WHITEPAPER

NEW EU MEDICAL DEVICE REGULATION ADOPTED APRIL 5TH

NSF Industry Forum Already Examined Impacts

By Howard Broadbridge, Business Development Manager, NSF Health Sciences Medical Devices

The year 2017 brings significant changes to the regulatory landscape across Europe, following the publication of the new European Medical Device Regulation (MDR) and In Vitro Diagnostics Regulation (IVDR). NSF International hosted an industry forum in the UK on November 30, 2016, to explore the likely impact of the changes on company planning, finance and human resources, particularly in the areas of quality assurance, regulatory and manufacturing functions. The forum also focused on identifying parallels with the pharmaceutical industry.

SETTING THE SCENE

More than 30 regulatory professionals from a wide range of medical device companies – from small start-ups to large corporations – manufacturing a broad range of medical products attended the forum. James Pink, VP for NSF Health Sciences Medical Devices Team, provided the forum with an overview of the two regulations. Since the PIP implants scandal and the product safety concerns associated with metal-on-metal resurfacing of implants came to light, the medical device regulatory framework has been under significant scrutiny.

To ensure a consistently high level of health and safety protection for EU citizens, it became apparent that changes were required in the medical device directives and that significant regulatory changes were also needed. For instance, competent authorities in some member states have neither regulated notified bodies effectively nor challenged them sufficiently to maintain consistency in the review of clinical data as well as applying the appropriate scrutiny when assessing the

manufacturer throughout their production processes.

The new regulations were proposed by the European Commission in February 2012, and the European Parliament voted on April 5, 2017, to adopt them. The industry is now subject to a three-year transition period for medical devices and a five-year period for in vitro diagnostic (IVD) products.

Notified bodies have also been significantly affected by the increased scrutiny, which has resulted in the loss of designation or voluntary withdrawal. The scrutiny has also affected manufacturers that have lost their notified body or have experienced delays in the issuance of CE certificates. Manufacturers will be further impacted by changes in product classification, possibly triggering portfolio rationalisation, and by additional scrutiny that may increase the difficulty of new product introductions due to indeterminate timescales and additional costs.

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Addressing all of these impacts requires careful business planning. Plans might include recruiting additional qualified staff to help manage the transition, ensuring that the organization has comprehensive clinical and technical data for their product families, being well prepared for audits, and reviewing the arrangements for postmarket surveillance.

IMPLICATIONS FOR IVDS

The first certificates for IVD products are to be issued by notified bodies within two years, and full compliance is required within five years. Doris-Ann Williams, MBE, represented the IVD industry at the forum. Chief Executive of the British In Vitro Diagnostics Association (BIVDA), she offered some remarks about the new IVD regulation.

Consistent with the MDR regulation, the new regulation for IVDs require reclassification of products based on the International Medical Device Regulatory Forum (IMDRF) risk-based classification criteria, but the certification requirement will have an even greater impact. Prior to the changes, most IVDs were self-certified, without the need for notified body involvement. However, this situation is about to be turned on its head, as the notified body will now be required to issue a CE mark for approximately 90 percent of products (classes B, C and D). Only instruments and specimen containers remain self-certifiable.

Another key change is the need for rigorous examination of the clinical evidence that supports the claims of a given IVD. The evidence needs to indicate compliance with general safety and performance requirements and must be updated regularly throughout the product's lifecycle.

Manufacturers also need to consider the impact of the changes on third parties, such as importers and distributors, which in many cases will be required to fulfill the role of an authorized representative within a given state of the EU. The impact will tend to be greater for smaller manufacturers than large multinationals and will affect both training and administrative costs linked to preparation of contracts and auditing.

Again, like their medical device counterparts, IVD manufacturers need to focus more on postmarket surveillance and vigilance; products in classes C and D also need a periodic safety update report (PSUR), at least annually, which forms part of the technical documentation. Timelines for reporting serious incidents have been reduced from 30 to 15 days under the new regulation. Both regulations require planning on behalf of manufacturers to ensure they have sufficient staff and adequate internal systems to meet the new requirements.

The changes discussed above may well spark a rationalization of manufacturers' product portfolios if, on review, certain products that are subject to increased regulation are deemed to have become less profitable as a result.

THE PHARMACEUTICAL PERSPECTIVE

Having considered the impacts of the new regulations on medical devices and IVDs, the forum welcomed Dr. Pete Gough, Executive Director at the Pharma Biotech Division at NSF Health Sciences. He provided some interesting information about the regulatory changes affecting the pharmaceutical industry. He focused primarily on clinical trial regulation, proposed new EU regulation for good manufacturing practice (GMP) and the new Falsified Medicines Directive (FMD).

The EU's new Clinical Trial Regulation (CTR), which will replace the Clinical Trial Directive No. 2001/20/EC, was introduced to halt the decline in clinical trial numbers and harmonize clinical trial regulation across EU member states. Additionally, the required content of clinical trial applications will be standardized and adverse incident reporting will be electronic/web-based. Implementation is expected during 2018.

The EU's proposed GMP legislation for marketed medicinal and investigational products will require organizations to adopt a risk-based approach and define new responsibilities for the Qualified Person. The requirement also holds for coming GMP legislation for advanced therapy medicinal products (ATMPs).

The FMD, which has been published and will go into effect in 2018, requires a number of safety features. Apart from a few exempt products, it requires

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organizations to verify their products' authenticity and to show whether outer packaging has been subject to tampering. Qualified Persons are legally required to ensure that safety features have been adequately incorporated in packaging.

In common with devices and IVDs, another area of change concerns the way in which products are identified throughout the supply chain. A unique device identifier (UDI) will provide the product, batch number, expiry date, strength, pack size and other relevant details. Unique to pharmaceuticals, there will also be a European Medicines Verification System (EMVS), designed to provide an additional level of control via national data repositories.

INDUSTRY IMPACT

To help gauge the likely effect of the new regulations on the industry, NSF used an electronic voting system to provide those attending the forum the opportunity to give their opinions on several different areas of impact they expect. In the first voting session, attendees were asked about the likely impact on human resources, training and company finances, and which changes will most influence their organization's strategic goals.

Seventy-eight percent of the 30 attendees who responded to the poll said that their company will need to invest in additional human resources to cope with the impact of the new medical device and IVD regulations, and half of the respondents reporting feeling that their organization is inadequately qualified to deal with the impact.

When asked for the most crucial impact on their companies' strategic goals, an overwhelming 30 percent of the respondents identified the impact on clinical data. Twenty-five percent identified the impact on remediating and updating technical information, followed by 15 percent identifying uncertainty about notified body certification, 15 percent UDI, 10 percent product up-classification, and 5 percent identified insurance and legal entities.

Ninety-four percent of the respondents agree that the financial impact of the new regulations will be significant, and 65 percent said that the implementation cost would exceed £50,000.

(See the appendix for the complete results of the poll.)

INDUSTRY PLANNING FOR THE NEW DIRECTIVES

In the forum's second voting session, NSF asked those in attendance to provide feedback on how their organization is planning to introduce the new regulations. The questions focused on internal communication, the need for external advice, access to notified bodies and the impact of Brexit.

Only 33 percent of the responding attendees reported that their company has prepared a plan for implementing the new regulations, and almost 40 percent said that they don't understand the regulations well enough to plan effectively for their impact.

Fifty-five percent of the attendees said that their organization has an internal steering committee or planning body with respect to the new regulations, but only 30 percent reported regular staff briefings to prepare for the regulations. At 59 percent, the organization's own research is by far the most common way that the attendees obtain information about regulatory changes, with conferences (18 percent), emails (14 percent), colleagues and external consultants (5 percent each) bringing up the rear.

Seventy-eight percent of the respondents said that their quality and regulatory assurance (QARA) personnel may need external advice or assistance with implementing the new regulations. Forty-two percent reported that access to services or advice from their current notified body has been difficult to come by; 32 percent said that it has not been difficult, and 26 percent didn't know.

Eighty percent of the attendees said that the UK's exit from the EU (Brexit) would, or perhaps would, have a significant impact on their business during the next five years. However, at this point, it is impossible to predict the effect of Brexit upon the medical device, IVD or pharmaceutical markets, given that trade negotiations have not yet commenced and are likely to take two years to conclude. However, irrespective of the negotiated final terms of the UK's exit, it is clear today that trading with the EU in the future

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will require UK companies to continue complying with European regulations.

(See the appendix for the complete results of the poll.)

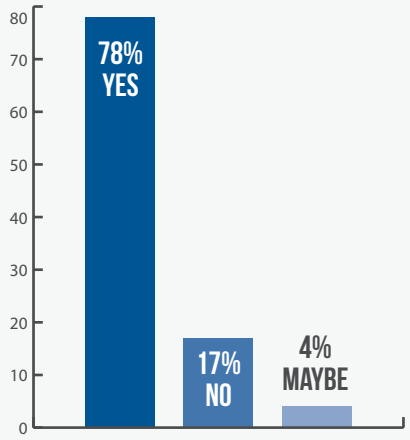
FUTURE DEVELOPMENTS

Because the impact of the new regulations is clearly very significant, medical device and pharmaceutical organizations need to keep a close watch on further developments and gather as much information as they can to predict and prepare for outcomes as well as possible.

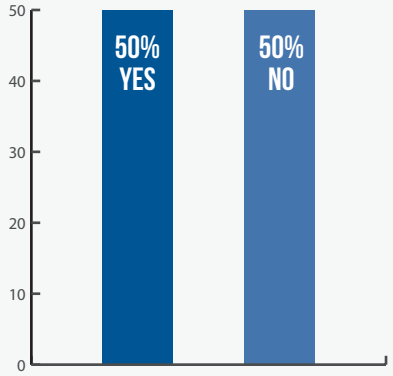
Appendix: Complete Polling Results

Impact of the New Directives

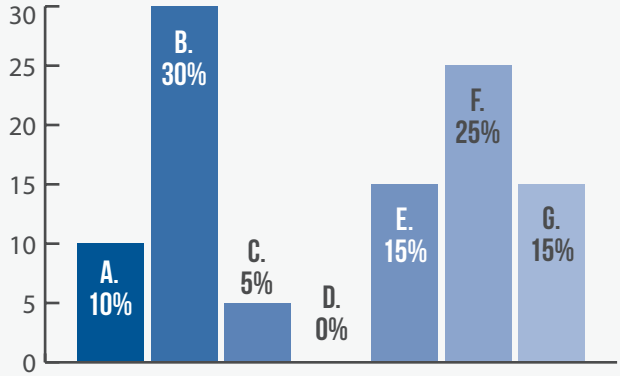
1 **Do you feel that you will need to invest in additional human resources to cope with the impact of the new medical device/IVD regulations?**



2 **Do you feel adequately qualified to deal with the impact of the new regulations?**



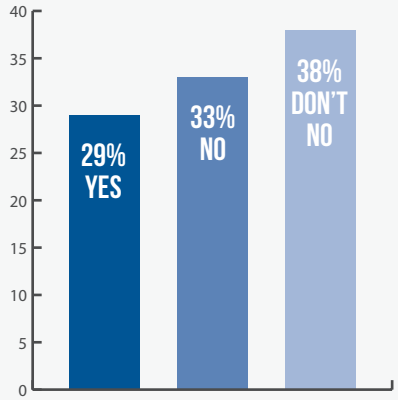
3 **What will be the most crucial impact that determines your company's strategic goals?**



A. Product Up-Classification - 10%
B. Clinical data - 30%
C. Insurance and legal entities (e.g. AR) - 5%
D. Person Responsible for Regulatory Compliance - 0%
E. UDI - 15%
F. Remediating/updating technical information - 25%
G. Uncertainty about Notified Body certification - 15%

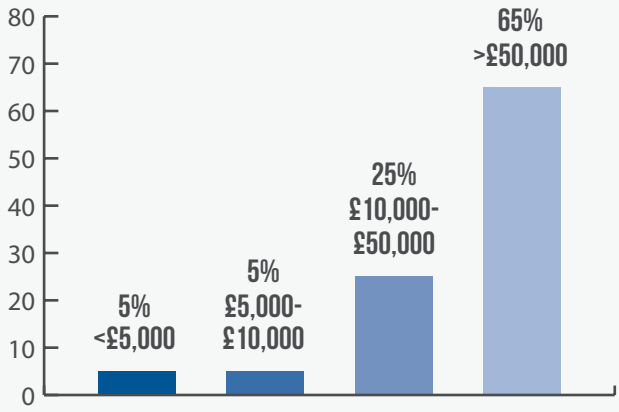
4

Do you feel that new medical device apps/software will have a significant impact on the way in which you implement the upcoming regulatory changes?



5

What do you think will be the approximate cost of implementing the new regulations?



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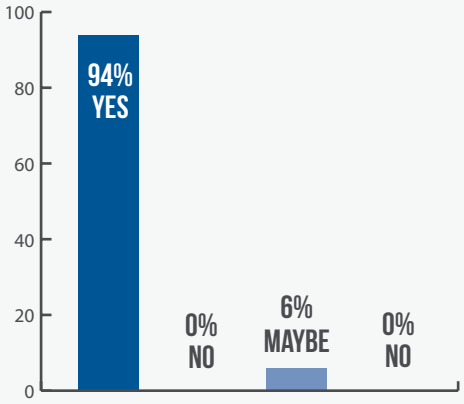
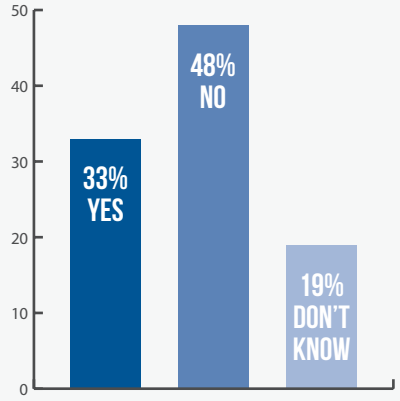
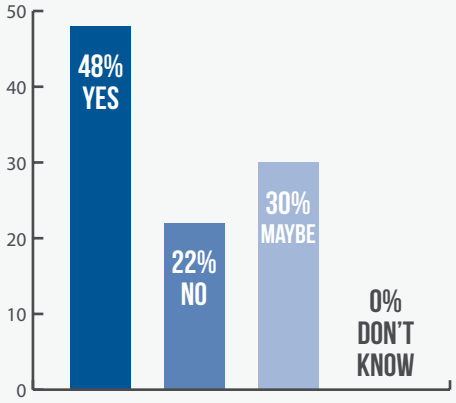
Do you think there will a significant financial impact as a result of MDR/IVDR?



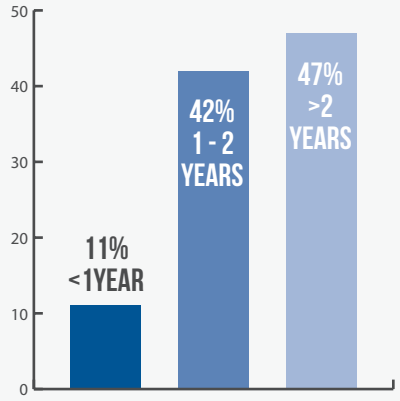
7 Has your company prepared a plan for implementing the new medical device/IVD regulations?



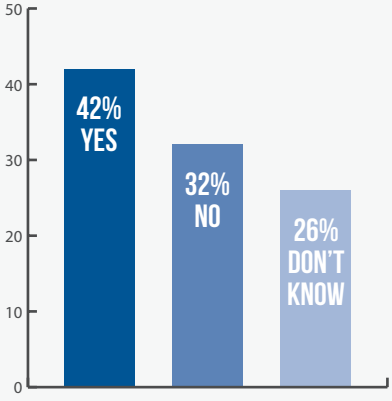
8 Do you feel that your QARA personnel will need external advice or assistance in implementing the new regulations?



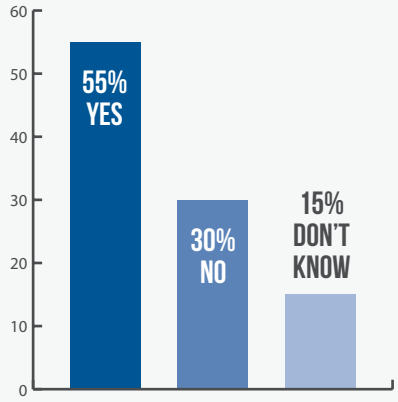
9 How long do you think it will take to implement UDI across your product range?



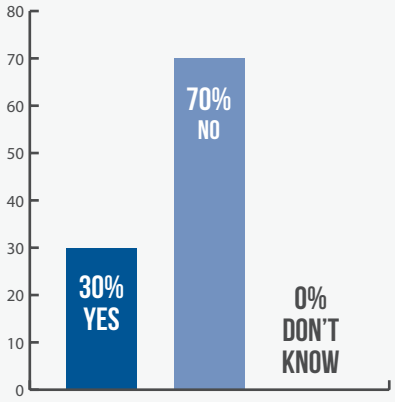
10 Have you had difficulty in accessing services or advice from your current notified body?



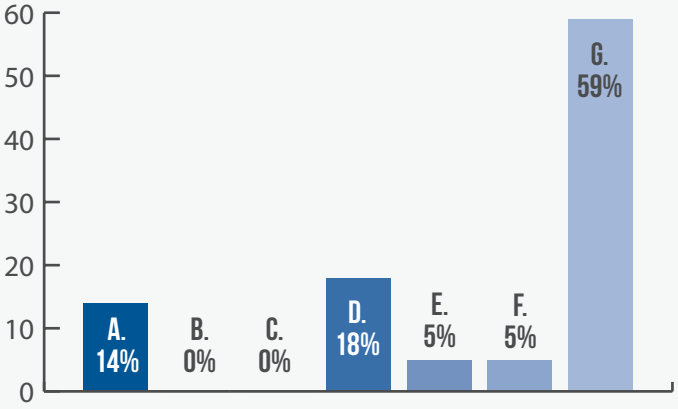
11 Within your organization, is there an internal steering committee or planning body with respect to the new regulations?



12 Do regular staff briefings take place in your company to prepare for the new regulations?

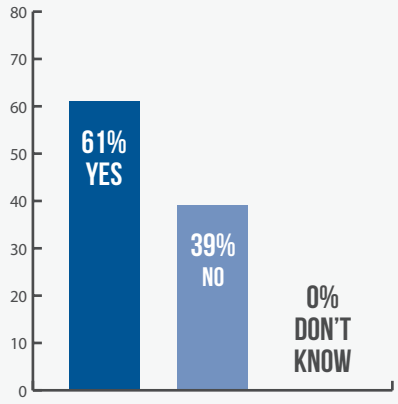


13 How do you mainly obtain information regarding changes to regulations?

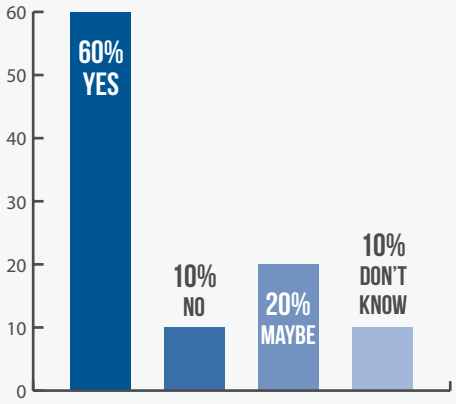


A. E-Mails - 14%
B. Advertising - 0%
C. Newsletters - 0%
D. Conferences - 18%
E. Colleagues - 5%
F. External Consultants - 5%
G. Own Research - 59%

14 **Do you understand the new regulations adequately to plan effectively for the impact?**



15 **Do you feel that Brexit will have a significant impact upon your business in the next 5 years?**



For more information on the new EU medical device regulations and the steps you can take to navigate the new regulatory environment, please contact **medicaldevices@nsf.org** or visit **www.nsfmedicaldevices.org**.

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