Considerations of lifecycle management in scope of the changing regulatory landscape

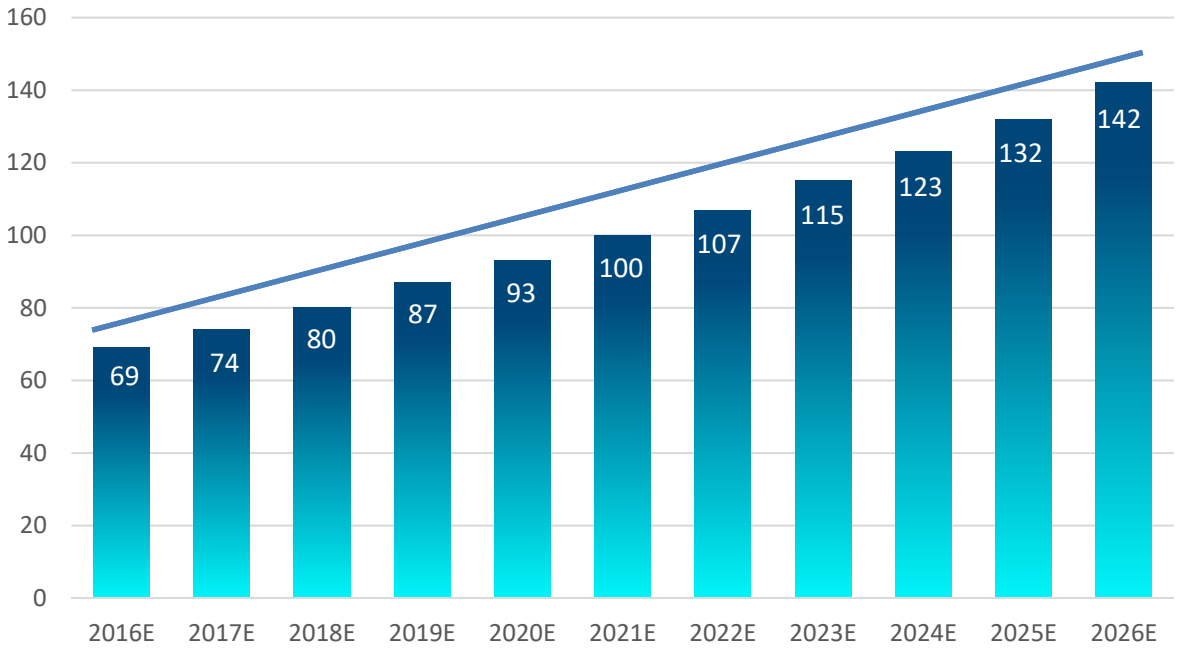
Rosemary Gonzales, Vice President Regulatory Affairs & Compliance, SHL Group

Overview

- Market trends and innovations as drivers of regulatory change
- A view of the fast-changing regulatory landscape
- Preparing for the future: a strategic roadmap for moving forward

Auto Injector Global Market Growth

Overall Auto Injectors Market
(Number of Units, Millions), 2016-2026



Source: Roots Analysis [1]

The auto injectors market is expected to increase from about 69 million annual units to approximately 142 million units by 2026, representing an annualized **growth rate of 7.6%.**

Market Drivers

The market is likely to increase from US$775 million in 2016 to US$1,243 million in 2026 due to [2] :

Patient Need:

- Growing prevalence of chronic diseases
- Urgent treatment required in emergency conditions

Industry Competition:

- Biosimilars

Health Authority:

- Sharps injury prevention regulations
- Reimbursement pressures to decrease cost, increase value, and enhance compliance for the user

Technology is Evolving and So Are Regulations, Standards and Guidance

Innovation drivers: Auto injectors can enable people to overcome concerns about self injections. Their benefits include:

- Easier administration
- Reduced anxiety (needle phobia)
- Improved treatment adherence
- Fewer sharps injuries
- More versatile (high volume drugs, high viscosity drugs, and lyophilized drugs)

As technology advances, regulators must continue to ensure **safe and effective products** and so regulations evolve as well

Sharps Injury Prevention

- About 16% of auto injectors on the market are used in hospital settings as a safer alternative for healthcare professionals [3]
- Auto injectors are contributing significantly to the 88% reduction in needle stick injuries [4]

ISO 11608-1
- section 3.16

ISO 23908
- in the process of revision

Lifecycle Changes

Potential post-market lifecycle changes to improve:

- Performance, safety, and usability
- Connectivity or other features
- Manufacturability
- Complaint rate

Regulations and Standards:

- 21 CFR 820 requires evaluation of changes
- ISO 13485 contains requirements for assessing design changes
- Consider upcoming ISO/CD 20069 - Change assessment of devices intended for administration of medicinal products

ISO: From 1 to 21,000+ Standards

Founders of ISO, London 1946[5]

- The International Organization for Standardization (ISO) is the world's largest developer of voluntary international standards
- It was founded in 1947, and since then has published 21,773 international standards covering almost all aspects of technology and business

Landscape of ISO Standards

ISO / IEC Standards impacting Medical Devices:

Syringe-related Standards:

ISO 9626: *Stainless Steel tubing*
ISO 7886-1: *Single use syringes*
ISO 7886-2: *syringes for syr. pumps*
ISO 11040-5,-6,-8: *Pre-filled syringes*

Other Standards which may apply:

IEC 60601-1: *Medical Elect. Equip.*
IEC 60601-1-8: *Alarms*
IEC 60601-1-11: *Home Healthcare*
EN 62304; IEC 80002-1: *Software*
IEC 15026-1,-2,-4: *Systems & Software Engineering*
IEC 60601-2 IEC 61000-4; CISPR 11 -14-1: *EMC*
IEC 60812: *Dependability*

Pump-specific Standards:

IEC 60601-2-24: *pumps*

…if the NIS is a rate-based pump

Other Standards which may apply:

EN 1615, 1618: *catheters, tubing*
ISO 594-2, ISO 80369-1: *connectors*
ISO 11070: *IV introducers + guide wires*

If the device is a Needle-Based Injection System:

ISO 11608 family of standard: *addresses:*

***Part 1** *Needle-based Injection Systems (NIS). Addresses the key requirements for needle-based systems. As the "parent" document for parts 2-7, it covers:*
- *General requirements, Risk Management*
- *Free-fall testing, Dose accuracy*
- *Determining and testing essential functions*
- *Visual inspection & Markings and Labeling.*

The NIS may also have to address the following:

***Part 2** *… if the NIS must be mated with a double-ended, separately-packaged, sterile needle to operate.*

***Part 3** *… if the NIS contains a non-syringe container or reservoir for the medicinal product.*

***Part 4** *… if the NIS contains electro-mechanical components, electronics, firmware, software and/or batteries.*

Part 5 *…if the NIS has an automated function (e.g., needle insertion or retraction, drug delivery, reconstitution).*

***Part 6** *… if the NIS is an On-Body Delivery System (OBDS)*

Part 7 *…If the NIS is claimed to be appropriate for persons with visual impairment*

+

ISO 23908: *…if the NIS is claimed to provide post-use sharps injury protection.*

If it is not a needle-based delivery system:

ISO 20072: *Aerosol Drug Delivery Devices*
ISO 21649: *Needle-free Injection Systems.*

… whether it has a needle or not, it may also need:

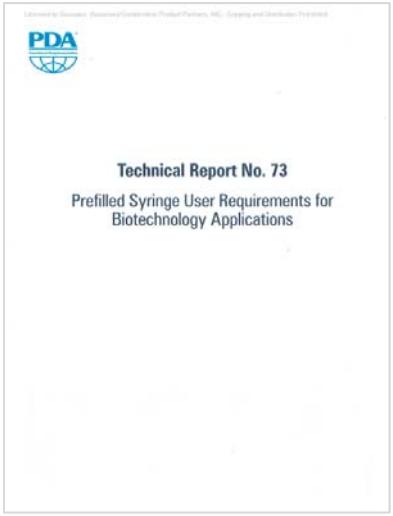
Process Standards:

ISO 14971: *Risk Management*
IEC 62366: *Usability Engineering*
ISO 10993-1: *Biological compatibility*
***ISO 20069:** *Change Assessment for Medical Devices*
ISO 11135: *Sterilization*
ISO 15223: *Symbols*

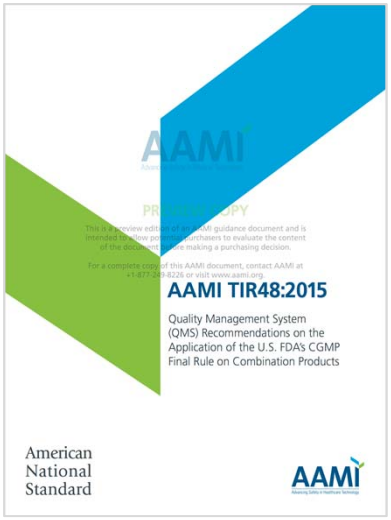
* *Denotes the standard is currently in development or undergoing modification*

Assessment as of July-2017 [6]

Additional Technical Guides



PDA Technical Report No.73
Prefilled Syringe User Requirements for Biotechnology Applications



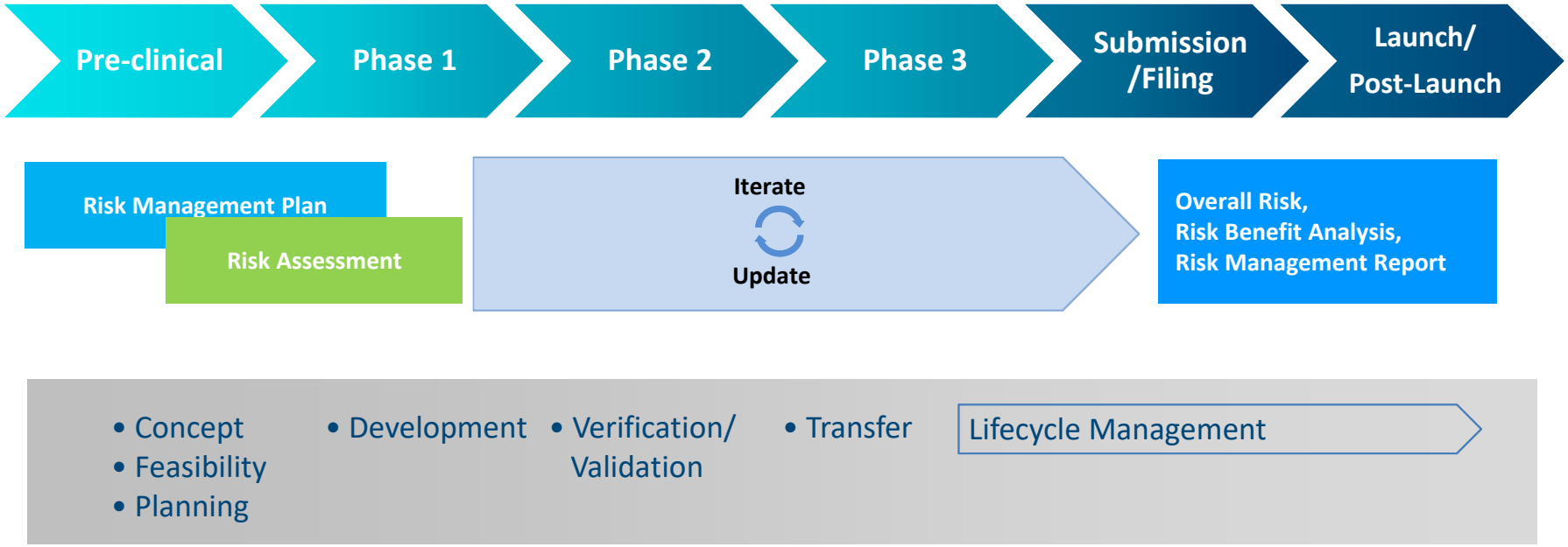
AAMI TIR48:2015
Quality Management System (QMS) Recommendations on the Application of the U.S. FDA's CGMP Final Rule on Combination Products

AAMI TIR59:2017
Integrating human factors into design controls

AAMI TIR50:2014
Post-market surveillance of user error management

Drug-Device Product Development Process

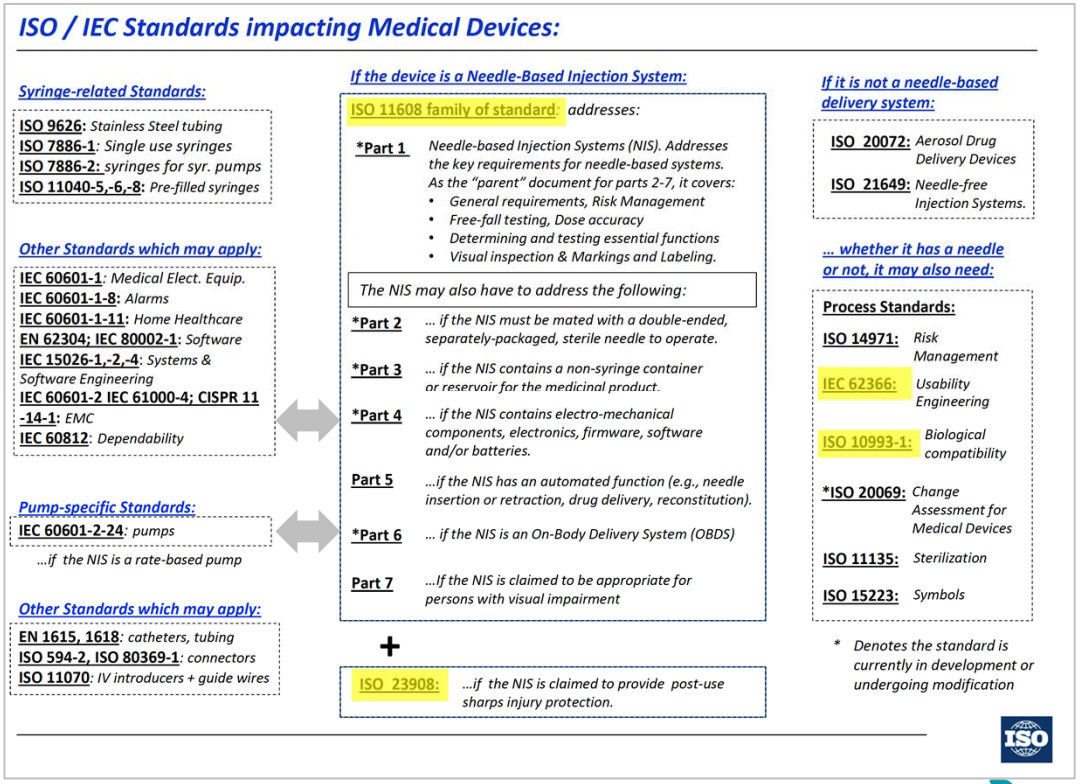
Aligned Combination Product Development Process



Reference **AAMI TIR48:2015**[7]

Keeping Pace with Changes in the Regulatory Landscape

- New or amended regulations, standards and guidance may occur during any point of development:
  - Medical Device Directive ➔ Medical Device Regulation
  - ISO 13485
  - ISO 11608
  - ISO 10993
  - ISO 23908
  - ISO 14971
  - IEC 62366



Ensuring Regulatory Competencies within the Organization

Regulatory Organizational Competencies		
Global Regulatory Strategy submission planning within and across products	**Regulatory Intelligence** surveying and providing input to regulations and guidance	**Regulatory Compliance** guiding the organization internally on past, current and future products

Support Organizational Infrastructure		
Structure and Processes Design Control Lifecycle Management	Quality Management System	Leadership

Source: Heidrick & Struggles International, Inc., 2017 [8]

Regulatory Activities and Product Development

- Following best practices
- Encouraging quality by design (QbD)
- Risk management activities
- QMS implementation – Pharmaceutical Quality System
- Pay attention to the supplier systems' compliance with regulatory expectations

Move from Project Focus to Broader Vision

2000-2005

Auto injectors
start to build momentum in biologic pharmaceuticals for treament of chronic diseases.

2005-2017

Regulations and guidance start to increase for combination products. Focus on sharps injury protection and human factors.

Prepare for the Future – Standards Evolution

Timelines to meet the EU MDR compliance requirements

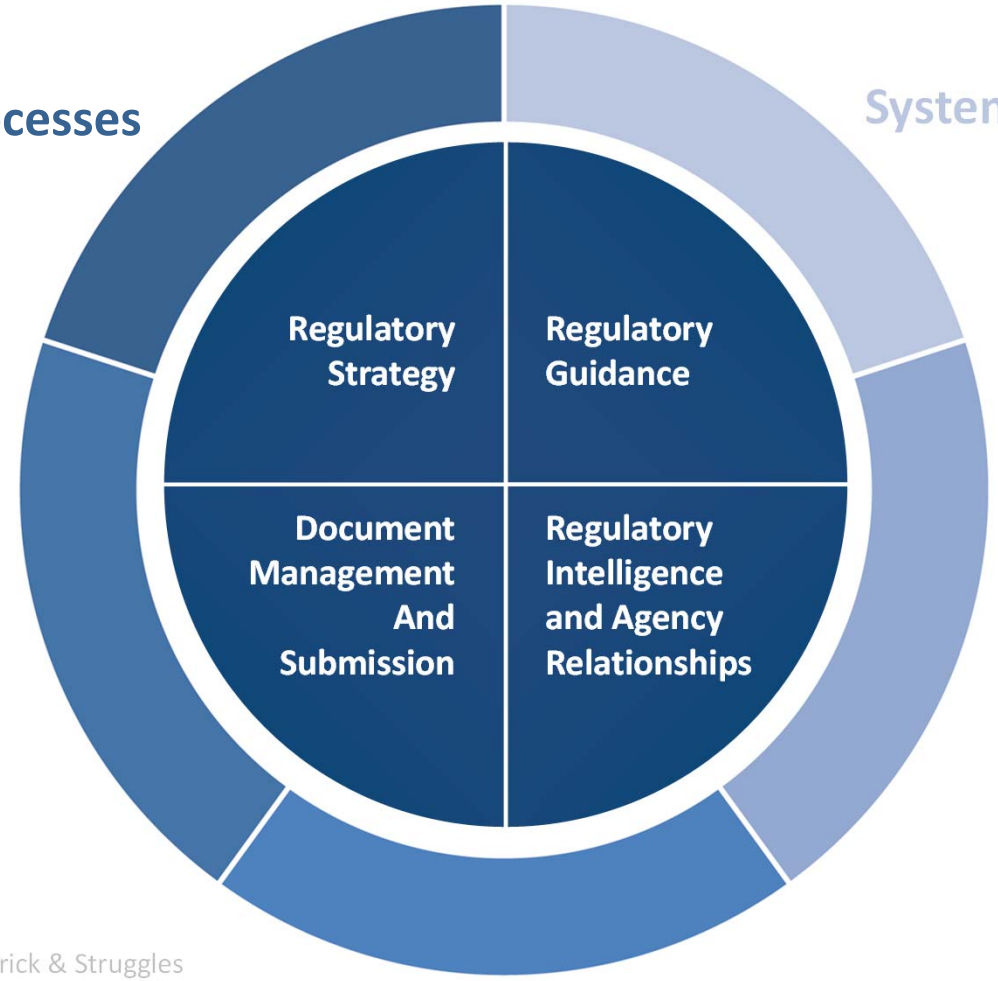
Source: Deloitte, 2016[9]

Medical Device Directive (MDD) to Medical Device Regulation (MDR) Comparison

Comparison	MDD 93/42 EEC	Medical Device Regulation 2017/745
Pages	60	177
Articles	23	123 (Consider 117)
Annex Published	XII	XVII (Consider Annex I)
Amendments	1998, 2000, 2002,2003, 2007	Now this is a regulation

Additional 80 legal texts are yet to be written and interpretations are not yet fully established. [10]

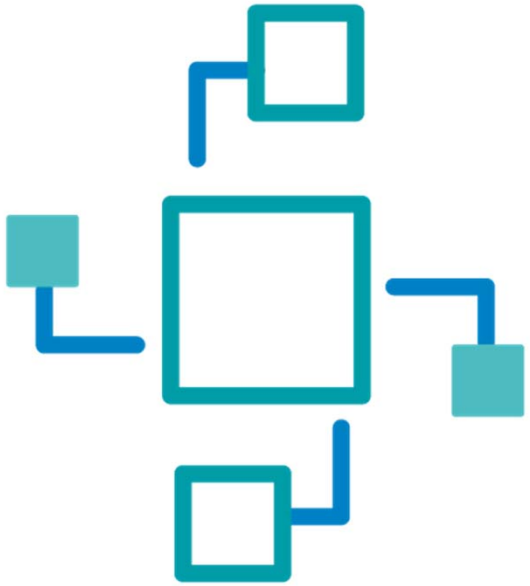
Prepare for the Future – Comprehensive View



Source: Heidrick & Struggles International, Inc., 2017[11]

Prepare for the Future – Responsibility and Coordination

- Coordination is essential from the early stage of development
- Everyone should be involved: primary container manufacturer, device developer, final assembler, the pharmaceutical or biotech company
- Each facility is responsible for CGMP requirements applicable to the activities performed at that facility
- Each facility should continue to be at the forefront of change in regulatory landscape



Conclusion

- Innovation and regulatory strategies must be aligned
- Consider your entire portfolio instead of working on a project by project basis
- Understand the regulatory change and be proactive vs reactive
- Does your organization have the right infrastructure to incorporate the complexity and change that we discussed?

Contact Us

If you have any further questions, please visit SHL booth X73-75 or send me an e-mail at: info@shl-group.com

References

[1] "Global Autoinjector Market, 2016-2026", Root Analysis, 2016

[2] "Global Autoinjector Market, 2016-2026", Root Analysis, 2016

[3] IMS Data

[4] http://www.businesswire.com/news/home/20060907005284/en/Amgen-Launches-Aranesp-Darbepoetin-Alfa-Prefilled-SureClick
http://www.futureinjectiontechnologies.co.uk/why-auto-injectors/

[5] Founders of ISO, London 1946, https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
http://ec.europa.eu/growth/single-market/european-standards/harmonised-standards_en

[6] ISO 11608 Family Coordination and Evolution , AbbVie, Inc. Robert R. Nesbitt Director, Human-Centered Design and Human Factors Co-Chair, US TAG, TC76 and TC84; member, AAMI Standards Board

[7] AAMI TIR48:2015 - Quality Management System (QMS) Recommendations on the Application of the U.S. FDA's CGMP Final Rule on Combination Products

[8] "Building a 21st-century global regulatory affairs organization", Heidrick & Struggles International, Inc., 2017

[9] "Preparing for the future: the new European Union medical devices regulation", Deloitte, 2016

[10] http://eur-lex.europa.eu/legal-content/ENG/TXT/PDF/?uri=CELEX:32017R0745&from=EN

[11]"Building a 21st-century global regulatory affairs organization", Heidrick & Struggles International, Inc., 2017