



WHITEPAPER

EU MDR 2021 and beyond.

Implications for an industry in transition.

With less than 12 months until the new MDR rules come into effect, will the European medical device industry be able to deliver the requirements? Or will it collapse under the compliance burden?

- Do organisations have the bandwidth to drive the behavioural and culture change required to transition to the new paradigm?
- What can be done to ensure organisations stay informed of new, changing and harmonised standards?
- Ultimately, will these preparations enable continued access to life-saving and life-changing technologies throughout the EU?

Why are European medical device regulations changing?

Since the European Union Medical Device Regulation (EU MDR) enforcement on 25 May 2017, organisations of all sizes have been preparing themselves for what is said to be one of the most significant disruptions to the medical devices industry in recent history. The MDR replaces the existing Medical Devices Directive (93/42/EEC) (MDD) and the Active Implantable Medical Devices Directive (90/385/EEC) (AIMDD) in May 2021.

Throughout this tumultuous 4-year transition period, it is important to maintain perspective on the catalyst for regulatory changes, and the implications of previous regulatory and legal shortcomings. The European Commission (EC) website provides a brief rationale for the changes and future expectations:

Problems with diverging interpretation of the current Directives as well as the incident concerning fraudulent production of the PIP silicone breast implants highlighted weaknesses in the legal system in place at the time and damaged the confidence of patients, consumers and healthcare professionals in the safety of medical devices.

Such problems should not occur again and the safety of all medical devices available in the EU has to be strengthened. Moreover, revision of the legislation was necessary to consolidate the role of the EU as a global leader in the sector over the long-term and to take into account all technological and scientific developments in the sector.¹

The Poly Implant Prothèse (PIP) silicone implants catastrophe was a significant catalyst for change. However, over the past decade there have been numerous other investigations globally into medical devices which have caused significant harm including transvaginal mesh implants, implantable cardioverter defibrillator leads, permanent contraceptive devices and hip replacement components.

Unsurprisingly, these events have attracted significant media attention and have had a profound impact on the medical device industry and the medical professionals that utilise and endorse the use of these devices. While it is not surprising to see that many of the shortcomings associated with these catastrophes have been addressed within the new EU MDR requirements, there is more to delivering better quality devices and safety for patients than declaring regulatory reform. Enabling the industry to meet the new requirements while maintaining timely patient access to treatment is the challenge currently being faced by companies supplying medical devices to the EU.

¹ Sourced 22nd March 2019; European Commission Website. Regulatory Framework: https://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework_en



What are the challenges as a result of the EU MDR?

Although regulatory frameworks have been in effect in Europe for more than 25 years, the new MDR imposes increased requirements for higher standards and improved regulation across the device lifecycle. It has been repeatedly acknowledged that demonstrating compliance with this latest update will be challenging for many organisations, as will the challenge of meeting consumer expectations which demand both proven safety and timely access to medical devices.

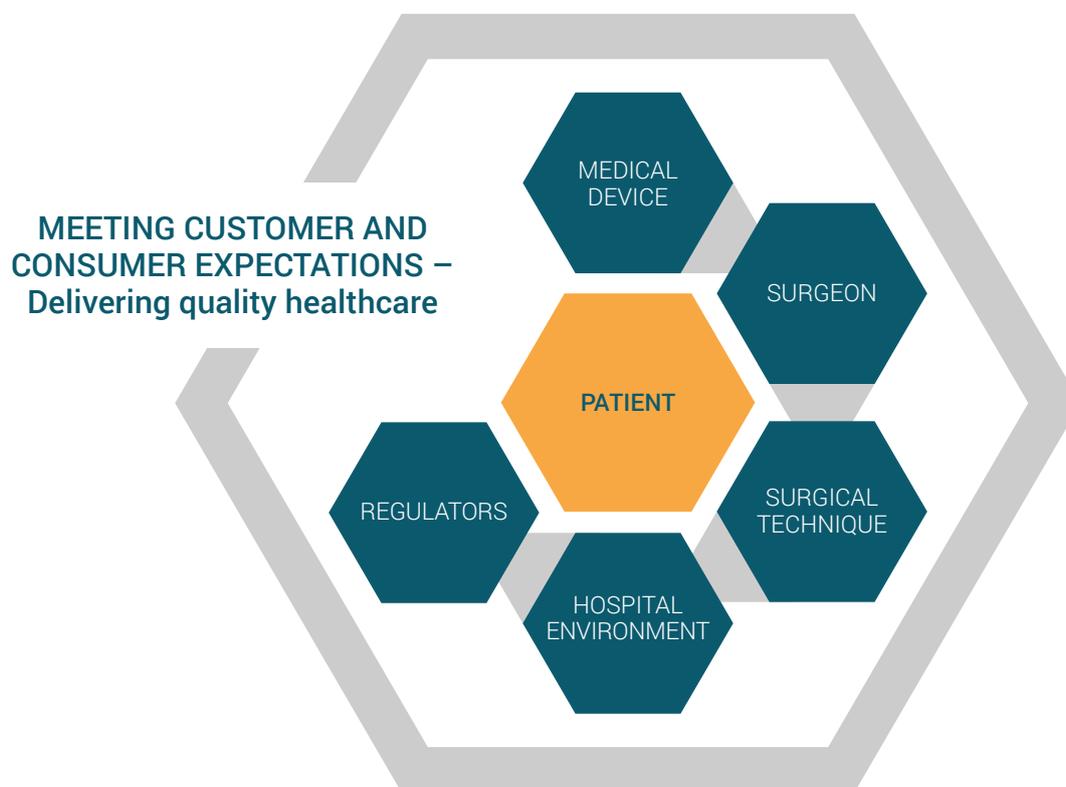
While all stakeholders agree quality and safety standards are paramount, regulation should not be so burdensome that the medical device industry is no longer viable, and patients lose access to life-saving and life-changing devices.

Patients in Europe have long enjoyed having earlier access to many medical devices, compared with more lengthy approvals in countries like the United States of America (USA). While the American Food and Drug Authority (FDA) is working to speed up their approval process, the EU MDR requirements will result in a longer wait for EU patients. In the worst case, the financial and time burden associated with the new clinical data requirements of the EU MDR may lead to withdrawal of existing products from market, or the decision to delay launch in Europe.

This has previously been the case in countries like Japan, where regulatory approvals have taken years after a devices approval and use in the EU and USA. One example is the endovascular stent graft (for abdominal aortic aneurysms) which was approved in Europe in 1997 and in Japan in 2008. Japan is now making efforts to harmonise with the FDA to streamline their regulatory process so Japanese patients can gain earlier access to medical device therapies.

The need to balance patient safety and economic viability for the medical device industry has been acknowledged in the second paragraph of the MDR.

“This Regulation aims to ensure the smooth functioning of the internal market as regards medical devices, taking as a base a high level of protection of health for patients and users, and taking into account the small and medium-sized enterprises that are active in this sector. At the same time, this Regulation sets high standards of quality and safety for medical devices in order to meet common safety concerns as regards such products. Both objectives are being pursued simultaneously and are inseparably linked whilst one not being secondary to the other.”²



² Official Journal of the European Union. REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.

However, the outcomes of this endeavour will vary based on the diverse, complex and dynamic interdependencies of stakeholders involved in the development of medical technologies and the delivery of healthcare. While compliance to the MDR seeks to deliver safety and quality improvements via regulatory reform, the real and positive outcomes will only be achieved when industry, regulators and medical professionals unite to deliver the essential changes in the real-world context.

The role of standards in achieving MDR compliance.

A common theme of the MDR changes is the reference to international standards as a compliance framework. By proactively complying with international standards, organisations can be confident they are well equipped to meet the MDR requirements. As previously noted, many of the MDR amendments will raise the current AIMDD/MDD requirements to align with international standards, particularly:

- EN ISO 13485: 2016 Medical devices. Quality management systems. Requirements for regulatory purposes,
- EN ISO 14155:2011 Good clinical practice for clinical investigations of medical devices for human subjects,
- EN 60601-1: Series of standards for medical electrical equipment, General requirements for basic safety and essential performance,
- EN 285: 2015 Sterilization. Steam sterilizers. Large sterilizers.

Other commonly applied medical device standards of relevance to the MDR include:

- EN ISO 14971: 2012 Medical devices – Application of risk management to medical devices,
- EN ISO 10993-1: 2009 Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,
- EN ISO 15223-1: 2016 Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements.

In addition to maintaining compliance with these and other core international standards, there is the anticipated arrival of approximately 230 harmonised standards to support MDR compliance. Furthermore, the MDR authorises the EU Commission to prepare Common Specifications (CS) in situations where harmonised standards do not exist and/or are insufficient to meet compliance requirements, and/or where there is a need to address public health concerns.

Not only will organisations need to monitor changes to international standards, they will need to develop frameworks that support an efficient understanding of the relevance and specific requirements of these standards to the devices within their portfolio. This knowledge is essential for organisations of all sizes.

Automated standard management systems are a valuable resource that can help companies stay ahead of new, updated and harmonised standards, as well as cross-referenced standards. Signals indicating the reference of a standard in legislation are also a key feature.

Customised collections folders enable efficient management of standards that specifically relate to an organisation's portfolio and can significantly ease the compliance burden by facilitating workflows, reducing human error and costly corrections if updated standards are not implemented in a timely manner.

What are the key MDR changes?

Compared with the previous Directives, the MDR places more emphasis on a life-cycle approach to safety, clinical evidence and international standards.

The EC have determined that most of the changes are extensions to existing requirements of the current AIMDD/MDD. In most cases, these new requirements simply bring the EU regulations up to date and into alignment with the requirements of other global regulators, as well as international standards. They have classified the changes into three categories: "Similar", "New" and "Novel".



SIMILAR

Many aspects of the current AIMDD/MDD have been retained in a similar form within the MDR, including:

- classes of device,
- classification rules,
- essential requirements (now known as general requirements),
- technical documentation,
- conformity assessment,
- registration,
- Notified Bodies (NB),
- the European database, EUDAMED, and
- vigilance.

IMPLICATIONS FOR INDUSTRY

While these requirements are mostly similar in form, under MDR they will have additional requirements for compliance, resulting in significant commercial and organisational implications for sponsors seeking to supply within the EU.

The following examples highlight a select few of the “Similar” topics that may have significant implications:

Classes of devices: While the current four classes; I, IIa, IIb and III are retained without change, some existing devices will be forced into a higher classification.

If a device’s classification changes, manufacturers must demonstrate compliance with the revised classification requirements. For example, in the instance where a device moves from Class I to Class IIa or higher, certification will change from a self-certified model to a Notified Body review model. This represents a significant change in the regulatory approval process and clinical evidence requirements for registration.

IF DEVICES ARE UNABLE TO DEMONSTRATE COMPLIANCE WITH A REVISED CLASSIFICATION, THEY WILL FACE DE-REGISTRATION AND IF SO, MUST BE WITHDRAWN FROM THE MARKET.

Devices in early development which change classification may face significant delays and un-forecasted costs such as expensive clinical trials. Developers may be forced to terminate commercialisation plans or seek strategic partnerships that would enable continued development. These additional requirements may mean that the EU no longer represents an attractive first market for global product launches, therefore delaying European patient’s access to new technologies.

Classification rules: These rules are based on the vulnerability of the human body and take into account the potential risks associated with the technical design and manufacture of a device. They are essentially the same as in the AIMDD/MDD, but with some new additions, most notably related to “software” and “substances”.

“Software as a Medical Device” (SaMD) includes the plethora of medical device diagnostic apps and medical wearables designed to inform clinical decision making which might have been Class I but will now be Class IIa or higher under the MDR.

“Substances” include the materials a device is made of as well as emissions from devices such as gases or energy will need classification. For example, substances that are carcinogenic, mutagenic, toxic for reproduction, endocrine-disruptors, latex and substances of human or animal origin, must be declared and may fall subject to a class change.

Notified Bodies: NBs will continue to act as delegates of the Health Authorities to perform pre-market assessments and routine surveillance audits. However, NBs will require more qualifications, greater scope of governance and will themselves be subject to closer monitoring and frequent audits.

NBs designated under the MDR will need to re-apply to obtain their designation, and must demonstrate they have the necessary capabilities and qualifications for their appointment. Furthermore, NBs will be monitored by authorities at least once annually, to verify that they are maintaining compliance with the extensive MDR requirements and are fulfilling their obligations as outlined in ANNEX VII. The increased requirements have raised concerns of a subsequent exodus of existing NBs that will not re-apply for designation, as well as a shortage of qualified people to undertake the required reviews.

To avoid market disruption and enable a smooth transition to the MDR, several transitional provisions have been established and outlined in Article 120. For example, some devices with certificates issued under the AIMDD/MDD may continue to be placed on the market until 27 May 2024 and made available until 27 May 2025.³ However fears of bottlenecks in the registration process remain and are an issue that the EU medical device industry association, MedTech Europe, have highlighted for urgent attention by the EC.⁴

The European database EUDAMED: Market surveillance on medical devices is a key component of the legal framework established by the MDR. Compared to the current AIMDD/MDD, the amount of data which will be available to the European Authorities in the future is one of the most significant changes being introduced.

EUDAMED aims to help European authorities conduct market surveillance on medical devices through information exchange and contains a vigilance module that will inform Member States on incidents or near-incidents in relation to certain devices on the market. The current database will be extended and in future some of the information will be made publicly available.

³ EU MDR Factsheet for Manufacturers of Medical Devices. ISBN: 978-92-79-89702-3 DOI: 10.2873/66341 20/11/2018 © European Union, [2018]

⁴ MedTech Europe; Implementing the New MD and IVD Regulations: Industry Calls for Solutions to Ensure Continuity of Care to Patients July 2018.

Article 33 of the EU MDR outlines the information that will be captured within the database. This includes comprehensive data on:

- the devices themselves, including the Unique Device Identification (UDI) data,
- all the economic operators associated with those devices,
- the Notified Bodies and the certificates they issue,
- clinical investigations conducted in Europe; and
- vigilance and post-market surveillance data.

Responsibility for data capture and uploading will reside with the manufacturers, importers, distributors and authorised representatives, presumably via the European database "portal" referred to in the preamble of the new EU MDR. The regulation allows 6 months from go-live to comply with the obligations to upload data.

Article 34 of the EU MDR obliges the EU Commission to make EUDAMED available by 25 May 2020 earlier. However, industry representatives anticipate that the go-live deadline will not be achieved and as such are expecting an extension, which incidentally has been accommodated for in Article 123 (d).

Data capture, upload and maintenance is likely to characterise the new era of the EU MDR. Some of the key, practical questions medical device companies should be addressing are:

- how is my organisation going to update the database?
- is an appropriate budget and staffing plan in place?
- does the wider organisation understand the actions required day-to-day in order to meet the obligations?
- who will be able to access the data and how will it be used?
- what reporting obligations fall from the data collected?

This aspect talks directly to just one of the multiple workstreams associated with the MDR transition which will require cultural and organisational adjustments to achieve compliance.

NEW REQUIREMENTS

The MDR introduces new requirements to secure and maintain compliance including increased reporting, staff awareness and data capture. These are resource and time intensive endeavours that require strategies in place to ensure companies can meet the requirements.

IMPLICATIONS FOR INDUSTRY

Post Market Surveillance (PMS): Investigations into medical device catastrophes revealed the inadequacy of post marketing surveillance activities, which were either absent or had fallen short in providing actionable information during investigations. This has been addressed in the MDR through the introduction of post-market surveillance reports and by reemphasising the requirement for all manufacturers to have a PMS system that is proportionate to the risk classification, device type and enterprise size. Additional requirements have also been assigned to Notified Bodies who will play a bigger role in supervising manufacturers' PMS systems.

Depending on the class of device, sponsors will now be required to produce either a PMS Report or a Periodic Safety Update Report (PSUR). These reports are an established practice under EN ISO 14971 and so should not be overly onerous for companies compliant with this standard. However, organisations not already exercising PMS in line with EN ISO 14971 might not appreciate the magnitude of this undertaking, and underestimate the cost, time and effort associated with the infrastructure and training needed to embed these practices and comply with this requirement.

Article 80 of the MDR outlines the Sponsor's adverse event recording and reporting requirements. A comprehensive PMS program will require the participation of every employee, (irrespective of functional responsibility or title). Employees are required to recognise when they are being told about an adverse event or device deficiency, be aware of their reporting obligations, and the methods by which to report the details of this event appropriately. Companies will need to ensure they have a robust adverse event reporting process in place, and the necessary training for staff to ensure they can meet their obligations.

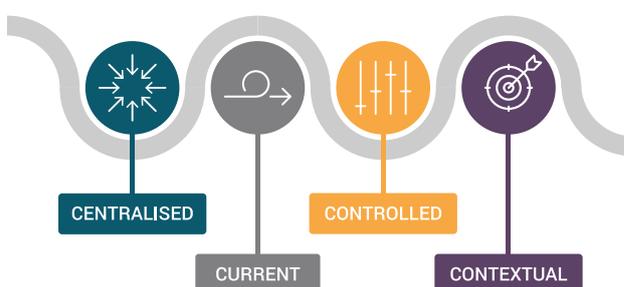
Depending on the quality of current PMS and methods deployed by organisations, compliance with this requirement can range from a slight adjustment to a wholesale cultural and operational overhaul.

THE KEY IN MANAGING THE VARIOUS IMPLICATIONS LIES IN SAI GLOBAL'S FOCUSED APPROACH;

- Understanding the crucial need for **centralisation**
- Believing in the importance of **control**, in cost and resource management
- Having confidence in information that is **current** and updated in real time
- Knowing that a **contextual** approach to the big picture is inspired by flexibility and collaboration

SAI Global empowers companies with knowledge, support, risk and compliance solutions that are critical to their capacity to continue to grow, thrive and provide outstanding care.

The below diagram outlines the key Priorities of Standards Management.



While the MDR has increased requirements regarding post marketing surveillance, the use of clinical registries as a means of effectively monitoring the use of medical devices and healthcare delivery has been in place for many years, and registries are expected to play a paramount role in the future.⁵

Whilst registries are costly and complex to establish and maintain, it is believed that:

“...registries can serve as a compelling foundational tool in developing evidence-based paradigms for best medical practices, provide real-time actionable feedback to stakeholders (industry, hospitals, health care providers), and improved quality of care and outcomes.”⁶

The combined outputs of improved PMS activities, more complete EUDAMED data and clinical registries will enrich the availability and quality of real-world evidence that is in high demand by key stakeholders such as governing authorities and payors.

Unique Device Identification: While new for Europe, UDI has been an established FDA requirement in the USA since 24 September 2013. However, the cost of updating artwork, components and packaging for devices currently supplied to the EU can be significant, as will be the costs of producing materials for the purposes of communicating these changes to the medical community.

A survey of EUCOMED* members in 2013 reported an estimated €7.5b (US \$ 8.1 billion) cost to industry regarding compliance with a UDI system, improvements in labelling and clinical performance data.⁷

Economic operators: The omission of economic operators in the AIMDD/MDD has been addressed in the MDR. ‘Economic operator’ throughout the MDR means to include manufacturers, authorised representatives, importers and distributors. Compliance responsibilities, quality management expectations, traceability of devices requirements and collaboration with authorities are just

a few of the requirements outlined in the MDR. Overall, economic operator requirements have been aligned with those established in other geographies.

NOVEL REQUIREMENTS

MDR introduces two Novel requirements. One relates to organisational accountability and the other extends the scope of the MDR which now includes non-medical devices that are similar to medical devices, such as coloured, cosmetic, non-corrective contact lenses.

IMPLICATIONS FOR INDUSTRY

Organisational accountability: One of the two mentioned “Novel” requirements is for at least one person in the organisation to be formally assigned the responsibility of ensuring regulatory compliance of the enterprise.

Although it is anticipated that this requirement will not be too onerous for medium to large organisations which already have a Quality, Regulatory Compliance or Safety Manager in place, challenges exist as the sphere of influence now required of people in such roles will be significantly greater than before.

The skillset and capabilities required for these elevated responsibilities in addition to increased demands of effort, time and focus must be recognised and supported by organisations in order to be effective in their execution of this requirement. Executive sponsorship of the EU MDR transition is crucial for success, and will require sponsors to:

- ensure alignment of workstreams with the overall company strategy,
- foster support from other senior executives and overcomes resistance,
- provide ongoing direction as the workstreams progress,
- create conditions for success that enable tactical implementation; and
- empower transition leads to deliver results.

⁵ APACMed/MTAA/Mecomeds Consensus Statement on the Future of Medical Device Registries Across Asia-Pacific and Middle East-North Africa.

⁶ Dokholyan RS, Muhlbaier LH, Falletta JM, et al. Regulatory and ethical considerations for linking clinical and administrative databases. *Am Heart J.* 2009;157:971–82.

⁷ EY How the new EU Medical Device Regulation will disrupt and transform the industry. © 2016 EYGM Limited. EYG no. 00379-164GBL. * EUCOMED - European Confederation of Medical Suppliers Association.



These few examples of MDR requirements and their implications highlight the diversity and complexity of issues that organisations are addressing in their preparations for transition.

How is the industry faring?

Medical technologies are developed in a framework of continuous innovation and iterative improvements based on developments in science, technology, and materials. This mindset of continuous improvement and design thinking, fundamental to medical device organisations is being applied in the preparations for MDR compliance. However, there are significant challenges to overcome.

Organisations that are already operating in line with international standards are expected to adjust more efficiently to the requirements of the MDR. For large organisations operating on a global scale, quality systems and processes for compliance with international standards may well be embedded within their operations. However, embedding a company-wide ethos that prioritises MDR compliance while still achieving timely patient access and balances with all other activities companies need to undertake to be successful could be a significant shift.

By contrast, small to medium organisations with less familiarity and/or experience with the demands of international standards alignment will have a more challenging transition. Limited human bandwidth and financial resources will inhibit preparations, as will absences or deficiencies in the necessary staff, systems and policies to deliver compliance.

Of all the challenges faced by organisations in transition, the one the industry is likely to struggle with the most relates to the time, financial capital and human resources required to conduct costly clinical trials. Whilst clinical evidence is important, challenges associated with funding, trial management and patient recruitment represent significant obstacles and will undoubtedly protract development cycles and delay delivery of innovative treatments to patients.

This will be a particular concern for small and medium enterprise that might not be able to conduct the clinical trials required to bridge data gaps, and therefore be forced to withdraw products from market, abort development plans or seek strategic partnerships to maintain the viability of commercialising their assets. It is also feasible that companies will no longer view Europe as an attractive territory for first launches, where previously they relied on the simplified and somewhat accelerated entry into the EU as their first market.

Barriers to entry will influence decisions of how, when and where to commercialise, and potentially divert launch activity towards more accessible markets. In fact, 74% of respondents in the latest Emergo Global Medical Device Industry Outlook for 2019 survey think that the current process of obtaining regulatory approval for a medical device (or IVD) in Europe is more difficult than it was a few years ago.⁸

In the worst-case scenario these requirements together with increased regulations threaten to stifle innovation and fracture the ecosystem that fosters medical technology advancement.

Conclusions

In the best-case scenario, the MDR transition will be smooth with limited market interruptions and increased consumers and medical professional confidence that the available medical devices meet their high safety and quality expectations. In the worst case, companies will fracture under the regulatory burden and innovation will grind to a halt, resulting in product deletions and patients being denied access to treatments. It is still too early to tell.

Whilst the medical device industry welcomes the regulatory reform, significant uncertainty remains regarding how these higher standards will impact productivity, innovation and patient access to transformative technologies. Changing organisational ethos and compliance framework implementation is an endurance event, not a sprint, and results of these efforts will accordingly take time to manifest. Organisational effectiveness will hinge upon well designed and implemented systems and processes that support these frameworks and improve workflow efficiencies. Therefore, compliance with the MDR should not be viewed as the destination.

As May 2021 fast approaches, transition preparations will continue, albeit with uncertainty and apprehension regarding the casualties of compliance, the effectiveness of the regulatory authorities, and the resilience and dexterity of organisations implementing the essential strategic, methodical and systematic approaches to deliver the desired patient outcomes.

Although losing perspective in the chaos of transition is a likely consequence for those involved, the promise of delivering life-saving and life-changing technologies to those who need it should be a beacon for all in the pursuit of excellence in safety and quality.

⁸ Emergo Global Medical Device Industry Outlook for 2019 survey.

To find out more visit www.saiglobal.com

Author: Helen Souris – OneFourNine Consulting Pty Ltd. h.souris@onefournine.com.au

SAI Global Limited ABN 67 050 611 642 © 2018 SAI Global Ltd. The SAI Global name and logo are trademarks of SAI Global Ltd. All Rights Reserved. 132097 05/19