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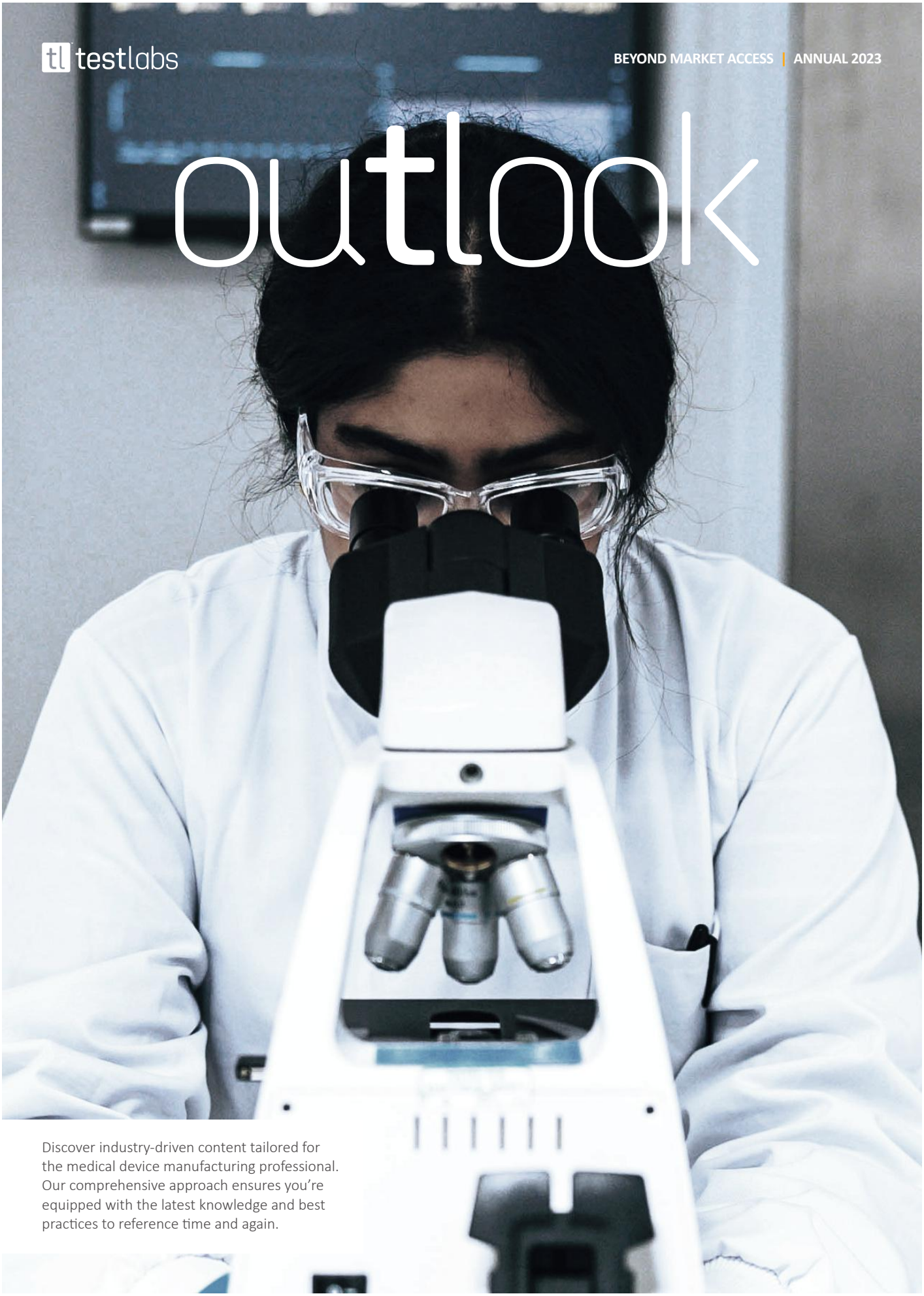

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Test Labs is a Medical Device testing laboratory with accredited Quality Management Systems. We work with medical device manufacturers providing expertise in clinical evaluation and reprocessing validation providing clients with tailored, highly customised solutions that go beyond market access.

'Outlook' is a Test Labs publication, curated from the past year's research and insight. Opinions expressed in Outlook are not necessarily those of Test Labs. Material contained in this publication may not be reproduced, in whole or in part, without prior written permission by Test Labs.

We would like to thank all our contributors for their input and support in delivering our inaugural edition. If you would like more information on an article or wish to contribute to future editions of Outlook, please email your request to: **outlook@testlabs.com**

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A FRESH OUTLOOK TO MEDICAL DEVICE TESTING

Hello and welcome to 'Outlook'.

As we embark on this exciting journey with the very first release of our yearly compendium from the world of medical device manufacturing and testing, I'm reminded of how important it is to pause and reflect on our achievements. It's in these moments that we gain a deeper understanding of the profound impact our work has, not only on the medical device industry but on the future of healthcare itself.

As an engineer, I've often found myself impatiently waiting to witness how the products we create are utilised, how they shape user interactions, and ultimately, the experiences they deliver. It's about looking beyond the confines of our internal processes, focusing on the broader impact, and finding the excitement that fuels our motivation for continuous improvement.

In our roles as scientists, engineers, and experts, we embrace the intricate details demanded of us. But this dedication never blinds us to the far-reaching influence our work has in the global landscape. We understand that product testing is not a mere check-box exercise; it's the foundation upon which healthcare systems worldwide rely.

Our commitment to excellence is fuelled by the knowledge that every test we conduct supports the delivery of safe and reliable medical devices to those who need them most. We call it "Beyond Market Access," as we believe it's a pathway to a healthier future.

The 'Outlook' annual is our perspective on navigating the complex regulatory challenges of our industry. It's presented in a confident yet calming and tranquil way that mirrors our vision of the medical device regulatory field and the dedicated individuals who work tirelessly to improve healthcare systems across the globe. We want our readers to recognise themselves, and the industry they serve, taking a moment to escape the pressures of the day while enriching their knowledge.

We want to open our doors and invite everyone to see what happens in the lab, and how medical devices are tested. We aim to shatter the secrecy that often cloaks laboratories, breaking the "servery hatch" analogy, where you don't know what happens when you hand over your device. So, we're lifting the lid on our lab for you to explore and demystify the process. Our team will share everything you need to know about what happens in the lab and beyond, offering an insider's view of our journey.

We are immensely grateful for the contributions of industry leaders and experts to this inaugural annual release. It's their insight and willingness to share that supports the growth of the industry – Thank you.

My appreciation extends to the entire Test Labs team, who are more than just a group of experts in medical device validation. They are a friendly and approachable team that genuinely enjoys working together. I am proud to be part of this team, and their enthusiasm is what motivates me each day to aspire for more.

We really hope that 'Outlook' provides you with a fresh perspective and understanding of behind-the-scenes testing and welcome you to join in with future editions. For more information on anything you've read within this annual or to visit the team at Test Labs HQ please contact **outlook@testlabsuk.com**

Tautvydas

Tautvyda Karitonas
Managing Director | Test Labs

CONTENTS

Welcome to Outlook. The following articles have been written by both members of the Test Labs team and a selection of industry professionals to bring you insight into the highs and lows of medical device testing.

PARTNERSHIPS ON GRANT APPLICATIONS: HOW IMPORTANT ARE THEY?

Eleanor Barnes discusses the role of partnerships when making grant applications, the implications and the advantages.

What is a grant partnership?

A grant partnership refers to a collaborative arrangement between two or more organisations that join forces to pursue a common goal or project using grant funding. While it is true that grant applications can be time-consuming and require extensive documentation, it is essential not to overlook a valuable and often required component: finding a project partner.

The trend towards collaborating partnerships continues to grow in the grant world. We have worked on several grants over the years and nearly all of them relied on some form of partnership collaboration, such as another SME, non-profit organisation, or academic institution. It may be a requirement of the grant agency that a portion of the award is given to the external partnering organisation, or it may be compulsory to receive outside financial contributions, such as in-kind offerings. So why are partnerships on grants so important, and why do funding agencies advocate it?

Why are they important?

Well, there are many reasons why partnering with another organization adds significant value to a grant application but key benefits include shared cost and complexities, broader support, new audience reach, and maximised resources. By forming a grant partnership, organisations can leverage their collective strengths, expand their capabilities, and enhance the overall quality of the project proposal. Collaborating with a partner offers several advantages:

- Complementary Expertise: A partner may bring skills, knowledge, or experience that complements your organisation's strengths. This collaboration allows for a more comprehensive and well-rounded project proposal.
- Shared Resources: Partnering organisations can combine their resources, including financial, technological, or human resources, to enhance project implementation. This shared pool of resources increases the chances of success and sustainability.
- Increased Credibility: Grant funders often view partnerships favourably as they demonstrate a collaborative and cooperative approach. A strong partnership can boost the credibility of your grant application and improve the likelihood of securing funding.
- Expanded Reach and Impact: Partnering with another organisation helps broaden the project's reach and impact. By tapping into each other's networks, the partnership can access a larger audience and achieve a more significant outcome.

While grant applications require focused energy on the narrative and supporting documents, it is crucial to dedicate time and effort to finding a suitable project partner. Partnering with the right organisation can greatly enhance the strength and competitiveness of your grant application, leading to increased chances of success in securing the desired funding.

What mistakes we have made?

Unfortunately, I did not prioritise partnership collaborations over the actual grant writing on previous applications. It pains me to admit it now, but I viewed them as nothing more than a requirement of the grant, a nuisance, in a way. Did we end up finding a partner in time? Of course. Were they necessarily the best choice for the project?

"While grant applications require focused energy on the narrative and supporting documents, partnering with the right organisation can greatly enhance the strength and competitiveness of your grant application."

In all honesty, no. Partnerships were forged with external parties who we already had an existing, trusted relationship with. They weren't necessarily the best fit for the project overall, but they were fine to feature on the application, as in, it ticked the box anyway.

But is it enough? No, in simple terms. 'Program Partners' came in at number 3 of the top 10 things assessors look for when evaluating a grant proposal.

- Are they experienced in the project programme?
- Do they have the right skills?
- Will they share the same project visions?
- Do they have the resources to commit to a long-term project plan?

These are the type of questions you should be asking yourself when seeking your partner because the assessors will be asking the same.

I cannot emphasise enough how important your partner is to the overall success of your grant application. So, where do you start? The following areas are my top three tips for building and sustaining partnerships for grant proposals.

1 Identify Your Partners Early

Don't wait until you are up against a grant application deadline to develop your partnerships. It will take time to allocate potential partners, discuss your project, and figure out who will be the best fit. Remember, the project could span months or even years, so it's important to partner with someone you know you can trust. Additionally, it is often a requirement from funders that you document your partners' role and commitment to the project by including formal letters of support and/or a list of their project contributions and associated costs to the application, which can be a time-consuming process.

2 Prepare a project plan

Draft a project plan and identify where you need to outsource support. Conversations can then be had with external parties who can help with that specific requirement of the project, and subsequently benefit from the best skills and expertise on the market. This will go a long way in convincing agencies to fund your project, by demonstrating a committed partnership to each project milestone.

3 Keep partners engaged throughout the project period

It is important to involve your partners early on as you implement your grant-funded project and keep them engaged throughout the project period. Sustaining these relationships may open doors for future grant opportunities, resource sharing and no-cost assistance from agencies across your community and beyond.

Maximise your chances of securing grant funding

Grant partnerships are a vital component of successful grant applications, offering numerous benefits and opportunities.

If you're looking to maximise your chances of securing grant funding and need assistance in forming strategic partnerships, we're here to help. Together, Test Labs can help create a compelling proposal and increase the impact of your project.

EVERYTHING YOU NEED TO KNOW ABOUT FDA MEDICAL DEVICE REQUIREMENTS

WORDS | TONI CARLTON

Toni Carlton has 6 years of experience working in an ISO 15189 UKAS accredited clinical biochemistry department within the NHS. During her time in the hospital, she achieved a Bachelor of Science degree in applied biomedical science at University of Westminster which incorporated her IBMS registration portfolio to become a HCPC registered biomedical scientist.

What does the FDA do?

The FDA is responsible for regulating the manufacture, repackaging, relabelling and/or import of medical devices. The regulatory requirements which must be complied with will depend on the intended use, indications for use and risk of the device. Below is a summary of the basic regulatory requirements that manufacturers of medical devices must comply with to place their products on the market in the US.

What is FDA establishment registration and device listing

Establishments (unless exempt) that are involved in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use must meet the registration and listing requirements outlined in 21 CFR Part 807. This may include any domestic or foreign establishment that:

- Manufactures a finished device to another establishment's specifications (contract manufacturer)
- Provides a sterilisation service for another establishment's device (contract sterilisers)
- Furthers the marketing of a device from a foreign manufacturer to those who deliver the device to the end user (initial importer)
- Manufactures components or accessories (including kit assemblers)
- Relabels, repackages or remanufactures a device
- Reprocess a single-use device that has previously been used on a patient

Unless a waiver is requested and granted by the FDA, owners or operators of establishments who are subject to compliance with these requirements must use the electronic device registration and listing system to complete the initial registration within 30 days of commencing operation. As part of the registration, they must provide the name, places of business, and information on all establishments (as detailed in 807.25) along with device listing information at that time.

Since 2007 an annual registration fee has been required and as part of this registration, the owners or operators are required to verify and update all information the FDA have on file. However, they are also required to document and report any changes made at any other time. For example, when a device is introduced, changes are made to a previously listed device, or when a previously listed device is removed from commercial distribution.

The requirements also state that any changes to the establishment registration information that is provided must be updated within 30 days of the change. Failure to submit this information on time will result in a "failed to register" or "failed to list" status, meaning the establishment may not appear on the FDA database until this information is provided and processed.

By having a maintained database of establishments and devices, the FDA can track the location of medical devices and where they are manufactured, enabling them to increase the nation's ability to prepare for and respond to public health emergencies.

Premarket Notification 510(k) process

The 510(k) submission is used to demonstrate to the FDA that the device intended to be marketed is substantially equivalent to one (or more) device already legally commercially available in the US. Devices cannot be commercially distributed until a letter of substantial equivalence from the FDA is received. Most low-risk devices (class I) and some slightly higher-risk devices (class II) are exempt from the 510(k) requirement: these devices can be found on the FDA website at fda.gov.

Devices which require a Premarket Notification 510(k) submission should follow the procedures outlined in 21 CFR Part 807 Subpart E. Submissions should be received by the FDA at least 90 days before the introduction or delivery of a device intended for human use which meets any of the following criteria:

- Being introduced into commercial distribution for the first time – meaning that it is not the same type as, or is not substantially equivalent to either a device in commercial distribution before May 1976 or a device introduced for commercial distribution after this date but has subsequently been reclassified into class I or II
- Being introduced into commercial distribution for the first time by a person required to register
- A device already commercially available (or being reintroduced) which is about to be significantly changed or modified in design, components, method of manufacture, or intended use

Each premarket notification submission should include the following information:

- The device name, including all names that it might be referred to e.g., trading name and classification name
- The establishment registration number, if applicable, of the owner or operator submitting the premarket notification submission
- The class of the device and, if known, its appropriate panel (or a statement if determined that the device should not be classified under section 513)
- Action taken by the person required to register to comply with the performance standard requirements
- Proposed labels, labelling, and advertisements sufficient to describe the device, its intended use, and the directions for its use
- A statement indicating the device is similar to and/or different from other products of comparable type in commercial distribution, accompanied by data to support the statement
- Appropriate supporting data to show consideration of the consequences and effects on the safety and effectiveness of the device from any significant changes or modifications made
- A 510(k) summary or a 510(k) statement
- A financial certification and/or disclosure statement
- A statement that the submitter believes, to the best of his or her knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.
- Any additional information regarding the device that may be requested

What is required for Premarket Approval (PMA)

Rather than a 510(k) submission, devices of a higher risk (class III) which pose a significant risk of illness or injury, along with class I and II devices which are not able to claim substantial equivalence will need to follow the PMA process as described in 21 CFR Part 814. This process is more involved than the 510(k) process and requires the submission of clinical data to support claims made for the device. The PMA process consists of a four-step review including:

- Acceptance and filing review – administrative and limited scientific review to determine completeness of the application
- Substantive review – an in-depth scientific, regulatory and quality system review
- Panel review – review and recommendation by the appropriate advisory committee
- Final deliberations, documentation and notification of decision

The FDA aim to complete all of the reviews within 180 days of the date of filing the PMA and issue either an approval order; an approvable letter; a not approvable letter or an order denying approval.

For each device that requires the submission of a PMA, the application must include:

- The name and address of the applicant
- A table of contents
- This should include separate sections on non-clinical laboratory studies and clinical investigations involving human subjects
- A summary section
- This should be written in sufficient detail to provide a general understanding of the data and information in the application (usually around 10 to 15 pages in length)

- This section must contain a summary for indications of use; device description; alternative practices and procedures; marketing history; summary of studies and conclusions drawn from the studies
- A complete description of the device; each functional component/ingredient; the properties of the device relevant to the diagnosis, treatment, prevention, cure, or mitigation of a disease/condition; the principles of operation of the device and the methods used in (and the facilities and controls used for) the manufacture, processing, packing, storage and installation of the device
- Reference to any performance standard, along with adequate information to demonstrate how the device meets the standard (or justification of any deviations)
- Technical information
- Shall contain data and information in sufficient detail to allow the FDA to determine whether to approve or deny approval of the application
- Must contain results of non-clinical laboratory studies including the microbiological, toxicological, immunological, biocompatibility, stress, wear, shelf life, and other laboratory or animal tests, as appropriate.
- In addition to results from clinical investigations involving human subjects including all pertinent information such as clinical protocols, number of subjects per investigator, subject selection and exclusion criteria, study population study period, safety and effectiveness data, adverse reactions and complications (note this is not an exhaustive list)
- One or more samples of the device, if requested by the FDA
- Copies of all proposed labelling including instructions for installation
- An environmental assessment
- Financial certification and/or disclosure statement
- Information concerning uses in paediatric patients
- Any additional information regarding the device that may be requested

For a PMA supported solely by data from one investigation, a justification showing that data and other information from a single investigator are sufficient to demonstrate the safety and effectiveness of the device and to ensure reproducibility of test results.

Investigational Device Exemption (IDE) for clinical studies

The purpose of an IDE is to encourage the discovery and development of useful devices which are intended for human use without effecting the health and safety of the public or ethical standards. An IDE allows for clinical studies to be carried out to collect safety and effectiveness data which is required as part submissions for the PMA process (and to support the small number of 510(k) applications that require clinical data). It can also be used for clinical evaluation of modifications of a device or new intended uses of legally marketed devices which would require a new submission to the FDA.

Unless exempt, all clinical evaluations of investigational devices must submit an IDE application as outlined in 21 CFR Part 812 to gain approval from the FDA and an Institutional Review Board (IRB) before initiating the study. Studies with devices with a non-significant risk only requires approval from an IRB. An approval then allows a device to be shipped lawfully (for the purpose of conducting investigations) without needing to comply with other requirements of the Food, Drug, and Cosmetic Act (FFDCA) which would normally apply. The IDE application should include:

- The name and address of the sponsor
- A complete report of prior investigations of the device and an accurate summary of those sections of the investigational plan
- A description of the methods, facilities, and controls used for the manufacture, processing, packing, storage, and, where appropriate, installation of the device
- An example of the agreements to be entered into by all investigators and a list of the names and addresses of all investigators who have signed the agreement
- A certification that all investigators who will participate in the investigation have signed the agreement, that the list of investigators includes all the investigators participating in the investigation, and that no investigators will be added to the investigation until they have signed the agreement
- A list of the name, address, and chairperson of each IRB that has been or will be asked to review the investigation and a certification of the action concerning the investigation taken by each such IRB
- The name and address of any institution at which a part of the investigation may be conducted
- If the device is to be sold, the amount to be charged and an explanation of why sale does not constitute commercialisation of the device
- A claim for categorical exclusion or an environmental assessment
- Copies of all labelling for the device
- Copies of all forms and informational materials to be provided to subjects to obtain informed consent
- Any other relevant information FDA requests for review of the application

What is Quality System (QS) regulation

To ensure medical device manufacturers produce products that consistently meet the applicable requirements and specifications the Quality System regulation which must be followed is outlined in 21 CFR Part 820. These requirements are known as Current Good Manufacturing Practice (CGMP) and relate to a range of processes and controls used for designing, purchasing, manufacturing, packaging, labelling, storing, installing, and servicing of medical devices. A few examples of requirement categories included are document controls, purchasing controls, identification and traceability, nonconforming product, corrective and preventative action.

Each manufacturer is required to establish procedures for conducting quality audits to ensure the quality system is in compliance with the established system requirements and to determine the effectiveness of the quality system. Each manufacturing facility will then also undergo inspections by the FDA to assure compliance with the Quality System requirements within the regulation.

The FDA recognises that the requirements of the latest edition of ISO 13485 provides a similar level of assurance for producing consistent medical devices which are safe and effective as the CGMP requirements. They also understand the benefits of harmonising requirements with other regulatory authorities and internationally recognised standards, which is why there was a proposal to update the Quality System regulation submitted by the FDA in early 2022. The proposed change would look to amend the current Part 820 to incorporate the reference of ISO 13485 to remove unnecessary duplicative regulatory requirements which currently impede market access and add additional costs.

What are FFDCA labelling requirements

The FFDCA defines labelling as 'all labels and other written, printed, or graphic matter upon any article or any of its containers or wrappers or accompanying such article' at any time while a device is held for sale after shipment or delivery for shipment in interstate commerce'. This means that for general devices the labelling requirements set out in 21 CFR Part 801 also extends to descriptive and informational documents associated with the product such as booklets, brochures, posters, instructions, and tags.

The minimum labelling requirements for all medical devices include the name and place of business; the intended use of the device and adequate directions for use for a layperson to safely operate the device. This means that the label (and associated literature) cannot include any false or misleading statements and must be displayed prominently in an appropriate location.

Further into Part 801 of the 21 CFR in Subpart H it also outlines the additional special requirements that should be complied with for particular medical devices. It should also be noted that the following Parts of 21 CFR also contain labelling requirements which may be relevant to particular devices:

In Vitro Diagnostic Products – 21 CFR Part 809

Investigational Device Exemptions – 21 CFR Part 812

Unique Device Identification – 21CFR Part 830

Good Manufacturing Practices – 21 CFR Part 820

General Electronic Products – 21 CFR Part 1010

Medical Device Reporting (MDR) FDA guidance

Device users, importers, manufacturers and distributors of medical devices should comply with the mandatory requirements of 21 CFR Part 803 for recording and reporting certain device-related events and problems with products to the FDA. This section is designed to help protect the public and ensure that devices continue to be safe and effective for their intended use.

The minimum labelling requirements for all medical devices include the name and place of business...

Device User Facility

Device user facilities such as hospitals, ambulatory facilities nursing homes or outpatient diagnostic/treatment facilities must submit reports as described in subpart C of Part 803. A report must be submitted to the manufacturer no later than 10 days after the user facility becomes aware of an incident which is considered a reportable event. This includes any death or serious injury which has been (or may have been) caused by a device, as well as events where the device may have contributed to the incident. In the event the manufacturer is not known, then these must reported to the FDA in accordance with the requirements of 803.12 (b).

Using Form FDA 3419, user facilities must also submit an annual report by January 1st as described in 803.33. A summary of all reportable events must be included, along with the reports submitted to the manufacturer/ FDA; however, if no reports were submitted during that year, an annual report is not required.

Manufacturers must report no later than 30 calendar days after receiving or becoming aware of adverse events or malfunctions...

Importer

Importers must submit reports as described in sub-part D of Part 803. No matter how the importer becomes aware of information (including from user facilities and medical or scientific literature) pertaining to a device causing or contributing to a death or serious injury, a report must be submitted to the manufacturer and the FDA, as soon as practicable but must be within 30 days of becoming aware of the event.

In addition to this, importers must report to manufacturers within 30 days of becoming aware of any possible device malfunctions or if a device is likely to cause or contribute to a death or serious injury if malfunction were to occur. Importers may become aware of this through any source including through their own research and testing, servicing, or maintenance of the device.

Manufacturer

Manufacturers must report to the FDA information no later than 30 calendar days after receiving or becoming aware of adverse events or malfunctions that may have, or has the potential to, cause or contribute to a death or serious injury. Manufacturers may become aware of information through the user facility, importer or other initial reporter and are responsible for obtaining, investigating, and submitting this information. Foreign manufacturers who distribute in the US should designate a US agent to be responsible for the activities outlined in Part 803.58 including reporting adverse events/ malfunctions to the FDA and maintaining the complaints files.

Manufacturers must also submit a 5-day report when an MDR reportable event necessitates remedial action to prevent an unreasonable risk of substantial harm to the public health or the FDA makes a written request for a reportable event. This report must be submitted with all the required information no later than 5 working days after becoming aware of either of these circumstances.

Information that must be provided in these (initial) reports include the patient information about the adverse event/device problem, device information, initial reporter information, reporting information (such as manufacturer contact information, report sources, date, type and number) along with any other information about the device and event. It is important to remember even though a user facility may submit a report for an incident that may involve multiple devices which are suspected to be involved with the incident, manufacturers must submit separate reports for each device involved.

Supplemental reports may also be submitted as follow-up to the initial report if information is obtained which was not originally submitted.

Distributors

Medical device distributors must establish and maintain complaint records (files) of incidents but are not required to report these incidents. These records must be clearly identified as device incident reports and filed by device name as well as include all the incident information. These files must be backed up and maintained in an electronic format and be retained for a period of 2 years from the date of inclusion or for the period of time equivalent to the expected life of the device, whichever is greater, even if this is after the point in which the device is no longer being distributed.

CLEANING VALIDATION WITH ATP: EVERYTHING YOU NEED TO KNOW

What does ATP stand for?

'Mitochondria is the powerhouse of a cell' is a phrase that should be engrained from many science lessons in school, but what exactly gives the mitochondria their power-like abilities? The answer is an intracellular small energetic molecule called ATP (Adenosine Triphosphate). ATP works by forming high energy bonds through the consumption of one of its phosphorus molecules, changing ATP into ADP. Although mitochondria are not present in many microorganisms like bacteria, they still produce and use ATP through different means, as ATP is the common 'energy currency' that provides fuel for most cellular activities. Therefore, ATP could be regarded as the 'powerhouse molecule' of most living organisms.

What is an ATP monitor?

Upon this concept, the use of ATP bioluminescence monitors was established. These devices measure the level of ATP amounts on a surface to determine whether there is residual organic matter present after the sanitization of an environmental surface, a medical device, or a surgical instrument. As mentioned previously, most living organisms produce and use ATP. The identification of ATP directly correlates to the presence of organic matter, this could be live or just debris from the impact of a sanitization process. For instance, here at Test Labs, we use ATP bioluminescence monitors as a secondary means of protein identification for IFU (instructions for use) validations (ISO 15883-5:2021).

Cleaning efficacy validation using ATP monitors

The validation of IFU is a requirement of the MDR EU 2017/745 to tackle the growing concern within the medical device scene about the reprocessing of medical devices and their effects on the intended use of the device. The ISO 15883-5:2021 standard comprises a cleaning process on a medical device based on the manufacturer's IFU, and subsequent analysis of at least two analytes that indicate the presence of organic matter, of which one analyte that Test Labs measure is ATP. Post-cleaning, any residual ATP is collected from the sample and measured using the ATP bioluminescence monitor. The importance of the ATP monitor in this standard is to quantify the level of debris in the form of ATP that remains after the cleaning procedure. The presence and quantification of ATP on a medical device would verify the cleaning efficacy. Hence, the ATP test measurement is essential in validating whether the instruction for use (IFU) is efficient in cleaning a sample. If the sample reads at an ATP level above the alert level (22 femtomoles of ATP/ cm^2) as per ISO 15883-5 acceptance criteria, then the IFU is deemed unacceptable. This similarly occurs in multiple hospital settings which utilize ATP bioluminescence monitor devices as an ATP-based sanitization monitoring system.

How do the monitors for ATP bioluminescence work?

ATP is measured through a bioluminescent reaction between the enzyme luciferase and the substrate luciferin. Only in the presence of ATP, the luciferase reaction occurs, producing a bioluminescent signal. This signal is proportional to the amount of ATP within a sample; hence a strong signal indicates high amounts of ATP, and hence a high amount of organic matter in a sample. However, ATP monitors do have their limitations. The biggest shortcoming is that ATP bioluminescence monitors are unable to detect viral organisms due to viruses not containing or producing ATP on their own.

In today's world, where hygiene is of paramount importance, the significance of sanitization cannot be overstated. ATP bioluminescence guns offer a reliable and efficient method for validating the cleaning of reusable medical instruments. By detecting residual organic matter on surfaces, these devices can confirm the efficacy of the cleaning process, ensuring that medical instruments are safe to reuse.

WORDS | RIWIA CHETIAN

With a BSc in Medical Microbiology and MA in Immunology, Riwia is well equipped with experience in handling in-vitro assays, techniques and methodologies that are utilised under many industrial settings

YOU'VE BEEN AWARDED GRANT FUNDING... SO WHAT HAPPENS NEXT?

WORDS | ELEANOR BARNES

You researched, drafted, wrote, drafted again, wrote again, and finally submitted that all important grant proposal. After what feels like an entire lifetime, you finally get that email notification you've been praying for – your proposal has been awarded funding.

Horizon's Inno4COV-19 was the first large-scale European funding competition we won. The grant was to support the rapid commercialisation of a new decontamination technology, capable of decontaminating small and confined spaces in hospital and healthcare settings, which was to be completed within the project deadline of one year. With a 7% success rate, and being the only UK county within the EU to be awarded funding, we were very proud of this achievement.

So, what are the next steps?

It seems we talk a lot about how to write grants, but not so much about what happens after funding is awarded. This is disadvantageous because how you handle the next steps plays a crucial role in the overall success of the project and the likelihood of securing future funding.

Below, I've listed the top 5 take-away points I learnt from the Inno4-COV19 funding process:

1 Make friends with your funder and don't delay communications

Once the funding offer letter is received, typically by email, the single most important next step is reading the terms and conditions, understanding them, and responding in good time. It sounds obvious, but delaying the acceptance of funds will only have negative implications further along. Gather the required documents and email them to the funders as soon as possible, not forgetting to thank them for their generosity in the process. For the duration of the project you will have regular communications with the funders, so it's essential you provide a great first impression and act promptly.

2 Re-read your proposal for out of date content

Project timelines and implementation activities listed in your proposal shouldn't be taken lightly. The funders will hold you accountable to these milestones and expect that they are completed accurately and precisely on time, so they must be realistic. The wait time between proposal submission to acceptance can be a very long-drawn-out process, so it's somewhat expected that certain unforeseen changes may have taken place during this period, forcing the project timeline to deviate from the original proposal. For example, a colleague may have left the business, or a particular resource is no longer available; whatever the reason if you suspect the milestones are no longer achievable, it must be communicated to the funders as soon as possible.

3 Project Planning

A lack of project tracking can lead to detrimental delays, which overtime snowballs into larger problems and before you know it the entire project is derailed. A well organised project management process must be in place and in constant review to enable successful completion of the project on time. With Inno4-Cov19, we shared updates on the projects progression by having a scheduled reoccurring meeting once a fortnight. Focus was on milestones achieved listed in the proposal, and what mitigating solutions were in place to ensure we wouldn't experience project creepage. Additionally, weekly meetings were conducted with the internal project team to ensure focus remained of the specific tasks required of them to enable successful project completion.

4 Project Reporting

Project reporting is a crucial part of the grant process and a lot of departments will need involvement, including finance, HR and collaborative partners. For inno4-COV19, stipulations included a video introduction discussing the new technology and intended use, advertisement of grant acceptance on social media channels, completion of a Technical Report and Third Party Monitoring Report, just to name a few. You need to keep on top of it all, so created a discipline and allocate protected time for all required activities.

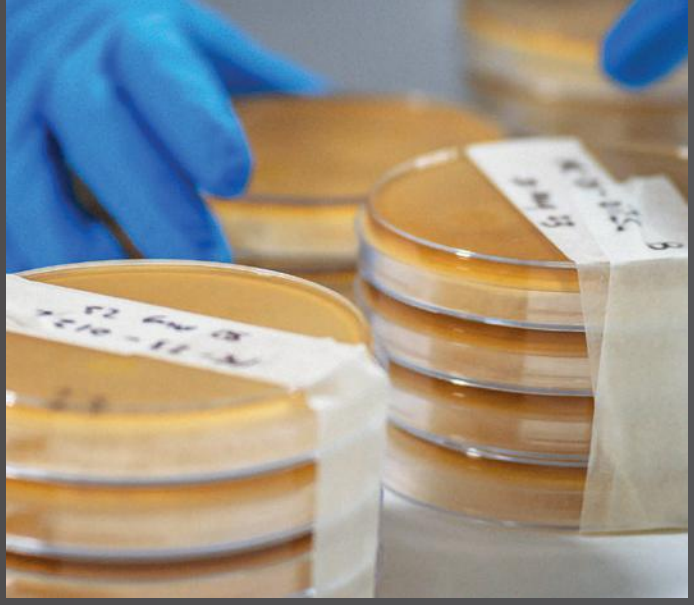
5 Closing the project

This is the most exciting part – in our case, we have delivered a physical unit, designed and developed to specification agreed with funders. Each project will have its own closing process and actions that must be completed. The Inno4-COV19 closing process included in-person product presentation, at an event where all other grantees were showcasing their project deliverables. Attending the event, completing final technical report and providing final presentation video were all critical in successfully closing the project and receiving the final funds.

As a closing note, it's important to remember that grants are basically contracts. Each grant will stipulate different rules and agreements for the intended use of funds, and it's essential that these are abided to at the very best of your ability.

OUR GUIDE TO GOOD LABORATORY PRACTICE

WORDS | TONI CARLTON



WHY WAS THE GOOD LABORATORY PRACTICE INTRODUCED?

Prior to 1976, scientists were trusted to provide complete, accurate and unbiased data which could be submitted to authorities without question. However, changes to regulations were brought about after a case in the US against a major drug and chemical company identified several serious flaws including false and completely fabricated records. The US FDA then discovered that this was not restricted to just one company. As a result, the US FDA developed a Code of Practice (GLP for Non-clinical Laboratory Studies) for the industry to promote the quality and validity of test data.

In 1978 the Organisation for Economic Co-operation and Development (OECD) was established to be the expert group on GLP. Although led by the US, there was also representation from 17 of its member countries, the Commission of the European Communities, the World Health Organisation (WHO) and the International Organisation for Standardisation (ISO). Using the basis of the GLP regulations published by the US, they developed the OECD Principles of Good Laboratory Practice, which was then formally recommended globally for use in 1981. 15 years later, another expert group, led by Germany was established to review and update the Principles of GLP to account for the scientific and technical progress that had been made in the field of safety testing. These principles are now within national law in many countries.

What are the Principles of Good Laboratory Practice?

Good Laboratory Practice is a defined set of principles to be implemented in a quality management system by an organisation (test facility) completing non-clinical health and environmental safety studies. It outlines how studies should be planned, performed, monitored, recorded, archived, and reported.

The principles of GLP state the requirements for the following components:

- Roles and responsibilities for those involved with GLP studies including the Test Facility Management, Study Director, Principal Investigator, Study Personnel and Quality Assurance Personnel
- The Quality Assurance (QA) programme
- The facility including archiving and waste disposal
- Apparatus, materials, reagents, test systems, and test/reference items
- Standard Operating Procedures (SOPs)
- The performance of the study and reporting of the results
- Storage and retention of the records and materials

WHAT DOES IT MEAN IF A STUDY IS CONDUCTED UNDER GLP?

In order to state that a study has been conducted under GLP, it must be completed by a test facility that belongs to an appropriate compliance monitoring programme and ensures that the study performed conforms to the principles GLP. A key component of a GLP system is the requirements for the QA department, which independently monitors the entire study. This includes verifying that all written procedures including the study protocol are followed correctly and that the report accurately represents the results produced.

By conducting a study under the principles of GLP, it provides the assurance that the study has been performed exactly as described in the study protocol (which is approved by the Study Director and the Sponsor/customer). It also gives confidence that the results reported are accurately represented. Due to GLP being accepted in many countries across the globe, it means that when a study is performed under GLP it allows for mutual acceptance of data among countries, meaning that duplicative testing can be avoided, thereby saving time and resources.

WHAT IS THE DIFFERENCE BETWEEN GLP, GCP, GMP AND ISO 17025?

Although GLP is most commonly associated with the pharmaceutical industry, it actually applies to many other areas relating to safety in the health or environment field. The key point is to remember that GLP is specifically designed to protect scientific data integrity for studies and testing which are non-clinical. This leads to clinical studies which are then governed by Good Clinical Practice (GCP) as well as other regulations intended to ensure the protection of human pparticipants such as the Declaration of Helsinki. One key difference is the role and responsibility of the Study Director who is a single point of contact who has overall responsibility for a GLP study, whereas GCP studies do not have this role and the overall responsibility including maintaining QA for clinical studies resides with the Study Sponsor.

Next, there is Good Manufacturing Practice (GMP) which is intended to demonstrate if individual batches of a regulated product meet the manufacturing pre-defined criteria. This means that GMP should apply to the entire drug manufacturing process, whereas GLP should be applied specifically to the safety testing phase.

Lastly, ISO/IEC 17025 is a quality management system standard which is also internationally recognised. However, the aim of this standard is to demonstrate that a testing and/or calibration laboratory has the technical competence and the ability to generate technically valid results for a defined scope, specified by their schedule of accreditation.

EVERYTHING YOU NEED TO KNOW ABOUT DENTAL INSTRUMENTS VALIDATION

For successful dental instrument validation, evidence must be provided in relation to the reuse of the device, in particular cleaning, disinfection, sterilisation, maintenance and functional testing and the related Instructions for Use (IFU). Within the IFU, there must be a detailed process which has been appropriately validated which ensures that the device is clean, sterile, moisture-free, and safe to use after every reprocessing cycle.

Medical Devices in Dental Industry

Many devices used within the Dental Industry should be classified as a medical device according to the Medical Device Regulation EU 2017/745 (MDR). The scope of dental devices ranges from the lowest risk classification (such as dental chairs) to the higher risk classifications (such as dental implants). Manufacturers must assess devices on an individual basis, taking into consideration the intended use of the device, as this can differ for the same or similar instruments. As a result, different requirements of the MDR will need to be met. For example, Endodontic instruments could be classified as Class Ir if used as a surgically invasive device, however, if used with a hand piece would be classified as a Class IIa device. Due to this, when submitting an application to a notified body in accordance with the minimum criteria outlined in Annex VII section 4.3 the risk classification justification will be detrimental to its approval.

Requirements of Manufacturers of Reusable Surgical Devices within the Dental Industry

With the reclassification of some Class I medical devices into the new subcategories manufacturers must now apply the procedures set out in Annex IX for devices intended to be supplied in a sterile condition (Class Is), have a measuring function (Class Im) or are reusable surgical instruments (Class Ir). As a result, these devices can no longer be self-certified and must have involvement from a notified body to ensure compliance.

Manufacturers of reusable surgical instruments, including those found in the dental industry, must demonstrate compliance against the general safety and performance requirements to a notified body. Evidence must be provided in relation to the reuse of the device, in particular cleaning, disinfection, sterilisation, maintenance and functional testing and the related Instructions for Use (IFU). Within the IFU, there must be a detailed process which has been appropriately validated which ensures that the device is clean, sterile, moisture-free, and safe to use after every reprocessing cycle. In addition to this, identification of the point at which the device is no longer safe to use must be detailed e.g., the maximum number of uses due to material degradation. As a result, verification methods should be performed for both aspects.

Manufacturers must assess devices on an individual basis, taking into consideration the intended use of the device, as this can differ for the same or similar instruments...

Cleaning, Disinfection and Sterilisation of Reusable Surgical Instruments

Cleaning is the first step in the multistage process to minimise the risk of microbial contamination for reusable devices. There are a range of different cleaning and disinfection methods that can be used including washer-disinfectors, ultrasonic cleaning, or manual cleaning. Even though using a washer-disinfector is the preferred method in the industry, due to the control and reproducibility of cleaning that can be achieved, this may not be appropriate for all types of devices.

WORDS | TONI CARLTON

Continued...

Cleaning and disinfection validation should be performed to demonstrate that all items can be cleaned by one of these methods reliably and consistently using predetermined and reproducible conditions. Evidence of the removal of residual debris left on the device after use must be documented due to the risk of inhibiting the effectiveness of the sterilisation process. Manufacturers can use the series of international standards, ISO 15883, which have been developed to specify the requirements and testing to be performed for the use of washer-disinfectors while testing based on requirements outlined in ISO 17664 can be used for other cleaning methods.

There are also a wide range of sterilisation methods used on medical devices, with the aim to prevent the potential of cross-infection between patients. The use of autoclaves to perform moist heat (steam) sterilisation is the most recommended method for reprocessing reusable dental instruments. The requirements for the development, validation, and routine control of a moist heat sterilisation processes for medical devices is specified in the ISO 17665 standard. The manufacturer must determine and validate the operating conditions required to effectively sterilise these devices including the choice of sterilisation cycle to be used (temperature, pressure, and time), the nature of the load, the loading pattern, wrapping, trays or containers and labelling.

The purpose of validating this process is to provide reassurance that when appropriately followed, the procedures outlined in the IFU will ensure the device is thoroughly cleaned and sterilised prior to being reused. Due to the high risk of the spread of infections associated with reusable surgical instruments, notified bodies will review this data as part of the conformity assessment that must now be performed to show compliance against the MDR.

Compatibility of reprocessing of dental instruments

When validating the reprocessing of dental instruments, manufacturers should also consider the compatibility of the device with the selected cleaning, disinfection and sterilisation cycle. After reprocessing, evidence that the device continues to meet any defined chemical and/or physical specifications required for the device's intended purpose should be documented. Manufacturers must also evaluate the impact of processes on material properties and the mechanical properties of the material used, such as strength and wear resistance and minimise accordingly.

Incompatibility of the reprocessing of dental instruments can impact the performance or safety of the product, leading to premature failure due to fatigue, discolouration, or residue remaining on the surface of the device. Quantitative and qualitative data can be collected on the most common material compatibility indicators including changes in visual appearance, texture, organic characteristics, and loss of functionality.

Some standards have been developed for testing materials used for dental equipment surfaces such as ISO 21530 which can be used to determine the resistance to chemical disinfectants. This standard includes three different methods of disinfection: immersion, spray, and contact. However, manufacturers must test against the whole process outlined in the device IFU for the number of cycles specified as part of their validation, not just each individual part. This will determine if the device can withstand the temperature, pressure and chemicals applied and at what point the device is no longer safe to use.

How is dental equipment successfully validated?

If you produce dental equipment it's likely that your products need to meet the requirements of the Medical Devices Regulation (MDR) 2017/745, and Test Labs can help. Our comprehensive IFU validation methods include simulated use cycle tests, automated cleaning tests, sterilization process validation, and compatibility assessment testing.

testing clarity in just 3-clicks

Discover all your testing requirements in just 3-clicks at **testlabsuk.com**

STREAMLINED, SWIFT AND SPECTACULAR: THE NEW TEST LABS WEBSITE

In a world driven by innovation and accelerated by digital advancement, Test Labs is proud to unveil a ground-breaking digital transformation that promises to reshape the landscape of accessibility for the medical device industry, saving you time and empowering your understanding of testing requirements in an ever-changing landscape.

Your Precious Time, Our Utmost Priority

In a bustling world where every second counts, the all-new Test Labs website sets out to revolutionise the way you access our vital services. We understand that in the medical device industry, you simply cannot afford to waste time.

The feedback we consistently receive from medical device manufacturers and regulatory affairs consultants is clear: what they need is swift access to information. They want to know if we offer a specific testing service and understand our typical lead times. This insight is crucial in their high-paced journey to bring their innovations to the market.

A Seamless 3-Click Journey

Visit **testlabsuk.com** where clarity, speed, and user experience reign supreme. Our aim is simple: to get you to the right service in just three clicks.

Select your device **category** from the options at the very top of our new homepage. After just one click you're selecting your **specific device** and a further click presents you with all the **services** relevant to your device, complete with clear information on lead times and accreditations.

Introducing the 'Device Card'

Find out all the information you need, at a glance with the innovative 'Device Card' (left). Every Device Card contains an overview, related resource links from our extensive Medical Device Resource Library, typical lead times, the number of relevant services available and the click-through to explore those services... No lengthy forms, no chat-bots and no delay in getting the insight you need.

Your Time, Your Success

At Test Labs, both online and in-person, we're here to match your pace and save you time. We understand that efficiency is paramount in your journey to market success. Time is your most valuable resource, and we're committed to giving it back to you.

From the moment you land on our website, it's about delivering the ultimate customer experience. We're not just helping you navigate a website; we're helping you navigate your path to success. With Test Labs, you're not just a visitor; you're a partner in innovation.

We invite you to join us in this new era of accessibility. This isn't just about browsing a website; it's about empowering your journey. The future is here, and it's built to put time back in your hands, where it belongs.

Welcome to a new era of accessibility. Welcome to **testlabsuk.com**

Ultrasound Scanners

These devices use extremely high frequency sound to create images in the body or measure certain characteristics such as blood velocity.

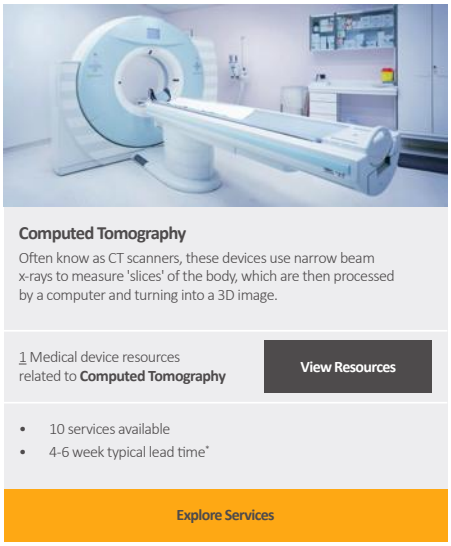
1 Medical device resources related to **Ultrasound Devices**

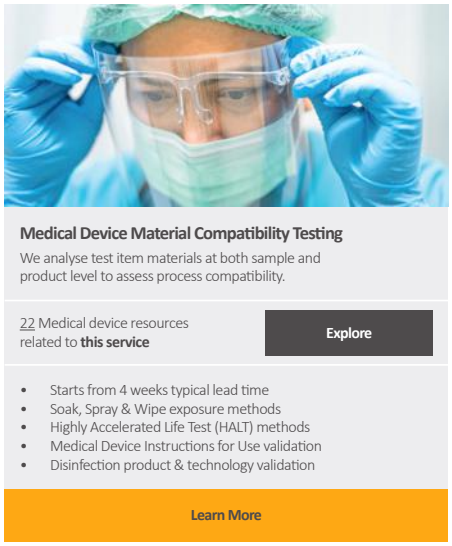
View Resources

- 10 services available
- 4-6 week typical lead time

Explore Services

Correct at time of print, November 2023. Further additions and enhancements are planned for 2024 and beyond. Stay up to date at **testlabsuk.com**





Streamlining Validation Services for Medical Device Manufacturers

Enhancing the Path to Regulatory Excellence

In the world of medical device manufacturing, precision is paramount. One significant challenge you face is ensuring that your devices adhere to the claims made in your Instructions for Use (IFU). In an industry bursting with diverse medical devices, finding the precise validation service you need can be akin to searching for a needle in a haystack.

Let's delve into one of our standout services, the Instruction for Use (IFU) validation.

The IFU Validation: Revealing the Secrets of Device Service Life

Consider the "service life" of a medical device as its endurance, the time it's expected to remain in optimal working condition once it's in use. Various methods typically determine this critical parameter. However, a common pitfall among manufacturers is failing to account for the device's real-world usage, which includes essential maintenance practices such as cleaning, disinfection, and sterilization. These real-world factors inevitably affect a product's longevity and regulators worldwide are increasingly demanding robust supporting data in this regard.

How we validate service life based on the IFU

We deploy cutting-edge, in-house HALT methods and technologies that repeatedly operate test devices and prototypes, extracting crucial data in an accelerated timeframe. Robotics and calibrated equipment work in harmony, accelerating the process and eliminating the need for human intervention.

For manufacturers looking to substantiate their service life claims, we simulate years of usage in a compressed time frame, generating data suitable for the device's technical file.

For those in the throes of prototyping new products, we meticulously log data during testing. Periodic assessments allow us to monitor performance changes.

Once we've mastered the service life, we pivot towards Reprocessing Validation, adhering to the rigorous standards outlined in your device's IFU.

Medical Device Material Compatibility:

Material Compatibility Testing safeguards your device's structural and surface integrity against potential damage caused by disinfectants and cleaning agents. It involves assessing the impact of these products on a wide range of materials that may accumulate over time. Our in-house tests encompass both sample and product levels, addressing potential structural and surface damage on visual, physical, and chemical fronts.

IEC 60601-1 Pre-Compliance Evaluation: A Precursor to Excellence

Our journey culminates with the IEC 60601-1 Pre-Compliance Evaluation, a service offering manufacturers a safeguard against the disappointment of repeated testing at certification facilities.

Before your device faces compliance testing, we conduct a comprehensive review of associated documentation, encompassing the risk file, markings, instructions for use (IFU), and more. We scrutinize your device's response to repeated cleaning, disinfection, and sterilization cycles, ensuring it thrives under the rigors of practical usage. This review extends to basic electrical, mechanical, and temperature safety evaluations.

This approach saves you both time and resources while ensuring that your device complies with critical safety and performance standards.

That's our way, and it's as swift and precise as our services themselves. We believe in serving you with excellence from the moment you land on our website, a reflection of our commitment to your journey in the medical device industry. Your success is our success, and we're proud to accompany you on this path of innovation.

CASE STUDY

WORDS | ELEANOR BARNES

HOW TO LOSE OUT ON GRANT FUNDING BY 2%

In the fiercely competitive world of grants, losing out on funding is not uncommon, in fact, the odds are largely against you. **Only 5% of applicants on average are awarded funding**, but that doesn't deter businesses from trying, I mean, what's not to love about free money to aid ambitious growth? But grants take time, a lot of time, and a lot of effort. Spending months complying what feels like an entire business plan, to then see the dreaded generic 'thanks, but no thanks' email land in your inbox, is to be honest, quite soul destroying.

So what have I learnt? Having both won and lost out on funding opportunities, and being so, so close to being awarded a grant worth millions from Innovate UK's lucrative Smart Grants Scheme, here are the top 5 reasons on how to lose out on grant funding by 2%:

1 Assuming the assessors would love the proposal idea

Without going into too much detail, our project idea was an AI infection prevention and control (IPC) predictive technology to reduce the risk of infections in healthcare settings. Smack bang in the middle of Covid-19, it couldn't have been more current. An innovative technology to aid IPC in the midst of a global pandemic, what's not to love? A lot, apparently.

On a panel of 5 assessors, one of them hated it, in fact I'll go further, loathed it. In the application feedback, he/she went as far as saying 'the unsubstantiated claim about NHS savings ran through the proposal like a message in a stick of Blackpool rock'. Wow.

2 Being WAY too ambitious

Following on from the assessor's comment above, too much forecasted growth can be viewed as 'unsubstantiated', even if these claims are broken down and justified in the project costings. From an assessor's perspective, approving R&D proposals for funding can be challenging as they are often deemed both high risk and high cost, so it's difficult to find that middle ground of showing ambition, but at the same time keeping it real.

3 Overloading supportive evidence page

One of the single biggest challenges I've found when writing grant proposals is restricting content to the word count. Supportive evidence pages, which can be submitted alongside proposals, are a great way of including additional information. However, it is easy to get carried away and start overloading content, to the point you can't really see the wood from the trees. As a result, the essential information is missed and you are downgraded for it.

4 Partnering with a collaborative business as an afterthought

Like many funding advisories, Innovate UK largely encourages business and research organisations to collaborate on funding proposals. It's easy to get carried away and have sole focus on the written application, but choosing a partnering organisation should also be at the forefront of priorities. After all, they must share your project vision, have the right skills, and reflect your business culture, just to name a few.

5 Spending £££ on various consultants

Finding a consultant to help assess or write a funding application isn't new, in fact, the internet is swarming with them. If you are new to the funding scene, they can provide crucial support in boosting your application to appear more worthy of funding. They can however be expensive, and we learnt the hard way that the greater expense doesn't necessarily mean greater results. Our first submission, supported by a sole trader grant consultant, scored significantly higher than our second application, consulted by a very large well-known funding consultancy. In fact, the score was downgraded by nearly 10%!

LESSONS LEARNED

It must be remembered that the assessing panel is made up of varying people from different professional backgrounds and expertise. To secure funding, it is absolutely essential that the proposal can be read and understood by a broad audience. As an example, no one will fall in love with a project they cannot technically understand, so use language and content that all abilities can follow.

Secondly, review the overall project size. If it is large, equating to acquiring millions in funding, it may be best to segregate it into smaller more affordable chunks. Grants that come from public funds in particular must be deemed good value for money, and large sums can be off-putting to assessors.

Thirdly, check and re-check the proposal content and make sure the essential information 'pops' and isn't lost within the proposal.

Next, research potential partnering businesses from the beginning, have conversations early and get a feel for them. It will take time to build trust.

Lastly, it can be helpful to receive proposal feedback from an outside source such as a consultant, they can pick holes in the application and guide you in the right steps towards a winning proposal. As with partnering businesses, it's essential to research, interview, and select the person that best aligns with your business culture. Big money doesn't mean better results.

"We take immense pride in supporting our customers amid the ever-changing regulatory landscape, offering them UKAS accredited reports for validating their reprocessing instructions."

Enrico Allegra, Laboratory Manager

TEST LABS ACHIEVES UNPARALLELED STATUS AS THE ONLY ACCREDITED UK LABORATORY FOR CRUCIAL MEDICAL DEVICE REPROCESSING

In a momentous progress, Test Labs has emerged as the sole UK laboratory accredited to conduct reprocessing procedure tests for medical devices.

This prestigious recognition comes as the company continues its trailblazing growth, expanding its scope of testing services to cater to the evolving needs of medical device manufacturers, while navigating the complexities of the regulatory landscape.

Why all the excitement?

Medical device manufacturers face stringent regulatory requirements to ensure the safety and compliance of their reusable products. One crucial aspect involves validating the cleaning, disinfection, and sterilization processes outlined in the instructions for use (IFU). This indispensable data is pivotal in applications for regulatory approval, as it demonstrates the device's adherence to patient safety standards and the effective minimisation of infection risks.

Recognising the growing demand for accurate and reliable medical device reprocessing testing services, Test Labs invested substantially to develop and implement technical procedures, extending its ISO 17025 scope to encompass tests associated with device reprocessing. The expansion is a testament to the company's unwavering commitment to quality and its dedication to provide comprehensive reassurance to customers.

Toni Carlton, Head of QMS, echoed the sentiment, affirming that this advancement was a major stride in assisting customers to adapt to regulatory changes, particularly the MDR reclassification. She emphasized the significance of UKAS accreditation as a symbol of confidence and reliability, providing manufacturers with much-needed assurance during uncertain times.

This milestone not only reinforces Test Labs' position as a leader in the industry but also instills trust among its customers. Amid mounting pressure on manufacturers to meet evolving regulatory standards, Test Labs' accreditation emerges as a beacon of reliability and a testament to their commitment to delivering unparalleled service.

As the medical device industry faces continuous advancements and challenges, Test Labs remains steadfast in its dedication to providing exceptional reprocessing medical equipment testing services, bolstering the sector's resilience, and advancing patient safety. By maintaining its UKAS accreditation, Test Labs stands poised to serve as the industry's go-to partner for essential reprocessing reusable medical devices procedure tests, cementing its reputation as a new leader in medical device testing.

INDUSTRY INSIGHT

ACCESSING THE UK MARKET

Do you understand the complex and un-established requirements to place your medical device or IVD onto the UK market? If you are finding it confusing, then I am not surprised considering where we were and where we are now with the regulatory framework.

The UK requirements, historically, involved following the current EU regulatory framework e.g. MDD 93/42/EEC. EU MDR 2017 for CE marking devices but since the United Kingdom (UK) left the European Union (EU) back in January 2020, there has been uncertainty on what the actual requirements will be from a legislation perspective: it's no wonder, we're left scratching our heads!

Current Regulation Status

Although the United Kingdom consists of England, Wales, Scotland, and Northern Ireland (NI), manufacturers will need to take into consideration separate regulatory requirements for access in markets in England, Wales, Scotland (Great Britain) versus NI.

So, what are the actual requirements at present? Let's look at the current requirements for both Great Britain (GB) and NI...

Great Britain

GB follows the Medical Devices Regulations 2002 (SI 2002 No. 618, as amended) (UK MDR 2002) which is presently in effect in UK law and has been for some time. The UK MDR 2002 points to the EU Directives;

- Active Implantable Medical Devices (AIMDD) 90/385/EEC,
- Medical Devices (MDD) 93/42/EEC and
- In Vitro Diagnostic (IVDD) 98/79/EC.
- Transitional arrangements to the UK MDR 2002 are required to facilitate supply of devices to GB under the transition measures and the UK will continue to accept CE-marked devices as follows:
- General medical devices compliant with the MDD or AIMDD with a valid declaration and CE marking can be placed on the GB market up until the sooner of expiry of certificate or 30 June 2028
- In vitro diagnostic medical devices (IVDs) compliant with the IVDD can be placed on the GB market up until the sooner of expiry of certificate or 30 June 2030 and,
- General medical devices, including custom-made devices, compliant with the EU MDR and IVDs compliant with the IVDR can be placed on the GB market up until the 30 June 2030

Class I medical devices and general IVDs under EU MDD or IVDD, for which the conformity assessment did not require a notified body, can only be placed on the GB market if the involvement of a notified body would be required under the EU MDR or IVDR.

On 26th July 2023, the World Trade Organisation (WTO) published a notification on the draft text of the UK post-market surveillance requirements Statutory Instrument (PMS SI). It appears that much of the proposed PMS requirements closely align with that of the EU Medical Devices Regulation 2017/745. You should review your current PMS processes for applicability against UK requirements.

Apart from the PMS draft text that was released for consultation, there has been little information on what the actual regulatory framework will look like. It is thought that this may closely align with that of EU legislation, but this is just speculation at present.

Northern Ireland

Although NI is classified as being part of the UK, the regulatory requirements differ from GB. Under the NI Protocol 2021 SI no.905, medical devices and IVDs are governed under the EU Medical Device Regulation 2017/745 (MDR) and In Vitro Diagnostic Regulation 2017/746 (IVDR) retrospectively. The date of application is in line with the regulation(s) date of applications, which means that any new product developed will now need to meet MDR/IVDR requirements and the market accessed according to these regulations.

For devices that require a third-party conformity assessment for certification, an EU Notified Body or a UK Approved Body can be chosen. If the UK Approved Body carries out the assessment for NI market access, a UKNI mark will need to be applied to your device labelling, alongside the CE mark.

IMAGE | LONDON, ENGLAND

Country/Region	Applicable Markings	Requirement	Conformity Assess ment
NI	UKNI	This marking is accepted in NI but is not valid for other EU member states.	Sterilisation (usually heat if heat-stable or chemical if heat-sensitive
	The UKNI indication is required if a UK Notified Body undertakes the mandatory third-party conformity assessment and should be applied next to the CE mark.	UK Approved Body, Self-certification	High-level disinfection by heat or chemicals (under controlled conditions with minimum toxicity for humans)
	CE	This marking is accepted in NI.	EU Notified Body, Self-certification
GB (Scotland, Wales, and England)	UKCA	This marking is accepted on the UK market but is not accepted in NI or EU.	UK Approved Body, Self-certification
	CE	Marking accepted for devices between 30 June 2028 – 30 June 2030 depending on classification. (subject to change)	EU Notified Body, Self-certification

Authorised Representative

There is now a requirement that non-UK manufacturers need to appoint a UK Responsible Person (UKRP) prior to placing their devices on the GB market. A UKRP can be an entity on their own or your importer or distributor if they have the required expertise, they can also act on your behalf.

If you are based outside of the UK or EU, to place devices on the NI market, manufacturers will need to appoint an EU or NI-based Authorised Representative.

For simplicity, it is probably worth engaging with a UKRP and EU Authorised Rep to allow for entry into both the GB and NI markets if you are based outside these territories.

In both cases, your Authorised Representative will need to register your devices with the Medicines and Healthcare Products Regulatory Agency (MHRA), the UK Competent Authority that govern both GB and NI prior to product release to these markets.

Labelling Requirements

At present GB and NI are accepting CE-marked devices onto the market under both the directive and regulation with the acceptance of UKCA (GB) and UKNI (NI).

The UKCA and UKNI markings must be clearly visible and legible, and affixed to the product. If that is not practical, you can attach it to the packaging or accompanying documents, such as your Declaration of Conformity or Instructions for Use (IFU).

The table above looks at the country region vs the applicable markings, requirements, and conformity assessment.

Where we are today

Even though GB and NI are part of the United Kingdom, it is clear from a legislative perspective that these regions are moving in different directions, with the landscape for GB still very uncertain. We anticipated PMS legislation in the summer of this year with implementation in winter 2023 or early 2024, only to learn that it has been postponed.

We are confident though, that the UK Government is committed to providing and strengthening the UK regulatory framework for the purposes of providing safe and effective devices. However, we are less confident that there will not be more delays with implementation dates slipping further away.

WORDS | LAURA FRIEDL-HIRST

LFH Regulatory

Laura founded LFH Regulatory; a regulatory, quality and clinical consultancy including UKRP services. Her vision was to create a consultancy and a team of consultants that have a pragmatic approach for navigating companies to their end goals.

Laura gained a BSc (hons) in Medical Biology at The University of Huddersfield. Since then, she has gained over 12 years' extensive industry experience working with varying sized organisations and with a diverse range of medical and in vitro diagnostics. Her knowledge and expertise spans over regulatory, quality, clinical and design & development.

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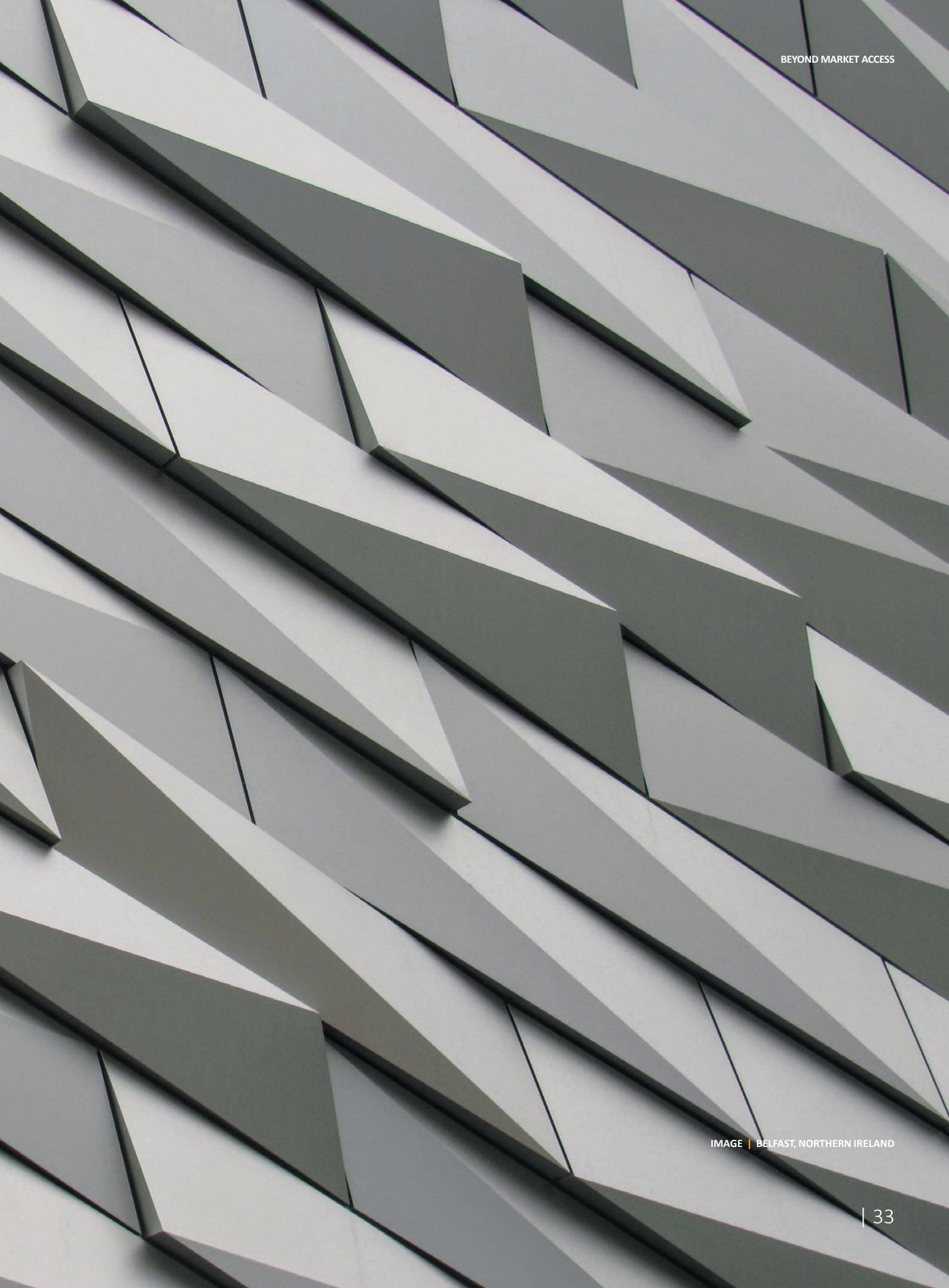


IMAGE | BELFAST, NORTHERN IRELAND

A GUIDE TO UKAS ACCREDITATION

WORDS | TONI CARLTON

Who are UKAS?

The United Kingdom Accreditation Service (UKAS) is the UK's national accreditation body. They are a private, not-for-profit organisation appointed by the government. Using their independence and expertise, they assess and accredit organisations that provide services such as certification, testing, inspection, and calibration against internationally recognised standards.

UKAS issues accreditation certificates and schedules, permitting the use of the UKAS mark accompanied by the UKAS Accreditation Number of the accredited body on the certificates/reports relating to those activities covered under an organisation's scope.

WHO IS UKAS ACCREDITATION APPLICABLE TO?

Organisations across a range of sectors, wanting to provide assurance to their customers for their products and/or services may wish to seek accreditation. UKAS can accredit organisations offering the following services against national and internationally recognised standards:

- Calibration laboratories
- Certification bodies
- Imaging services
- Inspection bodies
- Medical laboratories
- Medical physics and clinical engineering (MPACE)
- Medical reference measurement
- Physiological services (IQIPS)
- Proficiency testing providers (PTP)
- Reference material producers (RMP)
- Testing laboratories
- Validation/verification bodies for Greenhouse gases

What Is the Difference Between 'Accreditation' and 'Certification'?

'Accreditation' and 'certification' often get used interchangeably, and although they are closely related terms, they are distinctly different in quality assurance.

Although both require an assessment by an independent third-party via an audit of the organisation, certification is the procedure which gives written assurance that a product, process, or system conforms to specified requirements of a recognised standard or scheme. Whereas, accreditation, is a formal recognition by an accreditation body, such as UKAS, for the technical and organisational competence to carry out a 'specific service' in accordance with the standards and technical regulations, as described in their 'scope of accreditation'.

What Does It Mean If a Laboratory Is UKAS Accredited?

Accreditation underpins confidence that the laboratory can operate within defined procedures and to established standards which can be relied upon to ensure competence, independence, and performance of the organisation. UKAS ensure this by performing assessments on an annual basis, with a reassessment of the organisation every 4 years for the services outlined on the laboratory's schedule of accreditation. The assessment will review a range of aspects including the personnel and their expertise, the facilities and equipment as well as the systems/procedures in place but most importantly if these are being followed.

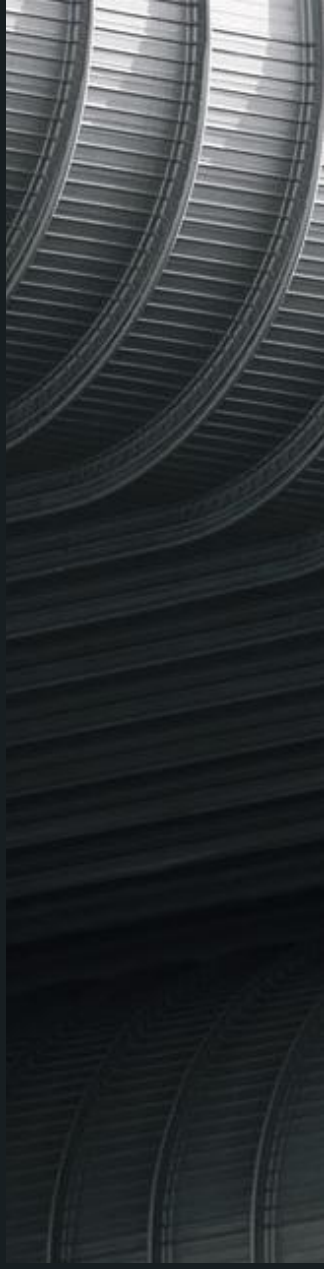
Having UKAS accreditation provides assurance in the quality, traceability, comparability, and validity of results issued by a laboratory. When organisations are looking for laboratory services, accreditation allows a means of identifying a proven, competent organisation and the selection of what laboratory to use can be an informed choice.

What is ISO/IEC 17025?

ISO/IEC 17025 is an internationally recognised quality management system standard for organisations that perform testing, sampling, or calibration. This includes government or industry laboratories as well as research centres, regulators, inspection bodies and other conformity assessment bodies. It is designed to enable laboratories to demonstrate technical competence and the ability to generate technically valid results. Technical competence can depend on a number of factors including:

- The qualifications, training, and experience of the staff
- The right equipment – appropriately calibrated and maintained
- Adequate quality assurance procedures
- Proper sampling practices
- Appropriate testing or calibration procedures
- Valid methods to recognised standards
- Traceability of measurements
- Accurate recording and reporting procedures
- Suitable testing facilities

As the standard is internationally recognised, having UKAS accreditation for a defined scope, as specified in the schedule of accreditation, helps to facilitate the acceptance of test reports and certificates from one country to another without the need for further testing.



INDUSTRY INSIGHT

MEDICAL DEVICE MARKET INSIGHT FROM A MEDICAL DEVICE CONSULTANCY PERSPECTIVE

Patient Guard

David Small has 20 years of experience in the Medical Device industry and is the founder of Patient Guard Limited, a medical device consultancy founded in 2017. Patient Guard has offices in the UK and Germany and has worked with hundreds of clients over the last 6 years helping them navigate the confusion of the medical device regulatory landscape.

WORDS | DAVID SMALL

The last few years have been a turbulent time for medical device manufacturers within the UK and the EU. First there was the EU MDR and IVDR that came into effect in 2017 with pressures on all medical device businesses to be compliant to the new regulations by May 2022 and May 2024 respectively, then came the pandemic causing the extension of the MDR grace period by 1 year to 2023, and then the extension of the grace period of up to 2028 for certain device due to the lack of Notified Bodies that were available causing a large backlog of companies being recertified under the new regulations, with the caveat that all medical device manufacturers were required to lodge an application with a Notified Body and on the waiting list to be certified by May 2024.

In addition to this, there was the fallout from Brexit, due to the UK leaving the EU, the UK left before the adoption of the EU MDR and IVDR, causing issues as it was not clear if CE-marked medical devices would continue to be accepted in the UK in the long term. Companies were now expected to register as a medical device manufacturer with the UK regulatory authority (MHRA) and apply a UKCA mark to their medical devices, resulting in dual regulation.

The UKCA mark for class IIa and higher medical devices could only be certified by a UK-registered Notified Body of which at the time there were only 3. If all this confusion wasn't bad enough there were different rules for Northern Ireland, and then the government announced that CE marked devices could be accepted in the UK indefinitely (but not for medical devices as there would be new regulations coming specific to them).

"A great many manufacturers still are not clear on what evidence they need to produce, and the level of data required to demonstrate regulatory compliance..."

There was the war in Ukraine which pushed up oil and gas prices leading to huge energy bills for medical device manufacturers, which also contributed to rapid inflation making it much more expensive and difficult for businesses to borrow money.

A whammy of effects lead to a perfect storm. As the dust settled in 2023, medical device companies have been cutting back on R&D spending, cutting projects or postponing them, wondering if this will be the last extension of the MDR and IVDR. Speculation has been rife about what the UK will do in terms of proposed new regulations coming down the line in 2025 (at the time of writing, we still know nothing about the details or their impact).

A period of uncertainty has spooked the market. What can we take from all of this? It's certain that Medical Device manufacturers need to be compliant with the MDR and IVDR if they wish to sell into the EU. Although there is an extension to compliance dates, this is really only for the Notified Bodies to catch up with the backlog of certifications. Medical Device Manufacturers really need to get ahead of the curve in terms of producing technical documentation for compliance needs. Notified Bodies are much stricter than they used to be and the number of rejections has increased significantly due to medical device manufacturers not producing enough or adequate data to support their medical device's intended uses.

A great many manufacturers still are not clear on what evidence they need to produce, and the level of data required to demonstrate regulatory compliance. We have found that a significant number of medical device manufacturers decide to 'have a go themselves' without input from experts in the field. This ultimately results in rejections and then panic, with additional expenses due to the cost of repeated Notified Body audit days and recertification costs. Trying to cut costs during the design and development stages of the medical device life cycle invariably leads to much larger costs when it comes to compliance checks before being able to place the medical device on the market.

In summary, although the medical device market has been at a confusing stage recently due to regulatory changes, the changes are here to stay, the benefits of selling medical devices on the marketplace will always be beneficial in terms of revenue generation for medical device companies. Getting the right help during design and development is critical in avoiding escalating costs of not getting it right the first time around.

EVERYTHING YOU NEED TO KNOW ABOUT IEC 60601-1

WORDS | JAMES TOLMIE

What is IEC 60601-1?

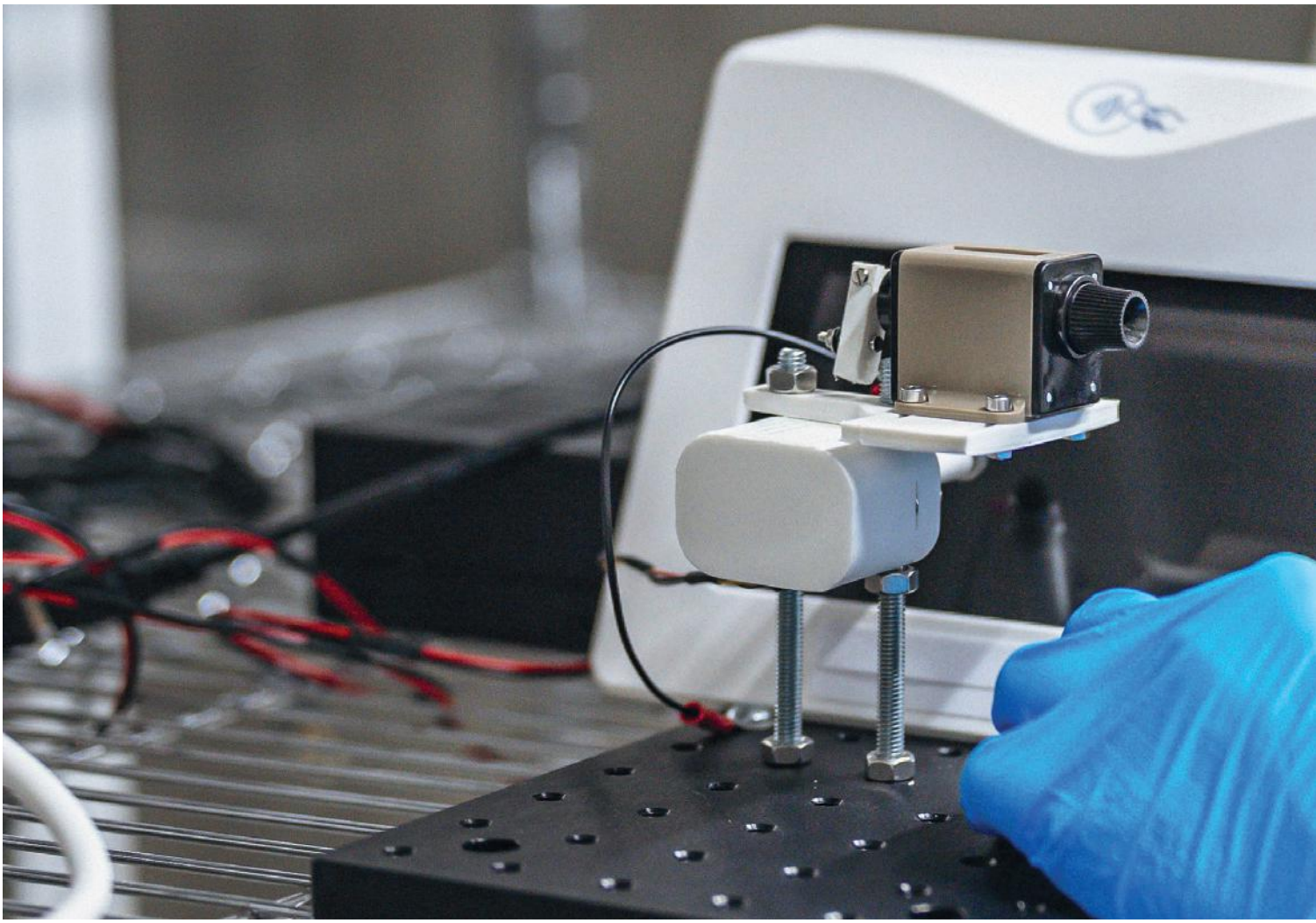
First published in 1977 by the International Electrotechnical Commission, IEC 60601-1 General requirements for basic safety and essential performance is the general standard of the 60601 series and gives requirements that must be met throughout the rest of the series. "General" here is a little misleading: the standard is enormous.

IEC 60601-1 is used both by technicians out in the field, manufacturers hoping to receive certification for a medical electrical device (ME device), and the test & certification houses that test ME devices for compliance to the standard.

What's in the IEC 60601-1 standard?

For technicians, the IEC 60601-1 Evaluation standard is mostly used for comprehensive electrical safety testing to verify that equipment is safe for both operators and patients alike. For manufacturers, the standard covers even more aspects of a device, from safety aspects beyond electrical safety, such as its ability to withstand high temperatures and its shielding from various forms of radiation to regulatory requirements like the correct markings that should be displayed.

The standard is split into 17 sections, beginning with the general requirements for the device (including risk control measures)



and the general requirements for performing the various tests in the standard. Further sections go into more detail regarding the classification, identification, markings, and documentation. The majority of the remaining sections (and the bulk of the standard) include detailed instructions for the various tests and requirements that ME devices need to meet during those tests.

The end of the standard is made up of nearly 200 pages of annexes, figures, and tables, which provide detailed examples of testing circuits, and test apparatus, as well as the exact limits for every test that a ME device needs to conform to.

...Medical devices need to conform to it, to meet EU regulations...

Conforming to the IEC 60601-1 standard

The reason the standard is important to manufacturers is that their devices need to conform to it in order for the devices to meet the requirements of Medical Devices Regulations such as MDR in the EU. In order for them to prove that this is the case, the device shall be subject to compliance assessment which is normally conducted by third-party test houses to the applicable requirements of the IEC 60601 series.

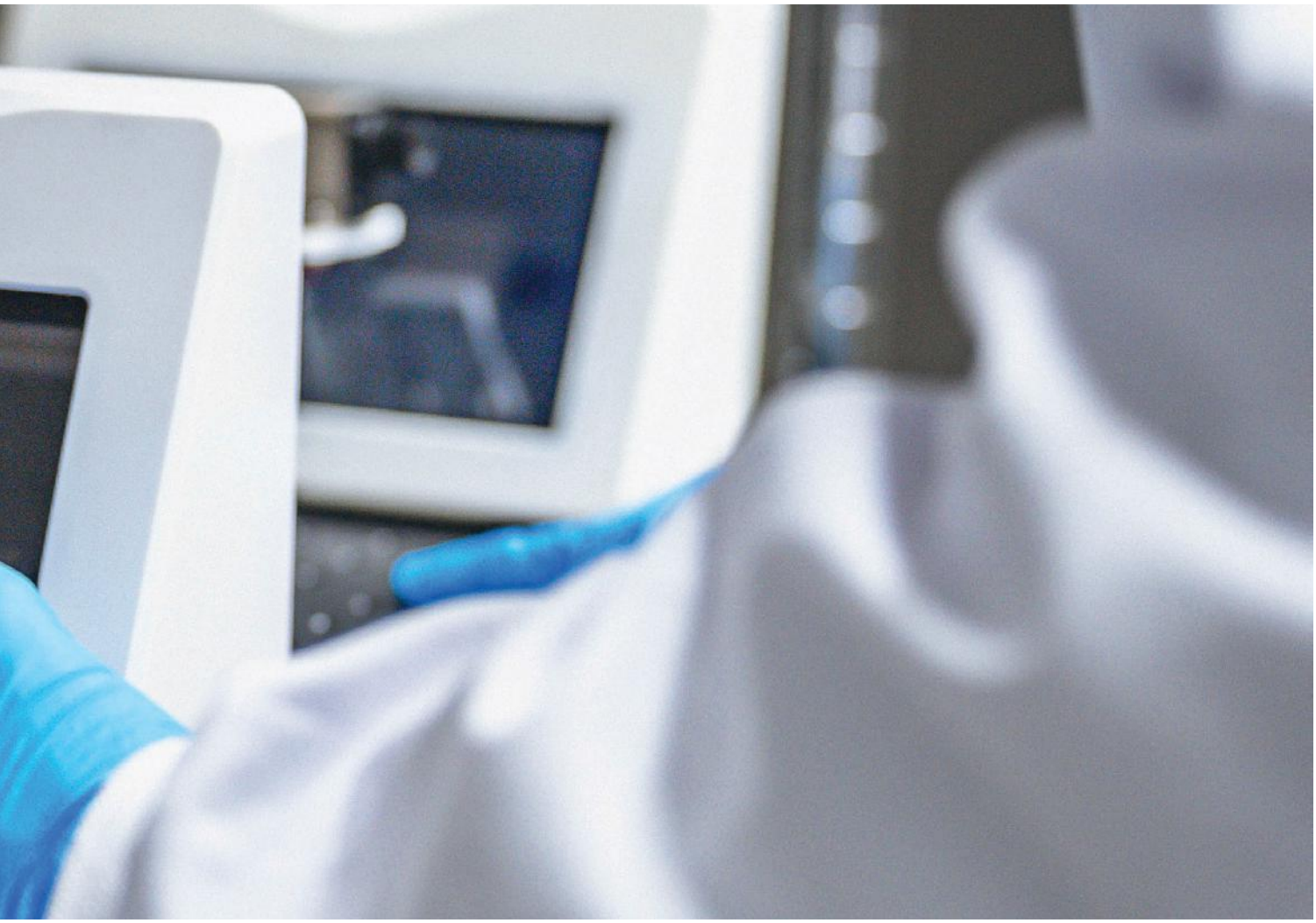
Performance requirements of multiple reprocessing cycles

Once all the testing was concluded and validated, for both the cleaning and sterilisation processes, the MD were then tested on multiple cycles to assess that repeated reprocessing would not affect the intended use or the safety of ME Equipment.

An example of reprocessing the dental ME Equipment applied part 50 times for cleaning and 50 times for sterilisation. After the 50 reprocessing cycles the intended use was assessed and compared to a brand new unprocessed MD. If it could be demonstrated that there was no difference in performance between the processed and unprocessed MD this would indicate the suitability of multiple reprocessing cycles and therefore full validation of the customer IFU.

Following successful validation of the IFU with BS EN ISO 17665-1:2006 and BS EN ISO 15883-5:2021 and with multiple cycles (50 in total) the IFU for the dental MD can be considered to be in compliance with ISO 17664-1:2021, fulfilling one of the requirements of the MDR.

James is a laboratory scientist with a focus on product testing. He has a degree in English Literature & Creative Writing and developed his product testing skills working as a Mastering Technician for over two years testing new products and software.



INDUSTRY INSIGHT

FUNCTIONAL SAFETY IN THE MEDICAL DEVICE SECTOR

One of the big challenges in the world of medical devices is the consideration associated with the safety of embedded systems. IEC 60601 the standard for the safety of Medical Electrical Equipment (ME Equipment) has a section on this very topic, the titled Programmable Electrical Medical Systems (PEMS). This section introduces the concepts of safe embedded product architecture, i.e. where we consider the interaction between hardware and software or in other words systems engineering. The challenge here is that the PEMS section IEC 60601 covers approximately half a page in in the standard, for a subject that is enormous. Other functional safety standards such as IEC 61508, ISO 13849 or ISO 26262 take hundreds of pages to describe the challenges and the solutions.

The challenges originate from the key functionality of a system where control or processing of data takes place. Software is by its very nature prone to produce unexpected results and hardware has a finite lifetime and is prone to upsets caused by environmental factors. These two points lead to developing the architecture in a way that mechanisms are built in to mitigate such malfunctions. In this article, we look at how some of these functional safety challenges are addressed and typical applications in the medical device sector.

Redundancy

If you have one programmable device, say a microcontroller controlling the inflation and deflation of a blood pressure cuff, if it were to malfunction then the cuff may inflate to a level that results in bruising to the patient's arm. A way of addressing that malfunction might be to add in a second programmable device, such that if device one malfunctions then device two can still deflate the cuff and avoid bruising. Modern microcontrollers often implement this architecture through a microcontroller and companion watchdog chip, which would deflate the cuff in the event of a problem.

Diversity

The example of the watchdog chip mentioned above brings another key topic to light: common cause failures. If programmable devices one and two were of the same technology or dependent on the same interfacing technologies e.g. power supplies of clock signals, they may both fail for the same reason. By bringing diversity into the architecture, the likelihood that both devices would fail for the same reasons is reduced. One issue here is that using redundancy has already increased the cost of your architecture introducing diverse devices could increase it further depending on the choices, hence the watchdog solution can provide diversity at a cost-effective price.

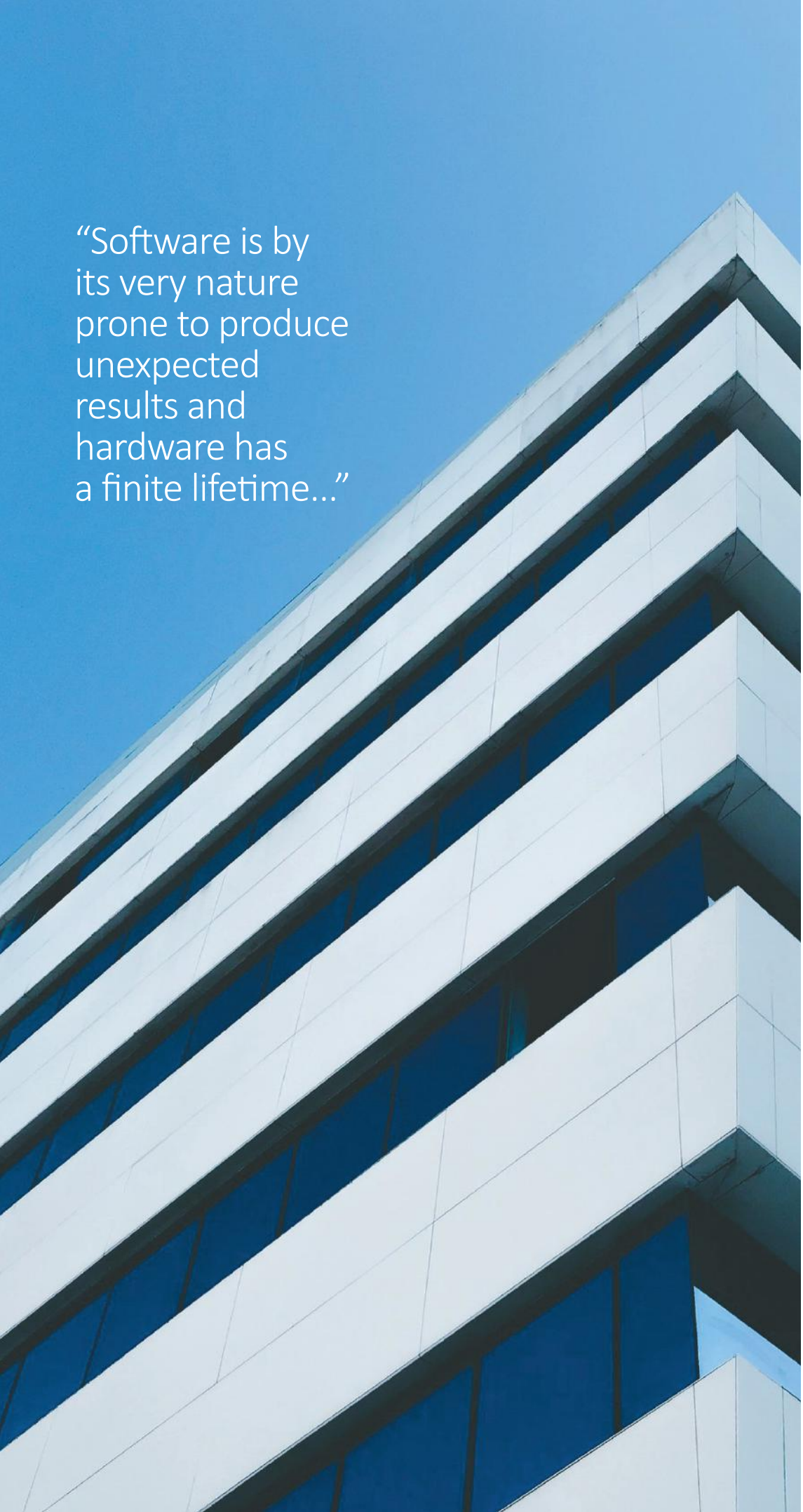
Fail-safe functions

Imagine if you have an ECG stress test system and the patient is running on a treadmill. The treadmill is controlled by a microcontroller and due to a static electricity discharge, the microcontroller stops its operation. In this case, the treadmill has no control input commands. This could in the worst case result in a sudden acceleration of the treadmill or rapid change in elevation, both could be hazardous to the patient. In such cases fail-safe function would mean that the treadmill is designed in such a way that it would come to a controlled stop and reduction of elevation in the absence of commands, to avoid harming the patient.

Diagnostic coverage

The two key factors in evaluating risks are the severity and how you can control the potential harm that could result. Diagnostic coverage is a term that indicates how effective your risk control measures are in a quantitative fashion. Instead of estimating how good the detectability is on a 1 to 10 scale as is done in Failure Modes and Effects Analysis (FMEA) diagnostic coverage is derived from sources such as IEC 61508 and is based on the architecture features in the product. If a power supply is only monitored for over or under voltage this would be a lowish diagnostic coverage, but if monitored for over and under voltages, spikes and oscillations then the diagnostic figure would be high approaching 99%. In functional safety standards, this value is used in conjunction with component failure in time (FIT) rates to calculate a residual failure rate that can determine if the risk is acceptable

The topic of functional safety is not well understood in the medical device sector, but there is nothing stopping companies using other standards and sources as state of the art.



"Software is by its very nature prone to produce unexpected results and hardware has a finite lifetime..."

Alastair Walker is an engineering consultant with more than 30 years experience in developing safety-relevant products in the medical, automotive and other industries.

He has developed and consulted on a variety of medical device products and has extensive knowledge of implementing safe 60601 programmable electrical medical systems (PEMS) architecture and Class C 62304 software. Alastair has extensive experience in system, hardware and embedded software development.

Alastair has many years' experience in risk analysis techniques such as fault tree analysis (FTA), failure mode effects and diagnostic coverage analysis (FMEDA) and hazard and operability study (HAZOP) and brings techniques from different industries to enable establishment of best practices in a given sector.

Lorit Consultancy

Lorit Consultancy specializes in providing consultancy, support, and training for functional safety projects within the medical and automotive sectors. In addition, we are your reliable partner for such topics as quality management systems and regulatory affairs.

Our extensive background in hardware and software development within the medical technology field enables us to assist you in navigating the complex landscape of international standards compliance.

Lorit Consultancy support clients worldwide in the successful development of innovative and safe products! Visit **lorit-consultancy.com**

CASE STUDY

GOING THE EXTRA SMILE WITH MATERIAL COMPATIBILITY TESTING

What is material compatibility?

Medical device safety testing includes material compatibility studies. Material compatibility is determining the resistance between a surface (or product) and disinfectant products and technologies. An adverse reaction resulting in the incompatibility of different components can impact the performance or safety of a product, leading to premature failure.

The EU Regulation 2017/745 (MDR) heavily focuses on the safety and performance of a medical device for the lifetime of the product to minimise risk as far as possible. As a result, there is growing emphasis on compatibility, risk of contaminants and verification of the cleaning, decontamination and sterilisation of a product based on its' instructions for use (IFU) to facilitate safe reuse.

Dental Material Compatibility Testing

Contracted for material compatibility testing using a dental chemical detergent, Test Labs performed an immersion test as per ISO 21530:2004 "Dentistry – Materials used for dental equipment surfaces – Determination of resistance to chemical disinfectants" on several dental products to evaluate the compatibility of using the chemical detergent on these materials. Despite the standard being specifically drafted for disinfectants, the sample principle can be adopted to test for a detergent used in the dental practice. This case study describes the procedure followed by the Test Labs team to conduct a 14-day immersion test and deliver results in under 4 weeks from when test samples were received in the laboratory.

As stated in ISO 21530:2004, materials that are used for dental equipment and are susceptible to being contaminated in normal use should be capable of undergoing disinfection/cleaning using relevant disinfectant/detergent, as per manufacturer's instructions, without deterioration or discolouration occurring.

In order to test for this, the standard outlines 3 exposure methods:

1. **Immersion**
2. **Spray**
3. **Contact**

Depending on the client's product and test samples, the relevant exposure tests are selected and testing carried out over repeated exposure cycles as outlined in the standard. In this case study, the immersion test was used as this exposure represented the intended use of the chemical detergent that was being tested.

The Immersion Test

The immersion test, according to the standard, is performed in 2 parts in parallel testing – a full immersion test, where test samples/products are immersed completely into the test solution, and a 50% immersion test, where only half of sample surfaces are covered in solution. In this case study, however, only the full immersion test was conducted.

The test was conducted over a period of 14 days on each test product (7 different products in total). The items were immersed in the test solution, which was replaced every 24 hours ± 2 hours with freshly prepared solution. Each type of product was tested in triplicate and placed inside sealable glass containers before the test solution was added such that they were fully submerged. The containers were sealed and left over the duration of the exposure time.

The effects of the repeated exposure were assessed in the form of visual and tactile measurements, as well as recording changes in mass of the products. The inspection assessments were conducted at an interim stage (after 7 days ± 2 hours), as well after the full 14-day exposure.

Inspection Assessments

ISO 21530:2004 outlines the general method of inspection of the materials at the interim and final stages of testing, where the tested products/samples are compared to reference samples of the same type that have not undergone any exposure to the disinfectant.

According to the standard, the products were visually assessed for changes in 1) Surface structure, 2) Surface colour and 3) Surface shine.

Test Labs in-house method of visual assessment involved the use of a Colour Assessment Cabinet with a Daylight 65 lamp to ensure inspections are carried out in consistent lighting conditions. Photographs were taken at different angles as a method of recording the visual observations.

Tactile assessment was conducted for which products were assessed for changes in 1) Surface texture, 2) Surface hardness and 3) Surface tackiness

For both visual and tactile assessments, changes were assessed according to Test Labs' own set acceptance limits (based on internal material compatibility validation studies) on a scale of 1-5, and compatibility was assigned if on average the score was ≤ 3 for each property.

1. No change
2. Slight change, barely noticeable
3. Noticeable change in one specific area of surface
4. Noticeable change in multiple areas of surface
5. Significant change

As part of the standard, it was also necessary to take mass measurements of the products before and after performing the immersion test. The acceptance limit for changes in mass of products from before and after 14-day exposure was set to ≤ 5%, in accordance with Test Labs internal procedure.

Once all inspections were completed, a Test Labs' report was issued to the client detailing all findings including both interim and final inspection assessments.

Tailored Material Compatibility Testing for Comprehensive Customer Outcomes

This study highlights how our tailored material compatibility testing can benefit customers by providing a wide range of quantitative measurements beyond the ISO 21530:2004 standard, such as changes in whiteness, opacity, and coating thickness. By selecting test methods based on standards and adapting them to suit the customer's needs, we can deliver a more comprehensive understanding of material compatibility, including both visual and tactile measurements.

At Test Labs, we are dedicated to providing our customers with the most comprehensive and accurate material compatibility testing available. Our internal validation studies have allowed us to gain a deeper understanding of the acceptance limits that should be applied to the results of our testing. By incorporating these acceptance limits into our testing processes, we can provide our customers with more detailed reports on the compatibility of their products.

Our commitment to providing accurate results means that we go beyond simply following industry standards. Instead, we tailor our testing methods to suit the unique needs of each customer. This includes taking into account the specific characteristics of their product, as well as any relevant regulatory requirements. By doing so, we can provide our customers with a level of insight and understanding that is simply not possible with a one-size-fits-all approach.

WORDS | SYEDA BEGUM

Syeda is a chemist, holding a bachelor's degree in Chemistry with Medicinal Chemistry and a research master's degree in Chemistry. Her thesis titled 'An Investigation of the Anion-Binding & Catalytic Abilities of Supramolecular Complexes' displays her competency in coordination compounds – an area of chemistry that is utilised in many industries including biological and medical – as well as her skill in scientific communication and writing.

INDUSTRY INSIGHT

BRIDGING REGULATORY AFFAIRS, ENGINEERING, AND QUALITY ASSURANCE IN MEDICAL DEVICE DEVELOPMENT

In the complex landscape of medical device development, a synchronized interplay between regulatory affairs, engineering, and quality assurance is essential. This collaborative effort forms the backbone of ensuring that medical devices not only meet stringent standards of safety and efficacy but also navigate the complex web of regulatory requirements seamlessly. While this triad of functions is instrumental in achieving success, it is not without its challenges and potential pitfalls.

Regulatory Affairs: The Compliance Architects

Regulatory affairs professionals serve as architects of compliance within the medical device industry. They are responsible for interpreting and implementing the ever-evolving landscape of regulations and standards that govern medical devices. Their role extends beyond just rule enforcement; it involves facilitating innovation while ensuring adherence to stringent regulatory boundaries.

Regulatory professionals play a pivotal role in medical device development by:

Navigating Regulatory Complexities: Regulatory affairs experts keep a watchful eye on the shifting regulatory landscape. They must not only understand current regulations but anticipate future changes. This proactive approach helps to prepare for forthcoming challenges and opportunities.

Setting Compliance Boundaries: They are the gatekeepers who ensure that product development stays within defined regulatory boundaries. This involves establishing a framework that encourages innovation while maintaining safety and efficacy standards.

Evaluating Regulatory Impact: Regulatory professionals evaluate the potential impact of regulatory changes on existing and future projects. This assessment helps teams adapt and ensure continued compliance.

Guiding Global Expansion: For companies looking to expand globally, regulatory affairs professionals navigate the maze of international regulations, ensuring that products meet requirements in different markets.

Michael B. Wetherington is the Founder of **DocuRegs**, a sister company of **MedicalRegs**, with a vision to foster collaboration across Regulatory, Engineering, and Quality domains through the provision of insightful tools and publications.

His extensive background spans various aspects of the medical device industry, including research and development, quality management, and regulatory affairs. Michael's experience also includes serving as a former Notified Body assessor and contributing to leading accredited testing laboratories.

This diverse expertise equips Michael to approach regulatory challenges with a holistic perspective, ensuring that all dimensions of a project receive the attention and care they require.

INDUSTRY INSIGHT

Engineering: The Creative Visionaries

Design engineers are the creative visionaries behind medical devices. They take ideas and turn them into tangible solutions, making innovation a reality. However, their creative brilliance is confined by regulatory frameworks and the need to address clinical requirements. Engineers bridge the gap between concept and reality, ensuring that devices are not only innovative but also robust, reliable, and user-friendly.

Engineers are responsible for:

Technical Vision: They shape the technical vision of the device, ensuring it aligns with clinical requirements and user expectations.

Innovation Implementation: Engineers translate conceptual ideas into technical solutions, transforming innovative concepts into functional devices.

Integration of Compliance: Their role involves aligning innovation seamlessly with regulatory demands, implementing technical solutions that meet safety standards, and simplifying the regulatory compliance process.

Technical Problem-Solving: When compliance challenges arise, engineers work alongside regulatory affairs professionals to find innovative technical solutions that ensure both compliance and functionality.

Quality Assurance: The Guardians of Consistency

Quality assurance (QA) professionals play a crucial role in maintaining consistency and reliability throughout the medical device development process. They establish and uphold quality management systems that underpin every aspect of the development life-cycle. From design controls to risk management, QA ensures that processes are meticulously defined, followed, and documented.

QA professionals focus on:

Process Adherence: They ensure that established processes and procedures are consistently followed, leaving no room for deviations that may compromise safety or efficacy.

Traceability: QA emphasizes the importance of traceability, documenting every step of the development process to ensure accountability and transparency.

Validation and Verification: They oversee the validation and verification of critical processes and components, ensuring that they meet safety and quality standards.

Consistent Performance: QA professionals are committed to maintaining consistent performance levels in both processes and end products.

The Interplay's Dual Nature

The dynamic interplay between these three pillars is both a catalyst for success and a source of challenges. When they collaborate effectively, regulatory affairs experts inform engineers about evolving regulations, enabling them to seamlessly integrate compliance into the project from its inception. Engineers, in turn, provide invaluable feedback to regulatory affairs, ensuring that the chosen path aligns with technical feasibility. Quality assurance professionals oversee every phase, verifying that processes are followed and that safety is never compromised.

Challenges and Potential Pitfalls

While the collaboration between regulatory affairs, engineering, and quality assurance is critical, it is not without its challenges and potential pitfalls. Let's explore some of these hurdles and how they can be overcome:

Regulatory Lag: One common challenge is that regulatory changes often lag behind technological advancements. This disconnect can hinder innovation, as engineers may need to adapt their designs to meet outdated regulations. The solution lies in proactive engagement with regulatory agencies, advocating for flexible frameworks that accommodate innovation.

Overly Complex Standards: Navigating a labyrinth of complex standards can be daunting for engineers. They may struggle to interpret technical jargon, leading to compliance gaps. Effective communication between regulatory affairs and engineering is key, ensuring that standards are understood and integrated cohesively.

Scope Creep: Expanding project scopes can strain resources and timelines. Regulatory affairs must ensure that the project adheres to defined boundaries. Clearly defined project scopes from the outset can mitigate this challenge.

Resistance to Change: Teams may resist changes necessitated by regulatory updates or quality improvements. Effective change management strategies, including education and training, can ease transitions and foster collaboration.

Working in Silos: When regulatory, engineering, and quality assurance work in isolation, vital information can be lost. Cross-functional teams and regular communication forums are essential to share insights and foster collaboration.

Lack of Risk Alignment: Misalignment in risk assessment between regulatory affairs and engineering can result in compliance gaps. A shared understanding of risk, facilitated by collaborative risk assessments, can bridge this gap.

Evolving Technologies: Rapid technological advancements can outpace regulations. Regulatory affairs should stay ahead by monitoring emerging technologies and advocating for adaptive regulatory pathways.

Inadequate Testing: Incomplete or ineffective testing can lead to non-compliance. A robust testing strategy, aligned with regulatory requirements, is crucial to identify and rectify issues early.

Conclusion: A Balanced Collaboration

The synergy between regulatory affairs, engineering, and quality assurance is a crucial driving force. It's a dynamic, evolving, and collaborative journey that can lead to ground-breaking medical technologies. When these functions collaborate harmoniously, they pave the way for innovation that enhances patient care while adhering to the highest standards of safety and efficacy. However, the careful navigation of this interplay is essential to avoid potential regulatory pitfalls that can stall progress in a rapidly evolving healthcare landscape. It's a delicate dance, but one that holds immense potential for the future of healthcare.

TECHNICAL FILE REQUIREMENTS FOR CLASS IR: EVERYTHING YOU NEED TO KNOW

What is a medical device technical file?

The EU 2017/745 Medical Device Regulation (MDR) requires that manufacturers of medical devices produce and maintain a technical file for each of their devices. The intent of this article is to broadly summarise the strict requirements these files must meet.

Before detailing the informational requirements, it's important to note that the MDR requires that a technical file should be "presented in a clear, organised, readily searchable and unambiguous manner". It is not just enough to list the required information, the file itself should be carefully presented.

Medical device technical file contents

While there may be some exceptions, most devices will need a technical file with the following information:

- A basic description of the device, including the product name, as well as an unambiguous and traceable way to refer to the exact model of the device (such as a product code or catalogue number, following the Unique Device Identification system described in Annex VI of the MDR).
- Why the device should be considered a medical device, the risk class of the device, and why this risk class was chosen (the guidance for this can be found in Annex VIII of the MDR). It should also include risk management information and a benefit-risk analysis (both of which are described in Annex I). Risk management must meet the following standard:
- ISO 14971:2019+A11:2021 Medical devices — Application of risk management to medical devices
- Who the intended users of the device are, how it is intended to be used (Instructions for Use or IFU), and what it is intended to be used for. It may also be necessary to demonstrate the scientific principles of the device.
- A description of the important parts of the device and their functionality, with diagrams and explanations if necessary. If applicable, the accessories, possible configurations and software of the medical device should also be described.
- An overview of previous or similar versions of the device, if they exist.
- The labels used on the device and its packaging and the instructions for use, which must meet the following standards, respectively:
- ISO 15223-1:2021 Medical devices — Symbols to be used with information to be supplied by the manufacturer.
- EN ISO 17664-1:2021 Processing of health care products — Information to be provided by the medical device manufacturer for the processing of medical devices.
- The raw materials used in the parts of the device that are key to its use or that will in some way interact with a human, as well as information about the suppliers of these raw materials with validation data regarding the manufacturing process. Furthermore, justification for the materials chosen should be present in the form of pre-clinical/clinical data gathered prior to submission of the technical file according to:
- ISO 13485:2016 Medical devices — Quality management systems — Requirements for regulatory purposes.
- ISO 10993-1:2018 Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process.
- Proof of conformity with the applicable general safety and performance requirements of the MDR, found in Annex I. This proof should include data that validates conformity, as well as justification for the solutions that were used to meet the requirements.
- Once the device enters circulation, the technical file should be updated with post-market surveillance data that verifies the device's safety and functionality in real-world situations. This data should include customer feedback and complaints, or any further testing that is performed (further information can be found in Annex III of the MDR).

Class Ir Requirements

Although the MDR doesn't mention the term "Class Ir" explicitly, the definition of this kind of risk class can be found in Annex VIII. It determines this risk class as class I devices that are "...intended for surgical use in cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or similar procedures, without a connection to an active device and which is intended by the manufacturer to be reused after appropriate procedures such as cleaning, disinfection and sterilisation have been carried out."

The EU 2017/745 Medical Device Regulation (MDR) requires that manufacturers of medical devices produce and maintain a technical file for each of their devices

Additional considerations are required for the technical file of a class Ir device, compared to a class I device, when it comes to the general safety and performance requirements. To ensure that the device is safe to be reused, the IFU must include instructions for a sterilisation process, a cleaning process, or a disinfection process, as appropriate. The instructions must be unambiguous and specific. For example: the exact sterilisation times and temperatures, or the specific disinfection agent and its procurement options.

Biocompatibility, material-compatibility, and shelf life must be considered when selecting materials used to manufacture a device intended to be reprocessed. Some materials may degrade or react with certain reprocessing techniques, or even become toxic. This is one of the reasons that all processes required for ensuring that the medical device is ready for reuse must be validated, and the data used for validation included in the technical file.

The following standards are applicable to validation of instructions for use:

- ISO 15883-5:2021 – Washer-disinfectors — Part 5: Performance Requirements and Test Method Criteria for Demonstrating Cleaning Efficacy.
- EN ISO 17665-1:2006 – Requirements for the Development, Validation and Routine Control of a Sterilisation Process for Medical Devices
- ISO 15883-2:2006 – Requirements and Tests for Washer-Disinfectors Employing Thermal Disinfection for Surgical Instruments, Anaesthetic Equipment, Bowls, Dishes, Receivers, Utensils, Glassware, etc.

The post-market surveillance mentioned in the previous section will also need to include reprocessing data to ensure the IFU are fit for use within a real-world setting.

WORDS | JAMES TOLMIE

EVERYTHING YOU NEED TO KNOW ABOUT FDA APPROVAL FOR MEDICAL DEVICES

Who are the Food and Drug Administration?

The Food and Drug Administration (FDA) is a government agency that is responsible for regulating an extensive range of food and health-related products in the United States (US). This includes drugs, medical devices, cosmetics, tobacco products, the nation's food supply and products that emit radiation. Their primary aim is to ensure these products (which make up about 20% of consumer purchases in the US) meet certain quality standards prior to being placed on the market.

The FDA conducts inspections and reviews facilities where these regulated products are produced, where the testing on animals and clinical trials are conducted and at the border where regulated products are imported. There are four different types of inspections the FDA may carry out including pre-approval inspections, routine inspections, compliance follow-ups, and "for cause" inspections. These inspections each have a different focus, however, the overall aim is to verify compliance with all relevant regulations to help protect consumers from unsafe products.

Medical Device Route to Market in the US

Although there are three routes to market that are commonly known, there are currently seven different pathways that can be used to bring a medical device to the market in the US. Depending on the specific circumstances of the device one of the following pathways can be used:

- Premarket Notification 510(k): this is the most common route to market for medical devices in the US that are not exempt from pre-market review.
- Premarket Approval (PMA): this application is required for new or high-risk (Class III) devices.
- De Novo: this is designed for "novel" devices without a predicate as an alternative pathway to be authorised a Class I or Class II device.
- Humanitarian Device Exemption (HDE): this pathway is for devices intended to treat or diagnose diseases or conditions affecting less than 4,000 individuals in the US per year.
- Customer Device Exemption (CDE): custom devices created or modified to meet the specific needs of an individual physician or dentist can use this pathway, so long as no more than 5 units per year of the particular device are made.
- Expanded Access Programme (EAP): this allows an investigational device to be used, outside trial in specific situations as compassionate or emergency use provisions.
- Product Development Protocol (PDP): this allows companies designing and developing technology that is well established in the industry to have an early agreement with the FDA where acceptance of outputs and milestones during development will result in an "approved" PMA at the end of the process.

Although some of these exemption routes mean that premarket approval is not required, it does not prevent them from having to conform to many of the other requirements to ensure the safety of the product.

...Although there are three routes to market that are commonly known, there are currently seven different pathways that can be used to bring a medical device to the market in the US.

Basic Regulatory Requirements for Medical Devices

Manufacturers of medical devices must ensure that their product complies with the basic regulatory requirements in order to distribute them in the US. Although some may not be applicable to all devices, the basic regulatory requirements include:

- Establishment registration – 21 CFR Part 807
- Medical device listing – 21 CFR Part 807
- Premarket Notification 510(k) or PMA, unless exempt
- Investigational Device Exemption (IDE) for clinical studies
- Quality System (QS) regulation
- Labelling requirements
- Medical Device Reporting (MDR)

What is a Premarket Notification 510(k)?

The Premarket Notification 510(k) is a process where manufacturers of medical devices notify the FDA of a new or modified device which they plan to sell on the US market. This submission then allows the FDA to determine whether the device is sufficiently equivalent to one or more predicate devices detailed within the application as well as that it meets all the relevant regulatory requirements. This route to market is the method by which the majority of medical devices within the US obtain marketing clearance.

Medical devices which require a premarket submission (and are not exempt or require a Premarket Approval) have three types of 510(k) submissions to choose from:

- Traditional
- Special
- Abbreviated

The traditional pathway is the most commonly used and is probably the first process that anyone thinks of when it comes to medical devices being placed on the market in the US. This is used for any original devices which have not been previously cleared (as well as modified devices that do not qualify for the Special 510(k) process). Manufacturers must be able to provide substantial evidence for at least one predicate device, taking into consideration the intended use and technological characteristics. The FDA aim to make a Medical Device User Fee Amendments (MDUFA) Decision within 90 days of receiving an application (compared to 150 days for De Novo applications and either 180 days or 320 days for PMAs, depending on if a panel meeting is required).

What is the special 510(k) pathway?

The special 510(k) pathway was developed in 1998 as an optional pathway "for certain well-defined device modifications where a manufacturer modifies its own legally marketed device, and design control procedures produce reliable results that can form, in addition to other 510(k) content requirements, the basis for substantial equivalence (SE)."

The special 510(k) may be appropriate if the following criteria are met for the modifications carried out:

- The change has been made to the manufacturer's own legally marketed device
- Performance is unnecessary (or well-established methods are available to evaluate the change)
- All the data can be reviewed in summary or risk analysis format
- The FDA aim to review applications within 30 days from receipt and will notify the manufacturer/submitter if the traditional pathway is required for their application. Due to the short time-frame additional considerations of circumstances also mean this pathway would not be appropriate, for example, changes in more than 3 scientific disciplines, changes from single-use to reusable or if complete test reports will be necessary to establish SE.
- Lastly, the abbreviated 510(k) pathway allows manufacturers to provide summary reports as part of the submission when it relies on one or more of the following:
- FDA guidance document(s)
- Demonstration of compliance with special controls for the device type, either in a device-specific classification regulation or a special controls guidance document; and/or
- Voluntary consensus standard(s)
- This process does not change the regulatory or other requirements that must be complied with, and all sections of the traditional 510(k) must be included, however in some cases it is more appropriate for a manufacturer to prove SE through the above points, rather than against a predicate device.

Regardless of the route that manufactures determine is most appropriate, or if they are exempt from premarket approval, all medical devices must be registered with the FDA. This helps to enable them to maintain several medical device databases including registered devices, recalled devices, product classification and establishments registered.

A GUIDE TO MEDICAL DEVICE BIOCOMPATIBILITY TESTING

What is biocompatibility testing?

Biocompatibility testing refers to a set of standards (ISO-10993) that defines the potential biological risks of a device upon encountering the human body, specifically evaluating patient contact time points and toxicity. This could range from 'local' effects such as burns or irritation of the skin, to 'systemic' effects including malignant illnesses.

Why should I conduct these tests on my medical device?

The ISO 10993-1 was prepared in collaboration with the medical device directive (MDD), re-emphasizing the recognition of these standards to provide patient safety and accurate evaluation of biological safety. In short, biocompatibility testing is fundamental in deciphering if a medical device is safe to use and is the penultimate step in introducing a device into the market.

Do all medical devices need biocompatibility tests?

In simple terms – yes. Annex I and II of the Medical Device Regulation (MDR) alludes to the notion that all medical devices which encounter human tissue should be subject to biocompatibility testing, and findings should be recorded in a comprehensive technical document. The updated ISO-10993 guidance document from June 2016 further highlights how medical device developers should test devices regarding both: the existing risks of a medical device and identifying the approach for potential risks. Therefore, the ISO 10993 standards act as a guiding tool to bridge the gap between the requirements of the MDR and the biological safety of a medical device.

However, under limited circumstances, your device may be exempt. This is dependent on a plethora of sufficient data to support the claim that your device has been thoroughly evaluated e.g., clinical, analytical, supplier, or from previous submissions, which is stressed in Annex II of the MDR.

In order to confidently submit your medical device to your regulator, medical device testing companies offer their expertise to choose which specific tests within the ISO 10993 standards are necessary for your medical device.

How does a medical device demonstrate the required Biocompatibility?

This process has been summarized into 3 helpful steps below:

1. BUILD A PLAN

- This plan should consider the biological risk profile of the medical device; it's application, duration of patient contact times, gaps in known data and potential toxicological threats.
- These types of plans are termed 'Biological Evaluation Plan (BEP)' and can act as a starting point to address the risks and possible testing solutions.

2. CONDUCT REQUIRED TESTS

- Consult with medical device testing experts to suggest the tests appropriate for your device, as highlighted in your BEP.
- These tests can include a broad selection of toxicological risk assessments, study designs to address potential risks, as well as identifying the presence of cytotoxicity within the chemical make-up of a device.

3. FORM A REPORT

- All the findings from the tests, and the evaluations performed on your device should be finalized in a report termed 'Biological Evaluation report (BER)'
- This report, alongside your test results, will be submitted for a conformity assessment by notified bodies to approve the medical device, as stated in Annex VII of the MDR.

WORDS | RIWIA CHETIAN

What is in vitro testing? >>

What is in vitro testing and how is it different to in vivo testing?

In vitro means 'in glass' which essentially refers to testing that occurs in glass vessels (e.g., test tubes), instead of in a human or animal (in vivo). It allows for the targeted testing of specific components of a living organism through the extraction of isolated cells. These isolated cells are then grown with specialised growth media to form a single layer of cells in a vessel, which would replicate similar characteristics as to the cells in the organism from which it was extracted. This is a reputable and acceptable method which is used in all of biocompatibility cytotoxicity testing.

Over the last 50 years, alternative solutions to animal testing have been considered a high priority within the biocompatibility testing field according to the principles of the 3Rs (Replacement, Reduction and Refinement). Hence, a key advantage to using in vitro biocompatibility testing is its positive effect on animal welfare by aligning with the 3Rs principle. However, the benefits of using in vitro biocompatibility testing extend beyond just being a sustainable alternative to in vivo testing. In comparison to in vivo testing, in vitro testing is more cost-effective as there is no extra charge for animal procurement or required registrations. Furthermore, in vitro testing is more time efficient due to cell reactions being faster in a controlled environment outside the organism. The only limitation to in vitro testing is on the accuracy of the extrapolated results and if they could be translated to 'real life.' Hence, in vitro studies have kept evolving to become more representative of the complex systems which are involved in organisms.
A key example of this is the RhE (reconstructed human epidermis) model used in the newest addition (part 23) to the ISO 10993 series of biocompatibility standards.

"...in vitro testing is more time efficient due to cell reactions being faster in a controlled environment..."

In vitro testing in ISO 10993-23

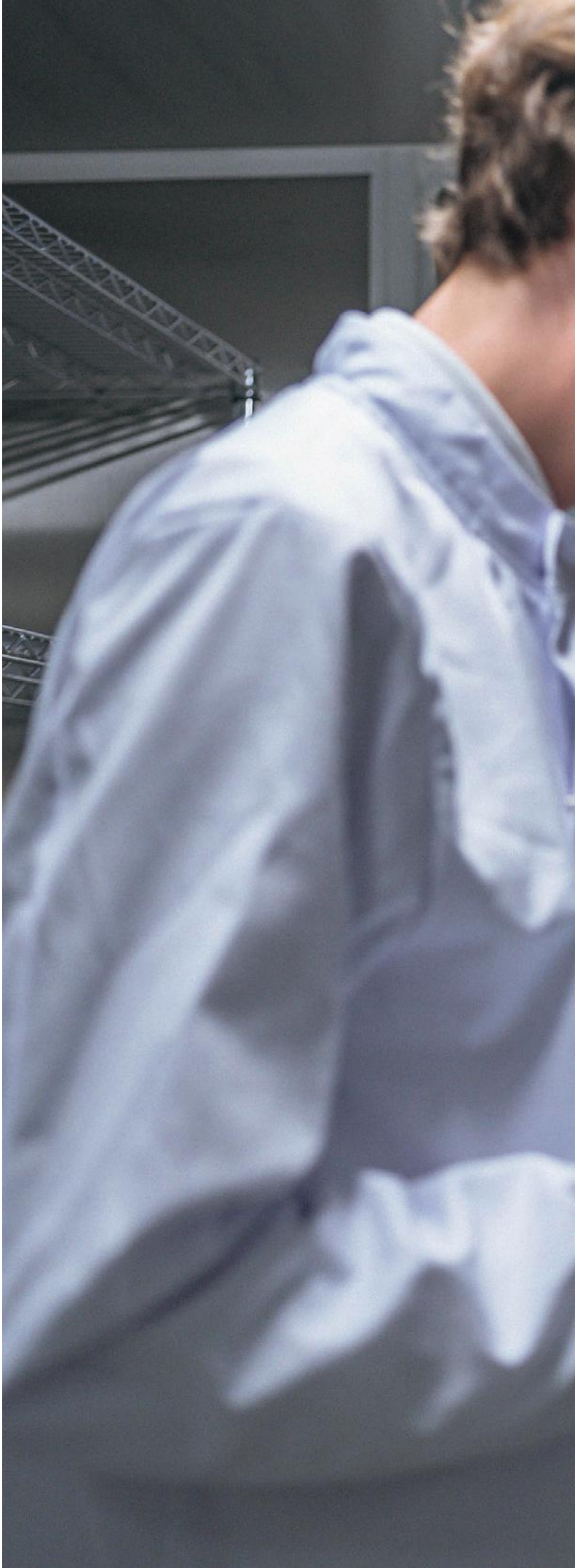
The release of part 23 of the ISO standard 10993 in 2021 highlighted the focus on in vitro testing for skin irritation potential in medical devices. Prior to this, irritation was primarily conducted in animals. The new addition to the standard introduced the use of a 'stepwise approach' when evaluating the potential biological risks of a medical device, in which in vitro testing is at the forefront of all testing procedures. Following an extensive chemical profile of the medical device material, further analysis of the irritation potential is assessed through three types of testing which are structured into hierarchical 'steps':

1 First begin by conducting in vitro testing.

2 If in vitro is not feasible, perform in vivo.

3 Perform non-invasive clinical studies if the irritancy potentials of the device have not been established in the prior testing.

As detailed above, the stepwise approach prioritises in vitro testing as the first test before all testing, showcasing the necessity of in vitro testing in demonstrating the irritation potential of a medical device.



"Over the last 50 years, alternative solutions to animal testing have been considered a high priority within the biocompatibility testing field..."

What are RhE models?

Reconstructed human epidermis (RhE) consists of human skin cells (keratinocytes) which are organised into a normal human epidermis structure, forming a 3D structure. These models overcome the limitations of traditional monolayer of cells which are used in cytotoxicity in vitro testing, as they represent more of the complex systems that occur in organisms. The RhE 3D structure includes an organized basal, spinous, and granular layer, as well as multi-layered stratum corneum (the outer layer of skin which acts as the main skin barrier). Interestingly, the first RhE skin model was made in 1980 by the well-known cosmetic company L'Oréal, to overcome the uproar against the infamous in vivo rabbit irritation testing in skin exposure and intracutaneous administration. Due to its structure, the RhE model is histologically similar to the epidermis found in our skin, and therefore mimics the human skin epidermis at a high level and is applicable to a vast range of manufacturers.

How does the skin irritation test work with the RhE model?

The irritation test allows the identification of potential irritants in a device that may encounter skin but is also applicable to implants and any other externally communicating devices.

The test is broken down into the following three steps:

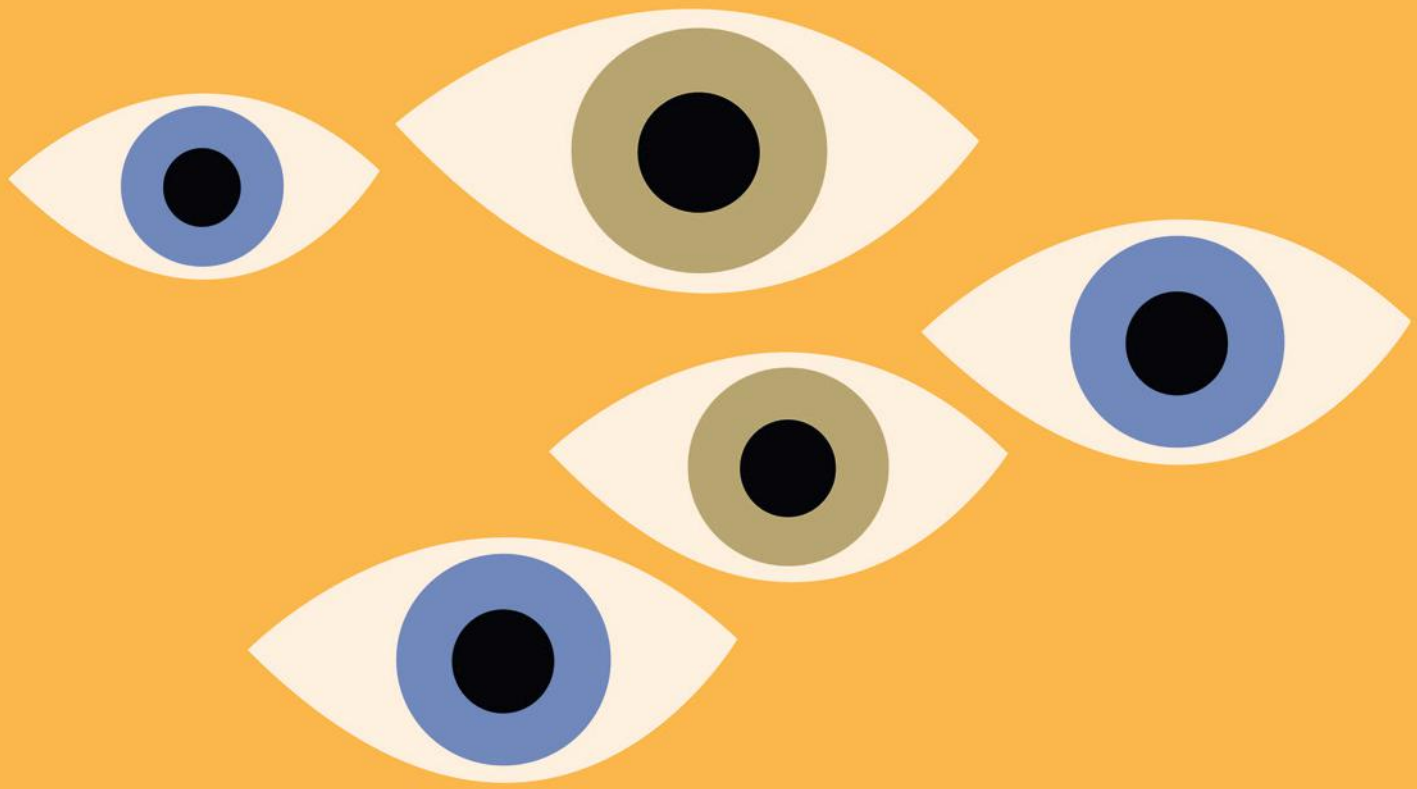
1 The test extract is topically exposed to the RhE skin tissue and incubated.

2 The sample is exposed to MTT dye, which is a yellow salt that measures cellular metabolic activity (commonly used in cytotoxicity testing).

3 If the cells in the RhE model are unaffected (viable) by the presence of the test sample, the yellow MTT salt will turn into purple formazan salt.

Thus, the degree of viable cells is proportional to the purple staining, and this can be quantitatively measured via optical density. If the mean tissue viability is less than or equal to 50% compared to the negative control, the device material is classified as an irritant, while a viability of above 50% classifies a non-irritant.

The test is limited to only two extraction solvents: polar or non-polar, hence it primarily accommodates solid substances e.g., polymeric materials commonly used in medical devices. Nonetheless, the RhE model in irritation testing opens a rapid, representative, and efficient alternative to in vivo testing for medical device manufacturers.



POST-MARKET SURVEILLANCE (PMS): EVERYTHING YOU NEED TO KNOW

What is post-market surveillance?

According to the EU 2017/745 Medical Device Regulation (MDR), post-market surveillance (PMS) is defined as all activities manufacturers must carry out to keep up to date a procedure for proactively collecting and reviewing evidence gained from a medical device. This includes devices they place on the market, make available to the market, or put into service for the purpose of identifying any need to immediately make changes to a device. This should also form part of the quality management system implemented by the manufacturer to ensure the quality of processes, procedures, and devices to achieve and maintain compliance with the provisions of the MDR.

The purpose of implementing a PMS system is to identify risks, not previously known, and opportunities for improvement in a timely fashion. This aims to ensure the continued safety of the medical device with accurately updated benefit-risk assessments, the monitoring of the performance of the device and initiate recalls, where necessary.

Understanding the post-market surveillance process

The PMS system implemented by the manufacturer should follow a similar "process approach" most management systems are often based on: "plan, do, check, act" which is also known as the PDCA cycle. This recursive and rigorous 4 step approach allows companies to maximise the control and continuously improve both processes and products.

The first step is for manufacturers to create a PMS plan for each medical device in line with Annex III of the MDR. As part of this plan, the manufacturer should cover the process for establishing, documenting, implementing, maintaining, and updating a post-market surveillance system, taking into consideration the risk classification of the device. The system should be designed to ensure that throughout the life cycle of the device, relevant data can be actively and systematically gathered, recorded, and analysed.

Once the plan has been established, ensuring that all the requirements have been met, the manufacturer can start to implement the plan (the "do" stage of the PDCA cycle). The plan should allow for a combination of both 'proactive' (anticipating events before they occur) and 'reactive' (responding after an event) activities to collect data. For example, processes which can be undertaken to be proactive include customer surveys, post-market clinical follow-up, expert user groups, field safety notices and adverse event reports. On the other hand, the management system should allow for reactive reporting from feedback including complaints, maintenance/service reports, monitoring and measuring analysis or literature reviews (which may form part of the devices' clinical evaluation).

The results from this should be able to provide the data for the "check" step within the cycle. Manufacturers should be able to perform root cause analysis to derive the necessary conclusions to determine and monitor the possible changes or improvements that can be made. This then leads to the final step "act" where any corrective or preventive actions are implemented.

In addition to this process, manufacturers must produce a PMS report or periodic safety update report (PSUR) depending on the class of the device.

Manufacturers of class I medical devices must prepare a PMS report which should present results and conclusions as a result of data gathered from the PMS plan, alongside rationale and description of any preventive and corrective actions taken. This report shall be updated when necessary and may be requested by a competent authority. Whereas medical devices within a higher classification must have a PSUR. This report is identical to a PMS report, but has a few additional requirements including:

- Conclusions of benefit-risk determination
- Main findings of the post-market clinical/performance follow-up
- The volume of sales of the device and estimate evaluation of the size or other characteristics of the population using the device
- The usage frequency of the device, where practicable
- The PSUR should be updated when necessary and at least every two years for class IIa devices, and at least annually for class IIb and class III devices.

What should be included in a PMS plan?

A PMS plan must be provided as part of the assessment which is carried out to obtain CE mark certification from a notified body. This plan should be based on the available clinical data and an assessment of residual risks as part of the risk-benefit analysis. The PMS plan should form part of the technical documentation of a medical device and include the following as outlined in the requirements of Annex III of the MDR

A proactive and systematic process to collect information from:

- serious incidents, including information from PSURs, and field safety corrective actions
- records referring to non-serious incidents and data on any undesirable side-effects
- trend reporting
- relevant specialist or technical literature, databases and/or registers
- feedback and complaints, provided by users, distributors and importers
- publicly available information about similar medical devices

Effective and appropriate methods, processes, and tools to:

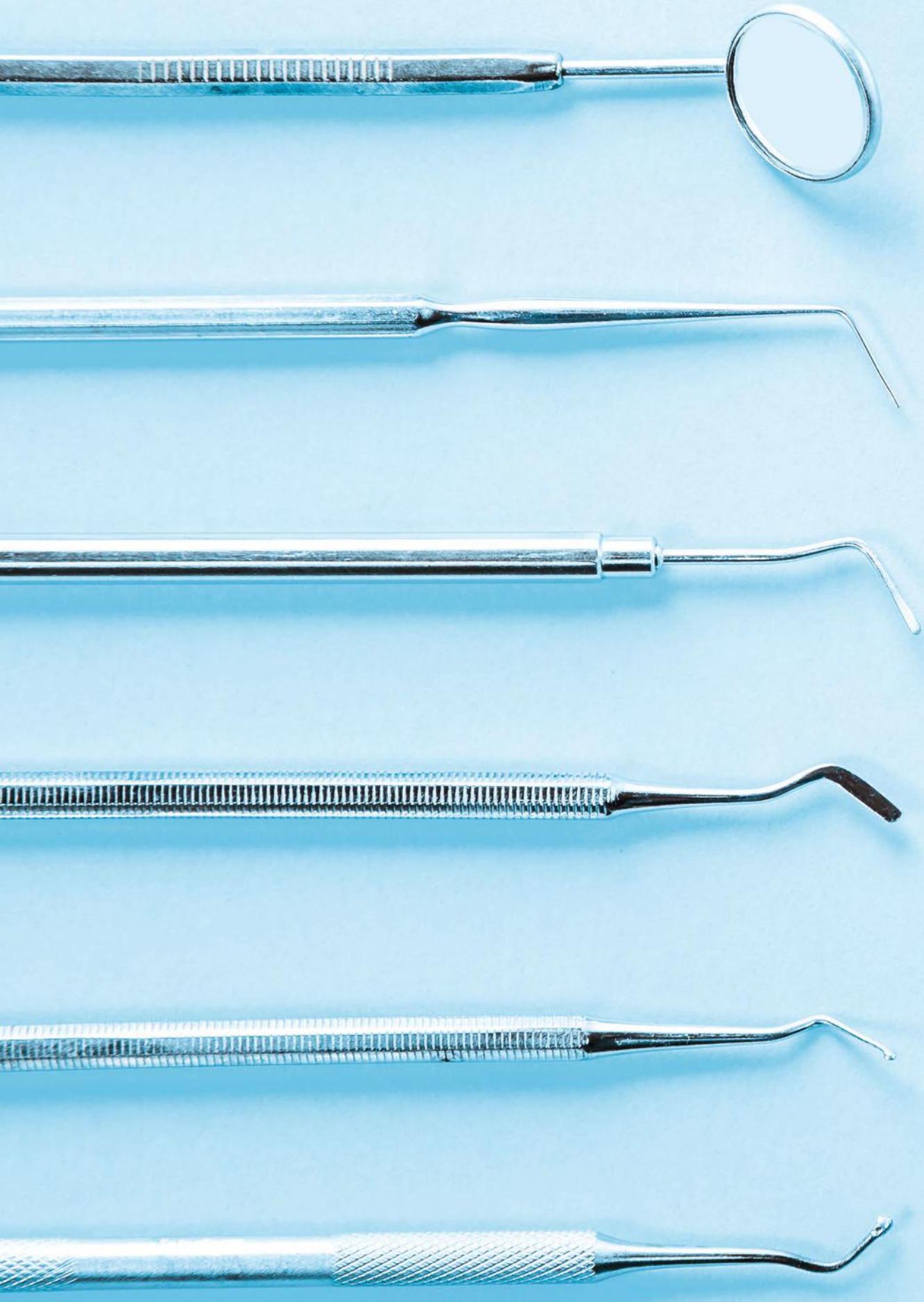
- assess the collected data
- investigate complaints and analyse market-related experience collected in the field
- manage the events subject to the trend report
- establish any statistically significant increase in the frequency or severity of incidents as well as the observation period
- communicate effectively with competent authorities, notified bodies, economic operators and users
- fulfil the manufacturer's obligation for a PMS system, PMS plan and PSUR
- identify and initiate appropriate measures including corrective actions
- trace and identify devices for which corrective actions might be necessary
- suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management
- a PMCF plan or a justification as to why a PMCF is not applicable

Who is responsible for post-market surveillance?

ISO TR 20416:2020 is an international technical report which aims to give guidance to manufacturers on the post-market surveillance process for medical devices. Section 5.4 of this report outlines the roles and authorities, stating that top management should define, assign, and communicate responsibilities and authorities for post-market surveillance activities. Depending on the size and complexity of the organisation, the number of those involved within the post-market surveillance team may vary but it should consider including cross-functional representatives.

Then according to Article 15 of the MDR, manufacturers must nominate at least one person with appropriate competence to be the person responsible for regulatory compliance (PRRC). This person is responsible for a range of aspects relating to the compliance of a product, including ensuring that the post-market surveillance obligation requirements are complied with. This means that the top management have overall responsibility for ensuring that sufficient resources are assigned for PMS to be performed, whereas the PRRC is responsible for coordinating the assigned PMS team and ensuring compliance against the regulations.

WORDS | TONI CARLTON



FDA VALIDATION REQUIREMENTS FOR REUSABLE MEDICAL DEVICES: 21 CFR 801.5

WORDS | CHRIS SIBANDA

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FDA Requirements for Reusable Medical Device Validation

The FDA requires manufacturers of certain reusable medical devices to include validated instructions for use and validation data on cleaning, disinfection, and sterilization in their 510(k) premarket notifications. In this article, we provide guidance on the requirements and criteria for validation data related to instructions for use, in accordance with 21 CFR 801.5.

Cleaning validation steps

According to the FDA, effective cleaning should:

"minimize the soil transfer from one patient to another or between uses in a single patient; prevent accumulation of residual soil throughout the product's use life";

According to ANSI/AAMI ST98:2022

1. Test soil choice and test soil validation:

ASTM F3293-18 offers guidance for an artificial test soil, the artificial test soil chosen should allow at least two clinically relevant soil components to be quantified for validation testing (e.g., total organic carbon, protein).

2. Inoculation and conditioning:

Soil inoculations should mimic worst-case clinical use conditions. All locations on the medical device likely to contact patient materials should be soiled, including all locations that are difficult to clean.

3. Cleaning of the medical device according to the IFU:

The personnel responsible for the IFU validation would then clean the soiled medical device according to the IFU with no deviation.

4. Extraction of residual test soil (analytes):

Devices should be subjected to a validated method of extraction for recovery of residual soil. The extraction method should be completely described for each device and its recovery efficiency should be determined as part of its validation.

Cleaning validation criteria

The following acceptance levels must be met in order to validate the cleaning instructions provided by the manufacturer:

ANSI/AAMI ST98	
Analyte	**Recommended Level**
Protien	≤6.4 µg/cm²
Hemoglobin	≤2.2 µg/cm²
Carbohydrate	≤1.8 µg/cm²
Total Organic Carbon	≤12 µg/cm²
ATP	≤22 femtomoles/cm²
No Visible Soil	

A minimum of 2 analytes must be measured for the medical device being tested regardless of standard.

Cleaning validation standards

- AAMI TIR30 – A Compendium of Processes, Materials, Test Methods, and Acceptance Criteria for Cleaning Reusable Medical Devices.
- ANSI/AAMI ST98:2022 – Cleaning Validation of Health Care Products – Requirements for Development and Validation of a Cleaning Process f or Medical Devices.
- ISO 15883-5:2021 – Washer-disinfectors — Part 5: Performance Requirements and Test Method Criteria for Demonstrating Cleaning Efficacy.
- ASTM F3293-18 – Standard Guide for Application of Test Soils for The Validation of Cleaning Methods For Reusable Medical Devices.

Sterilisation & Disinfection validation steps

Following cleaning, medical devices that are not returned into service will need to go through additional antimicrobial steps such as sterilisation and disinfection.

CDC considers the Spaulding Classification to offer rational guidance on the extent to which a medical device should be processed relative to criticality.

Category	Definition	Level of Microbicidal Action	Method of Decontamination	Example of Common Items/Equipment
High (critical)	Medical devices involved with a break in the skin or mucous membrane or entering a sterile body cavity	Kills all microorganisms	Sterilisation (usually heat if heat-stable or chemical if heat-sensitive	Surgical instruments, implants, prostheses and devices, urinary catheters, cardiac catheters, needles and syringes, dressing, stutres, delivery sets, dental instruments, rigid bronchoscopes, cystoscopies etc.
Intermediate (semi-critical)	Medical devices in contact with mucous membranes or non-intact skin	Kills all microorganisms, except high numbers of bacterial spores	High-level disinfection by heat or chemicals (under controlled conditions with minimum toxicity for humans)	Respiratory therapy and anaesthetic equipment, flexible endoscopes, vaginal specula, reusable bedpans and urinals/ urine bottles, patient bowls etc.
Low (non-critical)	Items in contact with intact skin	Kills vegetative bacteria, fungi and lipid viruses	Low level disinfection (cleaning)	Blood pressure cuffs, stethoscopes, electrocardiogram leads etc. Environmental surfaces, including the OR tables and other environmental surfaces.

Spaulding classification

The Spaulding Classification is a categorization scheme for patient-care items and equipment based on the degree of risk for infection involved in their use.
The classification, which was developed more than 30 years ago by Earle H. Spaulding, divides instruments and items into three categories: critical, semicritical, and noncritical. This approach has been widely used by infection control professionals to plan methods for disinfection or sterilization, and it is employed in various CDC guidelines for handwashing, hospital environmental control, and infection control in healthcare facilities.

Sterilisation validation at Test Labs 'Overkill method'

The goal of the overkill method based on EN ISO 17665-1:2006 and ANSI/AAMI/ISO 17665-1:2006, is justification of validity of a sterilisation process by demonstrating its effectiveness at killing a predesignated number of microorganisms.

The validation of an F0 value that gives a SAL of 10-6 (or a value determined to be satisfactory by the medical device manufacturer) should be performed by the overkill method partial cycle approach.

The method aims to justify a SAL of 10-12 as being achievable in real world conditions, using the F0 provided by the medical device manufacturer, if a SAL of 10-6 is achieved at half the provided F0 value.

The Sterilisation Validation Standards

EN ISO 17665-1:2006 – Requirements for the Development, Validation and Routine Control of a Sterilisation Process for Medical Devices

ANSI/AAMI/ISO 17665-1:2006 – Sterilization of Health Care Products – Moist Heat – Part 1: Requirements for the Development, Validation, and Routine Control of a Sterilization Process for Medical Devices

Disinfection Validation Steps

Thermal disinfection validation involves performing temperature mapping on the device being used to disinfect the medical device during the disinfection cycle.

According to ISO 15883-2:2006, during the disinfection cycle, the following requirements must be met:

- The operating cycle specified by the medical device manufacturer shall include a thermal disinfection stage which outlines a temperature that adheres to a minimum A0 of 600* for:

1. All surfaces of the load to be disinfected
2. All internal surfaces of the chamber and on the load carrier.

- A0 of 600 equivalent to 80°C for 10 minutes, or 90°C for 1 minute.

Chemical disinfection validation, based on ANSI/AAMI ST58:2013, medical devices are inoculated in the worst-case location providing the highest challenge to the disinfection process.

The biological indicator e.g., Mycobacterium to prove high level disinfection claims or Staphylococcus aureus for intermediate and low-level claims, is allowed to dry on the medical device.

The medical device is then disinfected according to the IFU, the disinfectant is prepared and applied to the medical device for the required contact time. The biological indicator on the medical device is then extracted, and log reduction testing is performed.

The Disinfection Validation Standards

ANSI/AAMI ST58:2013 – Chemical Sterilization and High-Level Disinfection in Health Care Facilities.

ISO 15883-2:2006 – Requirements and Tests for Washer-Disinfectors Employing Thermal Disinfection for Surgical Instruments, Anaesthetic Equipment, Bowls, Dishes, Receivers, Utensils, Glassware, etc.

Adhering to the criteria outlined in the aforementioned standards is essential for ensuring a successful submission of your 510(k) for reusable medical devices. By meeting these requirements and validating the instructions for use, as well as the cleaning, disinfection, and sterilization processes, you can demonstrate compliance with FDA regulations and enhance the safety and effectiveness of your medical devices. Meeting these standards not only facilitates regulatory approval but also instills confidence in healthcare providers and patients regarding the proper use and maintenance of the devices.

FDA MEDICAL DEVICE MATERIAL PERFORMANCE REQUIREMENTS

WORDS | SYEDA BEGUM

To prevent the spread of healthcare-associated infections (HAIs), it is vital that surfaces and devices used in healthcare settings undergo disinfection/ sterilisation. However, a growing problem is failure and damage to medical devices due to incorrect cleaning such as over-saturation, lack of rinsing, use of incompatible disinfectants, and lack of compliance from cleaning personnel. Aside from inadequate and/or unclear cleaning instructions where the use of incompatible sterilants/ disinfectants are used, medical devices can also become damaged through normal use if insufficient performance and compatibility testing has been done to demonstrate the materials chosen to manufacture the device are adequate for the device application.

A search for medical device recalls by the Food and Drug Administration (FDA) indicate these problems are prevalent and thus the importance of compatibility testing is revealed. For example, the problem of polymer components in a haemodialysis instrument becoming cracked from mechanical and thermal stress led to the device being recalled in 2006. Environmental stress cracking is a common cause of failure of thermoplastic polymer materials, and exposure of such polymers to liquid chemicals can accelerate this cracking process. More recently, in 2023, a type of ventilator was recalled due to potential adhesion failure with the silicone foam used in the device. This type of failure suggests insufficient performance testing was done on whether the different materials and components of the device are compatible with each other.

FDA Medical Device Material Compatibility requirements

As part of the FDA's safety evaluation process for medical devices, thorough review and assessment of the materials used in the device's manufacturing are conducted, including rigorous medical device testing. Although biocompatibility is a big part of the 510(k) submission by the device manufacturers to the FDA, this is more focused on the safety of the materials when used in contact with the human body.

Material compatibility considers the damage to the material surface that could potentially arise over time after repeated reprocessing or by cleaning practices prescribed by the manufacturer as part of their instructions for use (IFU). This type of compatibility testing is essential in ensuring the materials selected and used by manufacturers are appropriate for the intended use of the device and making sure the most suitable methods of cleaning and disinfection/sterilisation, pertaining to that material, are chosen to prevent potential failures.

FDA Medical Device Material Compatibility Regulations and Guidance

The FDA labelling regulations (CFR Title 21 part 801, AAMI TIR 12 and ISO 17664) require manufacturers of medical devices to state adequate directions for use, operating and servicing instructions, and either adequate warnings against dangerous uses to health, or information necessary for the protection of users. Aspects of the device label, in relation to reprocessing instructions, where material compatibility should be considered by the manufacturer include:

- The cleaning method, which should only recommend cleaning and/or disinfectant agents that have been demonstrated to be compatible with the medical device materials.
- The rinsing method, which should not leave harmful chemical residues that could adversely affect the materials or device performance, e.g. saline rinses are not recommended by the FDA as it could lead to corrosion and build-up of inorganic residues.
- Lubricating agents, if applicable to the medical device, should have been demonstrated to be compatible with the device.
- Instructions for visual inspection after cleaning should identify acceptance criteria related to the device performance, e.g. presence/absence of corrosion, discolouration, etc. and what to do if visual inspection fails.
- If the device is to be sterilised, it should include what materials are incompatible with the sterilisation load, e.g. cellulose incompatible with hydrogen peroxide sterilisation.
- Wrapped/contained devices should include a recommended minimum drying time since any moisture remaining after sterilisation could weaken the sterile barrier of the packaging materials and the seals used.

FDA Sterilisation Guidance

When choosing materials, medical device manufacturers need to consider what works best for the design and manufacture process, as well as the effect of sterilisation on the material, how the material will impact the application/function of the device, and how the sterilisation affects packaging and accelerated ageing of the material. The standard AAMI TIR17:2017/(R)2020 – Compatibility of Materials Subject to Sterilisation, is recognised by the FDA and provides guidance on 4 main areas:

1. Choosing materials compatible with sterilisation
2. Avoiding processing errors by optimising functionality of selected materials
3. Assessing functionality and safety of the product after sterilisation and aging
4. Applying accelerated aging programs to reduce cost and time for material qualification (see FDA recognised ASTM standard F1980-21 – Accelerated Aging of Sterile Barrier Systems and Medical Devices for guidance on developing accelerated aging protocols).

FDA Chemical Disinfection Guidance

Cleaning methods of medical devices that involve the use of chemical disinfectants require the manufacturer to consider how the active ingredients of the formulation affect the material of the medical device. One of the properties of an ideal disinfectant listed in the CDC Guideline for Disinfection and Sterilization in Healthcare Facilities is surface compatibility, stating that the disinfectant "should not corrode instruments and metallic surfaces and should not cause the deterioration of cloth, rubber, plastics, and other materials". FDA-cleared liquid chemical sterilant and high-level disinfectants (defined as "a sterilant used for a shorter contact time to achieve a 6-log10 kill of an appropriate Mycobacterium species"), that can be used to reprocess reusable medical devices, are recognised as safe to use in accordance with the label directions stated by the device manufacturer. The FDA-recognised standard ANSI/AAMI ST58:2013/(R)2018 – Chemical Sterilization and High-level Disinfection in Health Care Facilities provides recommendations on chemical material compatibility of all approved high-level disinfectants, liquid chemical sterilants, and gaseous chemical sterilants used for medical device sterilisation.


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