CAMBRIDGE DESIGN PARTNERSHIP

ISO 11608: WHAT THE NEW STANDARD MEANS FOR NIS MANUFACTURERS

Here, Steve Augustyn, Senior Consultant and Client Manager at Cambridge Design Partnership, looks at ISO 11608 and what it means for needle-based injection device manufacturers.

Over 16 billion injections are given every year. Since ISO 11608-1 was first published in 2000, the series has set the standards for how needle-based injection devices should be designed and verified. This year, the series received its biggest update in a decade. Here is what device manufacturers need to know.

WHY ISO STANDARDS MATTER

ISO standards set out the definitions, requirements and testing criteria that manufacturers should take into account when creating or redesigning products. ISO standards capture the absolute best practice for the industry, ensuring that devices are both safe and effective, and provide an assurance of quality that healthcare professionals and their patients can rely on.

Adherence to ISO standards is entirely voluntary for companies. However, these standards are still hugely influential – many countries' regulatory bodies expect compliance with the standards, making them de facto mandatory for devices destined for use in those territories. The US FDA, for example, is increasingly using ISO standards as part of its device review and approval process. Therefore, companies designing devices for the US market are highly recommended to demonstrate compliance with recognised standards. In the case of needle-based injection systems (NISs), the FDA directly references the ISO 11608 series in its published guidance for injection devices.

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ISO standards come with the advantage that they are designed to be relevant internationally: they are written in language broad enough to facilitate their application in as many different countries across the globe as possible. They are also informed by regulations within the US and Europe to reduce the compliance burden for device manufacturers operating internationally. The technical committees that develop the standards can comprise members from tens of countries, to ensure they reflect a global outlook and address concerns from across diverse territories.

Due to their global reach and popularity, it is becoming increasingly difficult for device makers to go to market without meeting ISO standards, particularly in territories where competitors and peers are doing so. For NIS manufacturers, adhering to ISO 11608 is critical to doing business worldwide.

MULTI-STAKEHOLDER STANDARDS SETTING

ISO standards are informed by expert opinion – the technical committees that develop the standards are made up of

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specialists and professionals from within the industry, as well as subject matter experts from consumer associations, academia, non-governmental organisations and government agencies including the FDA.

Patients and healthcare professionals also play a key role in ISO standard setting. ISO 11608 has been the embodiment of this patient-centric approach: during the writing of 11608-7, the contribution from a blind diabetic member of the group was enormously helpful. The final language in these documents considers the viewpoints of the different stakeholders and the unique perspectives they bring.

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ISO standards are periodically reviewed and updated, as in the case of ISO 11608, to ensure they accurately reflect the current market in the face of any new developments, significant trends, or challenges that have occurred since the standard was first published.

ISO 11608: WHAT IT MEANS FOR NIS

ISO 11608-1 was last updated in 2014, covering systems that deliver discrete volumes of a medicinal product, either through needles or soft cannulas, using intradermal, subcutaneous and/or intramuscular routes. It covers injection devices for single or multiple doses, which are refillable or disposable. It supplements the requirements for prefilled syringes covered in ISO 11040, and specific parts of the standards deal with different aspects of injector design.

A major review of ISO 11608 was published earlier in 2022, driven by advances in NIS technology, including on-body delivery systems (OBDSs) and growing numbers of electromechanical components used in NISs.

For device makers, there are notable benefits. The review aims to ensure the different parts of the standard are better aligned and integrated, as well as reduce duplication and define new concepts and device categories that manufacturers can use as they bring new products to market.

The 11608 series is formed of seven parts:

- General Requirements (11608-1)
- Double-Ended Pen Needles (11608-2)
- Containers and Integrated Fluid Paths (11608-3)
- Systems Containing Electronics (11608-4)
- Automated Functions (11608-5)
- On-Body Delivery Systems (11608-6)
- Accessibility for Persons with Visual Impairment (11608-7).

ISO 11608-1: THE STANDARD'S PARENT

As the "parent" part of the standard, ISO 11608-1 provides the foundation for the series, establishing the requirements and test methods for all NIS devices within its scope.

As well as adding OBDS requirements, described in more detail below, ISO 11608-1 introduces several new concepts, including "primary function" (a function of the device that allows it to be used safely and effectively) and "functional stability", which expands testing regimens to simulate whole-life testing for reusable devices. There is also more guidance on risk-based design approaches, and ISO 11608-1 adds more specific language to direct the manufacturer to consider the requirements of the medicinal product to be used with the NIS.

OBDSs AND ISO 11608

The growing interest in OBDSs has been reflected in several parts of the 11608 series, including 11608-1 (General Requirements), 11608-3 (Containers and Integrated Fluid Paths) and 11608-5 (Automated Functions). However, it is 11608-6 that is dedicated exclusively to OBDSs, setting out the requirements for these systems.

OBDSs were created to address several market needs, including extending medicinal products' delivery times; delivering more viscous medicinal products, such as biologics, more easily; and the possibilities of delivering medicinal products after a time delay. These features of OBDSs are useful in facilitating the medication of patients outside traditional healthcare settings.

Unlike infusion pumps, which are concerned with the rate of medicinal products' delivery, the performance of OBDSs is defined by the accuracy with which they deliver a volume of medicinal product – their dose accuracy. And whereas other NISs are designed to be held during the administration of the drug product, either by the patient or by a healthcare professional, OBDSs deliver the medicinal products while attached to the body. That means they can deliver a larger volume of medicinal product than other NISs over a longer time. As a result, OBDSs can typically deliver medicinal products in a way patients may find more tolerable and healthcare providers more appropriate for certain administration use cases.

The unique differences in function and delivery profile that ODBSs offer mean they needed their own equally unique set of requirements and design guidance. 11806-6 gives device manufacturers assistance in creating safer, more efficient products for the growing OBDS market and the reassurance to develop this novel class of system in a way that is likely to satisfy regulators.

CONTAINERS AND INTEGRATED FLUID PATHS

The increasing impact of OBDSs has also prompted changes elsewhere within ISO 11608. ISO 11608-3, which originally only defined cartridge geometry and performance, has now been expanded to cover NIS containers and integrated fluid paths.

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General requirements for soft cannulas and fluid line connections also now appear in ISO 11608-3 – another change due to increasing popularity of the OBDS device class.

Elsewhere, there are other notable changes for device manufacturers. The requirement for resealing the cartridge has been reduced from 1.5x the intended use to a minimum of 1x the intended life. There are new sampling requirements for particles generated through septum penetration that require the use of 5–100 cartridges, depending on the conditions of use. The requirements on particulates within the fluid path have been revised, and the standard now includes limits for the maximum permitted endotoxin-mediated pyrogenicity.

Meanwhile, the cartridge geometry definition is no longer mandatory and now forms part of an informative annex.

AUTOMATED FUNCTIONS

ISO 11608-5 supplements the general specifications in ISO 11608-1 by adding requirements for automated dose preparation, dose delivery and needle protection.

Under 11608-5, defining and measuring automated dose delivery time has become a requirement, while needles with automated insertion must meet a modified dose accuracy test to ensure that the dose is delivered at the correct depth.

11608-5 also defines the requirements around fenestrated needles (needles with holes in the side). It explores the implications of both non-perpendicular needle insertion and delivery of the drug product through a flexible cannula.

DOUBLE-ENDED PEN NEEDLES

Companies working with double-ended pen needles will also need to implement several changes introduced in ISO 11608-2.

The experimental procedure to determine flow rate has been defined more precisely, and the sample sizes have been brought in line with the requirements in ISO 11608-1.

Dose delivery and needle hub removal force are now part of the testing requirements to confirm compatibility between a needle and a specific NIS. The samples needed for functional compatibility have also been reduced while guidance has been introduced on requirements for the inner needle shield.

HOW TO WORK WITH ISO 11608

Manufacturers have a grace period of three years from the publication of the latest version of ISO 11608 (April 2022), during which they can still verify their designs to the old standards. Once the grace period has expired, manufacturers should verify new device submissions against the latest standards.

Device makers still have some time to consider how the standard will affect them and what changes need to be made to their products or their verification programmes. For those with devices looking to release products beyond the three-year horizon, a gap analysis is needed to ensure adherence to the standard when the device hits the market. For novel devices, more in-depth work may be needed to ensure the product meets the latest version of the standard.

It can be challenging to understand the changes that the ISO 11608 review has brought in, and its implications for device development and verification programmes.

Cambridge Design Partnership (CDP) develops and verifies many needle-based injection systems on behalf of its clients. CDP's clinical trial manufacturing capability gives the company a deep insight into the challenge of moving from design to commercial manufacturing. As one of a handful of British Standards-recognised experts on injection devices, CDP is well placed to advise clients on the implications of these changes in this latest version of ISO 11608.

The benefits of adhering to ISO 11608 are manifold; for some manufacturers, the demands of doing so can be too. For product developers struggling with device performance or needing expert support to meet the ISO 11608 standards, CDP has the expert teams to help overcome these problems.

ABOUT THE COMPANY

Cambridge Design Partnership is an end-to-end innovation partner, propelling global brands and ambitious start-ups to success. The company builds breakthrough products and services – from insight to ideas, prototypes to production – bringing innovation to life. CDP's teams are multi-disciplinary, uniting scientific rigour, design ingenuity and engineering excellence for consumer, healthcare and industrial clients. People-centred, deeply collaborative, and – above all – expert, CDP is uniquely positioned to shape the future for consumers, patients and industry. Even its ownership model is innovative: CDP is 100% owned by its employees, ensuring an open culture and a total commitment to your project's success.

ABOUT THE AUTHOR

Steve Augustyn is Senior Consultant and Client Manager at Cambridge Design Partnership. He has more than 20 years' experience in the design and development of drug delivery devices, and is also member of the ISO/TC84 – the ISO committee focused on standardisation of devices for administration of medicinal products and catheters.