow facial and pubic hair, and their voices deepen. Most girls grow pubic hair and breasts and start their period. They can be worried about these changes and how they are looked at by others. This also will be a time when teens can face peer pressure to use alcohol, tobacco products, and drugs, and to have sex. Other challenges can be eating disorders, depression, and family problems. At this age, teens make more of their own choices about friends, sports, studying, and school. They become more independent, with their own personality and interests. Children show more concern about body image, looks, and clothes, focus on themselves; going back and forth between high expectations and lack of confidence, experience more moodiness, show more interest in and influence by peer group, express less affection toward parents. They can also sometimes seem rude or short-tempered, feel stress from more challenging school work, develop eating problems, and can feel a lot of sadness or depression, which can lead to poor grades at school, alcohol or drug use, unsafe sex, and other problems. Children of this age have more ability for complex thought, are better able to express feelings through talking and have developed a stronger sense of right and wrong. This group will continue the use of mobile technology but will start creating and contributing to social media accounts.

A.3.5 Ages 15 years to 17 years — Middle adolescence

This is a time of continual and significant changes in how teenagers think, feel, and interact with others, and how their bodies grow. Most girls will be physically mature by now, and most will have completed puberty. Boys can still be maturing physically during this time. The teen can have concerns about his/her body size, shape, or weight. Eating disorders can be common. During this time, adolescents in this age group are developing unique personalities and opinions. Relationships with friends are still important, yet they will have other interests as they develop a clearer sense of who they are. This is also an important time to prepare for more independence and responsibility; many teenagers start working, and many will be leaving home soon after high school. Risk-taking is a common feature of early to middle adolescence, as individuals experiment with adult behaviour. Therefore, a certain level of parental guidance and oversight can still be needed.

A.3.6 Ages 18 years to 21 years — Late adolescence

By this age, most healthy adolescents have completed the process of physical maturation including attaining full adult height. At this stage of development, most of the secondary sexual characteristics consistent with normal development are evident. Their need for peer approval is diminished and they are largely psychologically independent from their parent with a sense of personal identity. Adolescents in this group can make independent decisions and are able to compromise. They want support from adults but seek it mainly in the form of guidance. By late adolescence, they are able to understand, plan, and pursue long-range goals, especially their vocational goals. Older adolescents are able to fully understand abstract concepts and are aware of consequences and personal limitations. The development of abstract thinking is an important factor in helping them manage treatment regimens independently as well as give informed consent. At this point they are beginning to transition to early adulthood.

A.4 Specific design considerations for paediatric age groups

The design characteristics given in Table A.3 should be considered for each age group.

Table A.3 — Characteristics to consider in the design of drug delivery systems for paediatric users

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
Perception **(Sensory)**	— **Sight** (field of view, colour, contrast, acuity). — **Hearing** (sound detection, speech discrimination, localization). — **Touch** (including proprioception).	**The paediatric perspective can differ from that of an adult.** Children see things in a "different light". Children learn through their senses. They want to see, touch, taste, hear, experience and experiment. The world seems exciting, interesting, and worth exploring[35].	Certain disease conditions/ disabilities can affect: — **Visual capabilities** (e.g. low vision, myopia, etc.) and cause defective vision (e.g. colour blindness, etc.). — **Hearing capabilities** and cause deafness.	— Design should consider children senses limitations (e.g. children who have visual difficulties and language limitations can benefit from warnings they can hear). — Design should consider children preferences and using appropriate senses for informing/feedback (e.g. it can be important to understand which sense(s) can be used for informing when a dose is fully administered, or understand if speech-based warnings can alert children that do not read easily to potentially hazardous situations[35]).

[a] Type of communication can be impacted by the level of education and the environment.

Table A.3 *(continued)*

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
		— A child between 4 years old and 6 years old might recognize the alphabet and be ready to begin reading. At 5 years old, the child might understand more than 2 000 words, time sequences (what happened first, second, third, etc.), sentences can be eight or more words in length, he describes objects, uses imagination to create stories. — The ability of both eyes to focus on an object simultaneously becomes more fully developed around 7 years of age. Most children can be somewhat farsighted (i.e hyperopic) but can see well at other distances.	— Certain disease conditions/ disabilities can cause: — **Touch disorders** or other impairments that can affect the abilities to use touch (e.g. affecting tactile pressure) — **Taste disorder** (e.g. hypogeusia, reducing the ability to taste sweet, sour, salty, and savoury).	— Consider adapting design (including training and IFU materials) to children visual capabilities. For example, adjust font size(s) on screen(s) and instructions for use for legibility. When using colours to convey information to children, avoid using too many colours on the same page. If a colour conveys a specific type of information, be consistent, ensure colour always means the same thing throughout the application. When using colour to convey information to children with colour deficiencies, locate important information in the same place each time it is presented. Some colour contrasts, such as grey and yellow, do not transfer well. Consider changing intensity of those colours instead[35].
[a] Type of communication can be impacted by the level of education and the environment.				

Table A.3 *(continued)*

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
		Also, a school-aged child can spend more than 1/3 of a typical academic day on activities that require hand skills[35]. Use of touch screen tablets by young children is increasing at home and in early childhood settings (e.g. children can interact with the tablet interface using a range of single and multi-touch gestures as one tap, double tap, long press, scroll, pan, flick, two finger tap and scroll, pinch, stretch, and spread)[34].		— Design should consider simple and age appropriate language (e.g. avoid complex wording and ensure appropriate speed). — Avoid complexity or too distractive systems, design appropriate protective measures for needle, etc.). — Design should consider familiarity with other model of device(s) and build design on child's previous knowledge/ experiences. — Provide age appropriate affordance.
Cognitive **(processing)**	— **Attention** (concentration). — **Recognition** (familiarity with technology, health literacy, training). — **Language and communication**[a] (literacy, verbal, nonverbal). — **Problem solving**. — **Memory** (working, long term).	**Paediatric patients can differ cognitively from adults.** They can take risks and lack judgment. They can test their skills, their adult supervisors, and their environment in their quest for independence. Because children's brains are more plastic than adult brains, children can learn certain new skills such as new languages more easily than adults can. It can also be expected that children interpret information and use products in ways that can make no sense to the adults who created those same information and products[35][36]. Examples of cognitive capabilities per age range[35]:	— Certain **disease conditions/ disabilities that can cause hyperactivity, impulsive behaviour, attention spans** (e.g. Attention Deficit Hyperactivity Disorder) **or any cognitive development problem**. — **Complexity of treatment, dose regimen, frequency of use, use environment** (e.g. does the paediatric patient have to take different doses of a solution at different times during the day?).	— Consider that children can have attention span limitations when using a device (e.g. presenting children with short, succinct tasks rather than long ones or making warnings "stand out" can capture children's attention). — Consider their familiarity with other model of device(s) and/ or their previous knowledge/ experiences that can influence their cognitive abilities when using the device (e.g. other products can work differently or children who are more familiar with a pictogram are more likely to understand and comply than children who are not[37]).

[a] Type of communication can be impacted by the level of education and the environment.

Table A.3 *(continued)*

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
		At 4 years to 5 years they might: — be able to categorize; — know primary colours; — often believe in fantasy and accept magic as an explanation; — develop and recognize a concept of time; — focus only on one aspect of a situation; — base much of their knowledge on how the situation appears; — recognize familiar words in simple books/signs; — speak fairly complex sentences; — be able to memorize their own address and phone number; — understand 13 000 words and use 5 to 8 words in a sentence; — understand that stories have a beginning, a middle, and an end; — attain 90 % of their adult grammar by the end of this age range; — follow three step commands.		— Consider that young children might not be able to understand the ramifications of an action taken when using a product (e.g. a warning) or might just explore[35][36][39]. — Consider that children can use products in unexpected ways compared to adults and that parents/caregivers can believe their children are better equipped to deal effectively with hazardous situations than is actually possible[36][38][40]. Also, consider that children can also be mistakenly attracted to dangerous products due to characteristics of the products packaging including colour, the container's shape, and the presence of symbols or other characteristics[35]). (**Birth to 6 years**) Consider use of simple language with descriptive and sensory words, and the benefits of repetition, rhythm and song, as well as animal and human characters to make content as appealing as possible.
[a] Type of communication can be impacted by the level of education and the environment.				

Table A.3 *(continued)*

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
		At 6 years to 7 years they might: — have longer attention span; — remember and repeat three digits; — have difficulty imagining others' points of view; — not consistently understand the consequences of their actions; — use expressive vocabulary of 2 600 words and use receptive vocabulary of 20 000 to 24 000 words; — reverse printed letters; — vocabularies for speak and listen increase to the double. At 7 years to 8 years they might: — increase problem-solving ability; — have longer attention span; — still have difficulty with considering all the logical, possible outcomes of their actions; — understand concrete, hands-on problems or situations and apply basic logic; — communicate thoughts and ideas.		— Consider that information or warnings can produce unintended effects if they are misunderstood bz children (e.g. some pictograms or symbols can be quite abstract and thus be misunderstood by children. Ensure that they are noticeable and comprehensible by the children; for example, the skull and crossbones pictogram can be interpreted as "pirate food" instead of "poison"[35]). — Consider avoiding labelling characteristics that can lead children to believe that the product is safer than it really is (e.g. colourful pictures, cartoon characters, etc.[35]). — Consider using unambiguous and adapted language (e.g. for older children or adolescents, warnings that include explicit language can be more effective and warnings can be especially valuable when combined with verbal warnings and instructions[35][41][42]).

[a] Type of communication can be impacted by the level of education and the environment.

Table A.3 *(continued)*

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
		At 9 years to 11 years they might: — plan future actions; — solve problems with minimal physical output; — still have difficulty considering all the logical, possible outcomes of their actions; — often have rituals, rules, secret codes, and made-up languages; — use cursive writing. At 12 years to 14 years they might: — engage in abstract thought; — use hypothetical reasoning; — speculate about future events; — use receptive vocabulary of 50 000 words; — have communication skills almost equal to an adult.		— Consider guiding adequately the child's steps to use the product (e.g. provide adequate dose completion notification). — Consider differences within and among age groups: children can change rapidly (e.g. what is intuitive for an 8-year-old can be not intuitive for a 6-year-old or even for another 8-year-old with a different background or maturity level[35]). **(7 years to 11 years)** Consider including allusions to stories about friendships, new skills or talents, daily occurrences that are opportunities for growth as well as testing one's values and critical thinking skills. **(12 years and above)** Consider the value of referring to positive role models with high moral standards, stories about balancing the influence of family/friends/media, non-pedagogical formats and guidance in helping channel the need for experimentation and independence into healthy life choices.

[a] Type of communication can be impacted by the level of education and the environment.

Table A.3 *(continued)*

User characteristics including user interface interaction	Developmental stage impact	Disease conditions impact	Specific design considerations
	At 15 years to 17 years they might: — question authority and society's standards; — think in complex ways; — be concerned about grades, appearance, and popularity; — be withdrawn or introspective. At 18 years to 21 years they might: — be aware of consequences; — seek independence; — challenge authority.		

[a] Type of communication can be impacted by the level of education and the environment.

Table A.3 *(continued)*

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
Emotional and Psychological **(Attitude)**	— **Attitude**: positive, neutral, or negative feeling toward the system. — **Motivation**: low, moderate, or high due to interest, fear (injection, pain, etc.), adherence or compliance to the system. — **Patience**: patience or impatience expected in accomplishing goal. — **Expectations**: kinds of reasonableness. — **Stress level**: high, some, or no stress generally resulting from task performance. — **Socio-economic and cultural influence** (family context, country, community, etc.).	**Paediatric patients can differ emotionally and psychologically from adults.** Children's motivations, interests and fears can be quite different from those of adults. Young children can have a little fear; they lack the experience that comes with encountering painful events such as falling, burning a hand, or pinching a finger[35][36]. Places and things that can seem scary from an adult point of view can be interesting to children. Children observe and mimic adults and can enjoy impersonating adults with child-size "adult" products. Also, some children need distinct kinds of challenges. Their environments should afford them opportunities to succeed and sometimes fail, and, with practice and perseverance, develop the ability to turn their failures into successes. They should be given safe environments, where failure is "ok" and seen as part of a learning process[35]. Most of children above the age of 8 can read and therefore, are able to take part in assisting in their own safety. As children get older, they tend to take on increasingly greater responsibility for their own safety[43]. Examples of emotional and psychological capabilities per age range[35]:	— **Patient education and training** e.g. asthma: asthma care requires a partnership between the child, its parents and the health care professional. Patients need to know about the causes of their disease, causes of exacerbations and, perhaps most importantly, how to use the prescribed medication and device reliably[33]. — **Severity of the disease conditions** e.g. does the child see a direct impact from taking the medicine? How tolerable it is for the child? — **Chronic vs. periodic disease**; chronic diseases (e.g. asthma, diabetes, etc.) or periodic/ intermittent diseases. This can influence abilities to be compliant to a therapy. — **Complexity of dose regimen, frequency of use, use environment** e.g. does the child have to take the medicine at lunch time (e.g. at school)?	— Consider that the socio-economic and cultural environment can be favourable or not to the use of the device e.g. how do the parents/legal guardian care for the paediatric patient? Are they involved in the treatment? Does their environment distract them and how does that affect the use of the device, etc.? — Consider that treatment compliance is known to be an issue for some children with chronic disorders, particularly those that do not result in immediate discomfort when scheduled doses are missed or delayed. Consider the importance of supervision and collaboration between the child/ adolescent and their parent/ legal guardian to ensure proper treatment compliance [44][45][46][47][48][49][50][51][52]. — Consider children attitudes/ preferences towards the treatment and their disease (e.g. consider engaging the child by opting for an appropriate, appealing, personalized design). — Consider their familiarity with other model of device(s) and/ or their previous knowledge/ experiences that can influence their attitude towards the proposed system.

[a] Type of communication can be impacted by the level of education and the environment.

Table A.3 *(continued)*

User characteristics including user interface interaction		Developmental stage impact	Disease conditions impact	Specific design considerations
		At 4 years to 5 years they might: — understand and obey simple rules, but often changes rules of a game as they go along; — persistently ask “why”?; — enjoy doing things for themselves; — enjoy playing with other children and developing “best friend” concept; — have a basic understanding of right and wrong. At 6 years to 7 years they might: — have strong desire to perform well and do things right; — be interested in rules and rituals; — enjoy active games; — be sensitive and emotionally vulnerable; — try to solve problems through emotions.		— Consider children can fear needle, pain, etc. When necessary, the device should be designed in a way that children can use them safely and fearlessly (e.g. system hiding needle, needle shielding, etc.).
[a] Type of communication can be impacted by the level of education and the environment.				

Table A.3 *(continued)*

User characteristics including user interface interaction	Developmental stage impact	Disease conditions impact	Specific design considerations
	At 7 years to 8 years they might: — see things from other children's points of view, but still very self-centred; — have difficulty handling criticism or failure; — see things as right or wrong, good or bad with little middle ground. At 9 years to 11 years they might: — start to see parents and authority figures as fallible human beings; — better understand other people's perspectives instead of only their own; — enjoy being a part of a club. Peers become very important.		

[a] Type of communication can be impacted by the level of education and the environment.