

Health apps: regulation and quality control

Summary of a joint meeting held on 19 November 2014 hosted by the Academy of Medical Sciences and the Royal Academy of Engineering.

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Disclaimer

This document reflects the views of participants expressed at the meeting and does not necessarily represent the views of all participants, the Academy of Medical Sciences or the Royal Academy of Engineering. For further information, please contact Dr Claire Cope, Policy Officer at the Academy of Medical Sciences (claire.cope@acmedsci.ac.uk, (0)20 3176 2164).

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Executive summary

Challenges and opportunities

Dozens of new health apps for smartphones and tablets are produced each month, adding to the hundreds of thousands already in existence. Some are focused on consumers' health and lifestyle, while others are intended to support the professional activities of clinicians or other healthcare workers.

Apps have the potential to increase the quality and efficiency of healthcare, and to empower consumers to manage their health better. A vibrant app development sector will also deliver economic benefits to the UK, in terms of employment opportunities and trade, as well as those associated with a healthier nation, such as increased productivity and reduced healthcare costs.

Health apps present a new challenge to regulatory authorities. Software intended for use in a medical context can be classified as a medical device, and health apps therefore potentially fall within the regulatory remit of bodies such as the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK and the Food and Drug Administration (FDA) in the USA. However, the sheer volume of health apps, and their rapid take-up by consumers and health professionals, raises questions about the appropriate levels of regulation and oversight, and whether current and impending regulatory frameworks are fit for purpose.

This joint meeting brought together individuals from multiple disciplines, including regulators, clinicians, app developers and engineers to discuss the current and evolving regulatory landscape and how it might be shaped in the future. The meeting featured an overview of the current regulatory and oversight landscape in the UK and internationally, as well as examples of apps that had successfully navigated regulatory pathways in the UK and USA. Invited speakers also covered procedures for assuring the safety of apps in the NHS App Library, the development of a patient-driven app library, and the approach adopted by the National Institute for Health and Care Excellence (NICE) for handling medical devices (including embedded software). Other presentations focused on software development practices in the automotive and nuclear industry, providing an opportunity to learn from other sectors.

Key issues identified

Discussions identified several important themes for future consideration:

- **Complexity of current regulation:** The current regulatory landscape was widely felt to be confusing. Developers would benefit greatly from clearer and more consistent advice and guidance from the regulatory sector on how to identify and navigate the appropriate regulatory pathway for their products. A roadmap providing clear guidance would be helpful for developers.
- **Suitability of current legal framework:** Delegates questioned whether current systems, set up to oversee physical devices, were still suitable for 'virtual' products.

New software- or app-specific structures might be needed, although this would raise resourcing issues. Intended use in a medical context, with associated risk-based assessment, as is currently the case, could be seen as a suitable basis for identifying products that warrant regulatory oversight. A challenge for this approach is the adoption of apps by healthcare professionals not originally intended for medical use. These apps may also be adopted by the public for use in a medical context. In terms of appropriate levels of regulatory oversight, participants acknowledged the tension implicit in the need for balance between ensuring safety and promoting innovation: health apps have the potential to lead to harm, yet excessive regulation could inhibit a field with opportunities to deliver considerable health and economic benefits. On the other hand, a strong regulatory framework can enhance standards and raise quality.

- **Vigilance and monitoring:** Questions were raised about the adequacy of current reporting and vigilance systems. Concerns were expressed that the MHRA was not always proactive in identifying issues. The respective roles of the MHRA and NHS England patient safety systems are not clear, and there may be merit in further discussions between the two groups and greater coordination between them.
- **Obstacles to app use and promoting app uptake:** Given their potential value to medical practice and public health, it was felt that more could be done to promote the use of apps with an appropriate evidence base in healthcare. Participants suggested that the use of apps in medicine, or recommendation of apps to patients, was being held back by a lack of clarity about liability, should patients be harmed.
- **Generating and evaluating the evidence of clinical utility:** There were suggestions that more evidence was needed to support the use of specific apps in healthcare. More centres specialising in app evaluation might be required. Consideration also needs to be given to the types of evaluation undertaken – lengthy randomised trials are not well suited to assessment of apps. Tools are required to support more systematic appraisal of apps, akin to those applied to assess the quality of information in conventional systematic reviews. Participants raised the possibility that NICE could play a greater role in evaluating medical apps and in promoting their implementation. This might, however, require additional funding and add red tape.
- **The role of aggregation services:** Participants suggested that app libraries could also play a more proactive role in quality assurance; for example, major app stores could facilitate peer review or note endorsements by learned societies. A similar role could also be played by specialist 'boutique' app libraries. Bodies such as the Royal Colleges could play a role in their specialist communities.
- **Software development practices:** There are widespread concerns that the software practices typical of rapid app development are not compatible with current regulatory appraisal systems. Although some of the principles adopted by software engineers in traditional engineering sectors might be applicable in app development, many would require a significant shift in mindset within the field of health apps, which is still in its infancy in comparison.

Introduction

Recent years have seen explosive growth in health and wellbeing 'apps' for smartphones and tablets. These range from simple lifestyle apps for consumers to sophisticated tools for use by medical professionals.

There is considerable scope for health apps to enable consumers to manage their health better and medical professionals to improve the quality or efficiency of medical practice. Clearly, apps designed for use by medical professionals have the potential to impact on patient health. However, by potentially influencing decision-making, even consumer apps could have health consequences, raising important questions about regulatory approval and oversight more generally.

Health apps do not fit neatly into the current regulatory framework. Some fall under the umbrella of medical device legislation, which includes medical software. In 2014, the MHRA published *Guidance on medical standalone software (including apps)*, which aimed to clarify when it considered an app to be a medical device and how it would be classified.¹ Various aspects of European legislation apply to health apps, and are currently being revised. The European Commission also published a consultative Green Paper on mobile health in 2014, to explore the issues surrounding mobile health and app development in particular.^{2,3} While safety is naturally a major issue, data protection and personal privacy are also highly relevant in this area.

Protection of patient safety and consumer health and privacy are central goals of regulation and oversight. However, app and other software development is a dynamic area of innovation, with the potential to deliver health and economic benefits through cost savings and wealth creation. One concern is that an over-zealous approach to app regulation could stifle the field, to the detriment of consumers and economic prosperity. Indeed, in the USA, concerted efforts are being made to limit regulatory oversight of app development.

This joint meeting brought together individuals from multiple disciplines, including lawyers, regulators, clinicians, app developers and engineers (a full list of participants is provided in Appendix II), to discuss the current and evolving legal landscape and how it might be shaped in the future. It included case studies of apps that have navigated

¹ <https://www.gov.uk/government/publications/medical-devices-software-applications-apps/medical-device-stand-alone-software-including-apps>

² European Commission (2014). *Green Paper on mobile Health ("mHealth")*. <http://ec.europa.eu/digital-agenda/en/news/green-paper-mobile-health-mhealth>

³ Subsequent to the meeting, the European Commission published its '*Summary Report on the Public Consultation on the Green Paper on Mobile Health*' (available at <http://ec.europa.eu/digital-agenda/en/news/summary-report-public-consultation-green-paper-mobile-health>). The report highlighted many similar issues to those discussed at the meeting, including: adequate data protection; the lack of a clear EU regulatory framework for mobile health (mHealth) and the complexity of legislation; the need to balance patient safety, user trust and mHealth reliability against the risk of over-regulation, which could stifle innovation and impede the potential benefits of mHealth; the difficulty in obtaining evidence to support the efficacy of mHealth use through long-term studies; the lack of clinical guidelines for the use of mHealth; liability, risk mitigation systems and reporting mechanisms; and international convergence of regulations. The Commission will propose a set of policy responses in the course of 2015, and, if needed, will carry out an impact assessment on future actions.

regulatory pathways in the UK and the USA. A particular aim was to examine whether lessons could be learned from the well-established regulatory regimes and approaches to software development in other high-risk areas of engineering, such as the automotive and nuclear industries.

Overview of presentations

The meeting covered the following areas (a full agenda is provided in Appendix I):

- The current regulatory and oversight frameworks in the USA and European Union (EU).
- Safety assessment of apps in the NHS Health Apps Library.
- Medical device evaluation by NICE and its potential application to apps.
- A patient-centred approach to app curation (myhealthapps).
- An MHRA-registered product (Mersey Burns App).
- An FDA-approved product (BlueStar).
- Software development for hybrid devices (Smartphone Vital Signs System).
- Software and system assurance in the nuclear industry.
- Software development processes in the automotive industry.
- Capturing good practice in software development (as documented in a recent report from the US National Academies).⁴

Appendix III provides brief summaries of the day's presentations.

⁴ National Research Council of the National Academies (2007). *Software for Dependable Systems: Sufficient Evidence?* The National Academies Press. Washington, DC.
<http://www.nap.edu/catalog/11923/software-for-dependable-systems-sufficient-evidence>

Discussions

Wide-ranging discussions after the presentations highlighted a number of issues surrounding the current legal framework and how it might be developed. In addition, it was widely felt that, alongside an effective and proportionate regulatory framework, there was also scope to encourage the development and uptake of apps to improve the quality and efficiency of healthcare and to support patient self-management.

Complexity of current regulation

- There is potential for people to be harmed by apps, particularly those specifically designed for use by medical professionals, but also those aimed at consumers, who may act on erroneous information. Some degree of regulatory oversight is required, but balance is needed to avoid stifling a dynamic market that is generating innovative products with the potential to improve the efficiency of healthcare and public health.
- To some degree, the app marketplace is self-correcting – successful apps thrive at the expense of those meeting consumers' needs less well. However, in technical areas, it may not be easy for consumers to judge an app's performance. Furthermore, unless apps conform to the standards required of equivalent medical devices, this could be considered an inadequate mechanism for weeding out ineffective or dangerous apps with the potential to cause harm.
- The current regulatory landscape is complex and it is often difficult for developers to identify what regulatory pathway they need to follow.⁵ In practice, it may be challenging to tell when an app or software is a 'medical device' for legal purposes. A roadmap or one-stop shop providing clear guidance would be helpful for developers, as current guidance, such as that provided by the MHRA, is still somewhat confusing.⁶
- International differences in regulatory systems are a problem for developers. UK law on medical software and apps is a national implementation of EU Directives, which aim to harmonise the law across the EU. These Directives are soon to be replaced by a more exacting regime that bypasses national legislatures so as to increase harmonisation across the EU.
- European data protection legislation could have major implications for apps using personal data. Potentially, it could add new obstacles to the development of medically useful apps and add further complexity to the app regulatory landscape.

Suitability of current legal framework

- The regulatory framework being applied to apps was developed for other products (such as tangible medical devices), raising questions about its suitability. Safety analysis often focuses on physical interactions with the body, which has little apparent relevance to software development. Potentially a new organisation (or section within an existing organisation) could be established with a more specific remit. This would,

⁵ Please see Mr Hitchcock's presentation entitled 'Health apps: the US and EU regulatory regimes' on pages 19-21 for further details.

⁶ <https://www.gov.uk/government/publications/medical-devices-software-applications-apps/medical-device-stand-alone-software-including-apps>

however, have to be developed within the context of European legislation. How it would be funded is another key question.

- Currently, there is no specific team within the MHRA dedicated to health apps. With growing demand, there are also questions over its capacity to provide extensive regulatory oversight. Because of its status, the MHRA is unable to charge fees for its services in this area. Whether it is adequately funded to manage rising demand is therefore open to question.⁷
- Many types of digital product are now used in healthcare, but not all are covered by regulation, raising questions about the reach of the regulatory framework. Training tools, textbooks (including electronic versions), websites and electronic health record systems sit outside the current framework, yet often have features in common with health apps.
- Categorisation of apps according to whether they are used by consumers or healthcare professionals has advantages, and regulation could focus on those clearly intended for healthcare use, drawing on criteria such as those adopted by the MHRA. However, the distinction is not always clear-cut, and some 'general' apps may be taken up and used within the medical sector. The reliability of results will be of paramount importance in healthcare use, but is also important to consumers making lifestyle or other decisions affecting their health. Risk assessment, the potential for apps to have harmful impact, could also be a good basis for regulating apps not covered by current legislation. This would include apps intended by the manufacturer for non-medical purposes.

Vigilance and monitoring

- As well as market authorisation, vigilance was raised as an issue. Only a handful of app-related incidents have been reported to the MHRA. The MHRA may not have the resources to police the entire app ecosystem effectively. Researchers or users of apps who identify examples of harm may not be aware of the reporting options available to them.
- NHS patient safety mechanisms provide an additional route through which problems with apps can be highlighted. While it may not always be clear if products fall under the MHRA remit, patient safety encompasses all areas of healthcare, so would equally apply to apps. NHS England could be alerted to potential problems and issue patient safety notices. The MHRA and NHS England should liaise in this area and closer working may be advantageous.

Obstacles to app use and promoting app uptake

- It is unclear what the consequences would be, were health app use to lead to patient harm in the health service. GPs are held accountable for their prescribing decisions, but it is not clear if app developers would be liable. This situation may make GPs reluctant to recommend apps to patients. Greater legal clarity would be helpful.

⁷ For examples of apps that have successfully navigated regulatory pathways in the UK and the USA, please see the case study presentations on pages 23-25.

- It may be beneficial to consider how uptake of innovative technologies, including apps, could be promoted within the NHS, perhaps initially through specific local initiatives.
- It may be necessary to develop incentives to encourage more development of medically useful apps.
- Some form of 'traffic light' system might be helpful to guide clinicians, based on how well an app meets a set of defined criteria.
- More education of healthcare professionals and the public about apps and their use might be beneficial, to promote more appropriate usage. However, the experience from other industries is that it is unrealistic to expect consumers to adapt to the product – product developers have to work with consumers' known behaviour.

Generating and evaluating the evidence of clinical utility

- To promote increased use of apps with appropriate evidence of effectiveness and/or clinical utility, there is potential for NICE to play a greater role in their review; although it cannot mandate their use, NICE could encourage greater take up or recommend their use in clinical guidelines.⁸ However, NICE would probably require additional funding to carry out this role. Although their roles are distinct, closer liaison between the MHRA and NICE could be advantageous in this area.
- It would be useful for guidance to be available on how clinical investigations and other studies should be carried out in order to generate appropriate evidence for NICE.
- It may be necessary to provide funding to support clinical investigations and other studies to generate evidence, particularly of apps from small developers. There are currently few incentives for developers to carry out such trials.
- It may also be helpful to develop research expertise in the assessment of health apps and to develop more centres specialising in their evaluation.
- Particularly for apps used in healthcare, more systematic appraisal would be helpful. There are groups already working on a systematic framework for assessing the evidence associated with health apps.⁹

The role of app aggregation services

- App aggregation services – for example, app stores and libraries - have a potentially important role to play in quality assurance, complementing formal regulation.¹⁰ App registries might also be useful. Many organisations act as 'gatekeepers' to particular communities and could take a lead in evaluating apps and providing guidance to professionals or lay consumers. Bodies such as Royal Colleges could do more in this area, but other organisations could take on the role of 'app-curation' to wider audiences or develop 'boutique' app stores in focused areas.

⁸ Please see Dr Dillon's presentation entitled 'NICE: evaluating the cost of healthcare apps' on pages 21-22 for further details.

⁹ Lewis TL & Wyatt JC (2014). *mHealth and Mobile Medical Apps: A Framework to Assess Risk and Promote Safer Use*. Journal of Medical Internet Research **16 (9)**, e210. <http://www.jmir.org/2014/9/e210/>

¹⁰ Please see Dr Baker and Mr Singh's presentation, 'NHS health apps: evaluating the safety of healthcare apps', on page 21 and Dr Wyke's presentation, 'myhealthapps: patient endorsement of healthcare apps', on pages 22-23 for further information.

- App stores are crucial parts of the health app landscape, and have the potential to be more involved in quality assurance and ensuring that hazardous health apps are revoked or disabled once identified as such. Some form of peer review could be considered for health apps, or rankings could be adjusted to reflect 'quality marks', such as endorsement by learned societies or professional bodies, or clear signposting of CE-marking and/or regulatory approval. However, the owners of app stores may feel that they are working well and may be reluctant to adapt a well-tried model, or to instigate a separate model specifically for health apps. The sheer numbers of apps submitted to app stores might also present issues for more rigorous assessment.

Software development practices

- A lack of involvement of medical professionals in the development of apps, including those used by healthcare professionals, is a cause for concern. An industry code of conduct, developed by EUCOMED¹¹ across Europe or the Association of British Healthcare Industries (ABHI) for the UK, could be considered to encourage adoption of best practice.
- The customer support available for apps may also be important. For sustainable use, app developers need to consider issues such as user training and customer support as well as technical functionality.
- There is currently a mismatch between regulatory mechanisms and software development practice. App development is extremely rapid. Regulatory approvals may take months, while formal research-based evaluations may take years.
- The industry is also relatively young, and many developers do not have experience in interacting with regulators.
- Software development is often also based on beta-testing and post-launch debugging with frequent upgrades. However, conformity with medical device standards is subject to specific operating systems and is invalidated on upgrade. Furthermore, innovative 'agile' systems of software development may not necessarily be compatible with the more formal approach of industry standards or in the context of ensuring patient safety. Indeed, software and devices will have to be designed and built to 'enable privacy by design' under the impending Data Protection Regulation.
- Although lessons could be learned from the established engineering industries, the degree to which their high-integrity approaches could be adapted to health apps was queried.¹² The industries are mature with well-established practices; they have a strong emphasis on safety and there are powerful commercial reasons for maintaining high standards. Health app development, by contrast, is an immature field dominated by mostly small players. Nonetheless, some delegates thought that, in time, and with some innovation, specific health app assurance approaches could be developed that were appropriate for the technology used in health apps and the differing safety significance of the applications.
- Although regulation can be seen as an obstacle to rapid product development, an effective regulatory framework can help to drive up standards and the quality of products.

¹¹ EUCOMED represents the medical technology industry in Europe.

¹² Please see Session 2 presentations on pages 25-28 for further information.

Appendix I Programme

Wednesday 19 November 2014 at the Academy of Medical Sciences

09.30	Registration
Welcome and Background	
09.55	Welcome and introduction Dr Martyn Thomas CBE FEng, Non-Executive Director, Health and Safety Executive
Session 1 – Regulation and oversight of health apps Chair: Dr Martyn Thomas CBE FEng	
10.00	Health apps: the US and EU regulatory regimes Mr Julian Hitchcock, Counsel, Lawford Davies Denoon
10.15	NHS Health Apps: evaluating safety of healthcare apps Dr Maureen Baker CBE, Chair of Council, Royal College of General Practitioners
10.30	NICE: evaluating cost-effectiveness of healthcare apps Dr Bernice Dillon, Technical Adviser – Medical Technologies Evaluation Programme, NICE
10.45	Myhealthapps: patient endorsement of healthcare apps Dr Alex Wyke, Chief Executive, PatientView
11.00	Q&A
11.10	Tea/coffee break
11.25	Case study – Mersey Burns App: developing a CE-marked healthcare app Mr Rowan Pritchard-Jones, Consultant Plastic Surgeon, St Helens and Knowsley NHS Trust
11.40	Case study – BlueStar: world's first FDA-approved Mobile Prescription Therapy Mr Ryan Sysko, Chief Executive Officer, WellDoc
11.55	Discussion: <ul style="list-style-type: none"> • What are the key challenges with, and gaps in, current regulatory/oversight mechanisms? • What are the appropriate evidentiary requirements to validate safety and efficacy? How should these be obtained? • What are the ideal regulatory/oversight mechanisms for health 'apps'? How can these be achieved?
12.55	Feedback
13.15	Lunch
Session 2 - Regulatory systems and standards for other software Chair: Professor Lionel Tarassenko CBE FEng FMedSci	
14.00	Regulation and oversight for developing embedded medical software Dr Chris Elliott FEng, Director, Léman Micro Devices SA
14.15	Regulation and oversight for developing software for the nuclear industry Professor Robin Bloomfield FEng, Professor of System and Software Dependability, City University, London
14.30	Regulation and oversight for developing automotive software Dr Michael Ellims, Director, Sybernetic Limited
14.45	Overview of the conclusions from the US National Academies of Sciences

	report, <i>Software for Dependable Systems – Sufficient Evidence?</i> ¹³ Dr Martyn Thomas CBE FEng, Non-Executive Director, Health and Safety Executive
15.00	Tea/coffee break
15.15	Discussion: <ul style="list-style-type: none"> • Can lessons be learnt from the regulation and oversight of other types of software? If so, how can these be applied? • In light of these experiences, have your views on the ideal regulatory/oversight mechanisms for health ‘apps’ changed?
16.05	Feedback
16.25	Conclusions Professor Lionel Tarassenko CBE FEng FMedSci, Head, Department of Engineering Science, University of Oxford
16.30	Close

¹³ National Research Council of the National Academies (2007). *Software for Dependable Systems: Sufficient Evidence?* The National Academies Press. Washington, DC.
<http://www.nap.edu/catalog/11923/software-for-dependable-systems-sufficient-evidence>

Appendix II Symposium delegates

Dr Maureen Baker CBE, Chair of Council, Royal College of General Practitioners

Mr Mark Bartlett, Managing Director, Geneix

Mr Nimish Bhatt, Business Development Manager – UK, Uniquedoc

Ms Jessica Bland, Senior Researcher, Technology Futures, NESTA

Professor Robin Bloomfield FEng, Professor of System and Software Dependability, City University, London

Dr Richard Brady, Specialty Registrar Colorectal Surgery, Edinburgh

Ms Julie Bretland, Director, Our Mobile Health Ltd

Mr Robert Chesters, Innovation Lead, NHS England

Dr Andre Chow, Co-founder and Chief Operating Officer, Touch Surgery

Dr Bernice Dillon, Technical Adviser - Medical Technologies Evaluation Programme, NICE

Dr Michael Ellims, Director, Sybernetic Limited

Dr Chris Elliott FEng, Director, Leman Micro Devices SA

Ms Valerie Field, Head of Unit, MHRA

Mr David Grainger, Senior Medical Devices Specialist, MHRA

Mr Julian Hitchcock, Counsel, Lawford Davies Denoon

Mr Sejal Jiwan, Technology Manager, Faculty of Medicine, Department of Surgery and Cancer, Imperial College London

Professor Jonathan Kay, Clinical Informatics Director, NHS England and Professor of Health Informatics, City University London

Professor Sanjeev Krishna FMedSci, Professor of Molecular Parasitology and Medicine, St George's University of London

Mr Charles Lowe, President, Telemedicine & eHealth Section, Royal Society of Medicine

Mr Mohammad Mobasher, Clinical Research Fellow and Surgical Registrar, Imperial College London

Dr Omer Moghraby, Partner, Psychiatry-UK

Professor Mike O'Reilly, Vice President Medical Technology, Apple

Dr Ashish Patel, Clinical Technology Director, Babylon

Mr Jaymeen Patel, Senior Government Affairs Manager, EMEIA, Apple

Mr Rowan Pritchard-Jones, Consultant Plastic Surgeon, St Helens and Knowsley NHS Trust

Mr Ryan Sysko, Chief Executive Officer, WellDoc

Professor Lionel Tarassenko CBE FEng FMedSci (Chair session 2), Head, Department of Engineering Science, University of Oxford

Dr Martyn Thomas CBE FEng (Chair session 1), Non-Executive Director, Health and Safety Executive

Professor Robert Walton, Clinical Professor of Primary Medical Care, Bart's and The London School of Medicine and Dentistry

Mr Francis White, EU General Manager, Alivacor UK

Professor Jeremy Wyatt, Leadership Chair in eHealth Research (Health Informatics) and Director of the Yorkshire Centre for Health, Leeds Institute of Health Sciences

Dr Alexandra Wyke, Chief Executive, PatientView

Secretariat

Dr Claire Cope, Policy Officer, Academy of Medical Sciences

Mr Ian Jones, Medical Writer

Ms Philippa Shelton, Policy Advisor, Royal Academy of Engineering

Dr Rachel Richardson, Policy Intern, Academy of Medical Sciences

Dr Naho Yamazaki, Head of Policy, Academy of Medical Sciences

Appendix III Summary of presentations

Session 1: Regulation and oversight of health apps

Health apps: the US and EU regulatory regimes

Mr Julian Hitchcock, Counsel, Lawford Davies Denoon

Introducing the current regulatory framework, Mr Hitchcock highlighted the complexity of systems and a lack of clarity in the USA and Europe, as well as the considerable state of legislative flux.

In the USA, the key regulator is the Food and Drug Administration (FDA), which classifies medical devices (including software) according to three levels of risk. Intended use in a medical context is a key criterion, and general health and lifestyle apps typically fall outside of its remit. The FDA issued guidance in 2013 which included the potential to apply discretion in regulation, but it is unclear when this discretion is likely to be exercised – potentially problematic when the default classification, class III, presents particularly onerous responsibilities on manufacturers to demonstrate safety and efficacy.¹⁴

The ‘Sensible Oversight for Technology which Advances Regulatory Efficiency Act’ of 2013 (the SOFTWARE Act), introduced into the House of Representatives, and the ‘Preventing Regulatory Overreach to Enhance Care Technology Act’ of 2014 (the PROTECT Act), introduced into the US Senate, would each, if enacted, significantly curtail the FDA’s regulatory role in this area.^{15,16}

In Europe, no specific legislation has been developed for health apps, but numerous EU statutes apply. These include the Medical Devices Directive, and the Active Implantable Medical Devices and In Vitro Diagnostic (IVD) Medical Devices Directives (where the app is deemed to be an ‘accessory’), and the Data Protection Directive. To add complexity, all these Directives are scheduled for replacement by EU Regulations. Unlike Directives, EU Regulations apply directly in each EU Member State, bypassing national legislatures. These are the Data Protection Regulation, Medical Devices Regulation and IVD Medical Devices Regulation. Each has cleared the European Parliamentary stage, but debate continues within the Council of the European Union over the extent of these new instruments, which extend and deepen regulatory obligations and will have considerable relevance to the regulation of mobile apps. It is not certain when the various Regulations will come into effect; possibly in 2019.¹⁷

A key question is whether an app or other standalone software counts as a ‘medical device’ for the purposes of the EU regulatory regime. If it does, it may only be placed on

¹⁴ <http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf>

¹⁵ SOFTWARE Act of 2013. http://blackburn.house.gov/uploadedfiles/hr_3303_bill_text.pdf

¹⁶ PROTECT Act of 2014. http://www.fischer.senate.gov/public/_cache/files/7b25f3a3-2d8b-4638-aba9-b12cc68fde0d/tam14031.pdf

¹⁷ See <http://medicaldeviceslegal.com> for updates.

the market in Europe if it bears a CE-mark to declare its conformity with specific EU regulatory requirements.¹⁸

Software in its own right can be considered a 'medical device', with intended use in a medical context again a critical principle. The definition plainly captures many apps: '*software... intended by the manufacturer to be used for human beings for the purpose of:*

- *diagnosis, prevention, monitoring, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*
- *investigation, replacement or modification of the anatomy or of a physiological process,*
- *control of conception....'*

Software falling outside of this definition will nevertheless be regulated as a 'medical device' if it is intended by its developer to be used as an 'accessory' to one or more medical devices; i.e. to enable something that *is* a 'medical device' to be used as its manufacturer intended. Many apps may, therefore, be classified as accessories. The 'medical devices' they serve, wherever located, will fall under the same EU legislative regime.

Apps designed specifically for use in healthcare typically fall within categories requiring evidence of safety, including in many cases clinical investigations, prior to CE-marking. Guidance published by the MHRA helps developers judge whether their apps are likely to be classified as medical devices and suggests likely risk classifications.¹⁹ However, in contrast to the US position, developers do not file applications with the regulator. Instead, applicants either self-certify the conformity of the devices they intend to market, in the case of Class I devices, or obtain certification from an independent 'notified body'. Class I manufacturers must also register with the MHRA.

Data protection and personal privacy are also highly legislated in the EU and beyond. Safeguarding personal data and consent for data processing must therefore be a high priority for developers, given the potential for large fines (up to 5% of worldwide turnover is suggested in amendments to the proposed EU Data Protection Regulation) for organisations found to be in breach of data protection regulations.²⁰ Regulation relating to management and processing of personal data, including genetic data, is the subject of debate within the Council of the EU, with legislation imminent. It has significant implications for app developers.

Interpretation of the legislation surrounding IVD medical devices adds further complexity. For example, software developed to support bioinformatic processing of information generated by use of IVD devices could be considered to fall within the remit of such legislation. Potentially, this could prevent such apps from being made publicly available (since such devices should not be marketed directly to consumers). The international

¹⁸ There is an exemption for devices manufactured in-house, which would extend throughout an NHS institution.

¹⁹ <https://www.gov.uk/government/publications/medical-devices-software-applications-apps/medical-device-stand-alone-software-including-apps>

²⁰ The original proposal of 2%, which may be agreed by the Council, is still significant.

context, under which apps operate through international networks with remote processing systems and databases, presents a further challenge.

NHS health apps: evaluating safety of healthcare apps

Dr Maureen Baker, Royal College of General Practitioners and Inderjit Singh, NHS England

As well as formal regulatory regimes such as those managed by the MHRA, professional bodies can add a layer of oversight by independently evaluating health apps. In a presentation developed with Inderjit Singh of NHS England, Dr Baker described work examining the safety of apps in the NHS Health Apps Library on the NHS Choices website.²¹

The key question, Dr Baker suggested, was whether patients could be harmed if anything went wrong with an app. With the current deluge of apps, the NHS 'brand' has a potentially important role to play in signposting users to safe, high-quality resources.

Drawing on the principles adopted for ensuring safety in health IT systems, Dr Baker and colleagues have developed the world's first process for assessing the safety of health apps. An app submission process has been developed, which begins with an initial triage to assess safety implications, carried out by clinicians and software safety engineers.

Apps identified as medical devices – a categorisation that is not always easy to make – are directed to the MHRA. Other submissions are then assessed to see whether the ISB0129 safety standard applies. If so, manufacturers are required to carry out a risk analysis, examining questions such as how the app might go wrong, how often, and how the impact of errors would be mitigated.

Of 246 submissions to date, 174 have gone through safety assessment. In 150 of these cases, ISB0129 was not applicable, while 24 apps were found to be ISB0129-compliant. Close liaison with developers has helped to ensure that no apps have yet had to be rejected. While the emphasis to date has been on safety, there are hopes that quality and usefulness can also be addressed, for example through an NHS kite-marking scheme, as announced in November 2014.²²

NICE: evaluating cost-effectiveness of healthcare apps

Dr Bernice Dillon, Technical Adviser, Medical Technologies Evaluation Programme, NICE

For app use within the healthcare sector, NICE has a role to help promote NHS adoption by issuing of NICE guidance, which highlights the clinical and cost-effectiveness of the technology.

NICE has established relatively new systems for medical devices, which can be assessed under the Medical Technologies Evaluation Programme or the Diagnostics Assessment Programme.^{23,24} Some apps would not need evaluation by NICE, because they perform an

²¹ <http://apps.nhs.uk/>

²² <http://www.england.nhs.uk/2014/11/13/leaders-transform/>

²³ <http://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-medical-technologies-evaluation-programme>

existing task; for example, transmitting test results more simply and efficiently. NICE would only consider apps categorised as medical devices, but has not yet undertaken any such evaluations.

NICE concentrates on the information needs of decision-makers, particularly evidence of clinical efficacy and health economic impact. Assessment of medical devices follows the same principles, although the evidence base is generally less extensive.

NICE has established mechanisms to decide whether technologies are appropriate for it to consider, and which of its programmes would be most appropriate. In the Medical Technologies Evaluation Programme, key issues for an evaluation include whether the performance matches manufacturers' claims, how a device would impact on patient care pathways, and what its economic impact might be. A relatively simple health economic analysis is carried out, based on the potential for cost savings or for more patient benefits to be delivered at the same cost. In recognition of the rapidly evolving nature of technologies, the Programme has been designed to have relatively quick timelines (10 weeks for selection and routing, 38 weeks for guidance development).

These systematic evaluations, currently only of single technologies (rather than comparisons of different products), are considered by the Medical Technologies Advisory Committee in the development of NICE medical technologies guidance. The Programme can also highlight where additional research is required, and provides advice on implementation of recommended devices.

myhealthapps: patient endorsement of healthcare apps

Dr Alex Wyke, Chief Executive, PatientView

With the numbers of health apps available running into the hundreds of thousands, and dozens of new apps appearing each week, regulatory bodies can in reality assess only a tiny proportion. However, suggested Dr Wyke, there is potential for patients and consumers to step into this breach and provide feedback to enable users to make more informed choices, thereby providing a form of quality assurance. This is the principle of the myhealthapps library.²⁵

Dr Wyke made the point that the voice of patients and consumers is often neglected, yet they can play an important role, having direct experience of health conditions and the value of tools to support the management of their condition. High-quality apps have the potential to improve quality of life for patients, because, in principle, they empower patients to improve their self-management and care, which also should reduce demand on healthcare professionals.

In the myhealthapps approach, apps are nominated by patient groups. These apps are subsequently assessed to give users an indication of their provenance (such as sources of funding), costs, technical specifications and CE-marking. The site operates a grading

²⁴ <http://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-diagnostics-guidance>

²⁵ <http://myhealthapps.net/>

system based on five criteria of importance to users, including the app's trustworthiness, ease of use and whether it enables users to manage their condition. myhelathapps seeks to represent a visually straightforward way for users to assess and compare apps, as well as identify apps of use to their own personal situation with ease. But the greatest value comes from the feedback left by users.

As at November 2014, the site had more than 400 apps and 8,000 returning visitors. A social media campaign is being planned to drive up usage, and Dr Wyke's organisation is also involved in multiple joint ventures to promote high-quality health app development reflecting patients' needs.

Case study – Mersey Burns App: developing a CE-marked healthcare app

Mr Rowan Pritchard-Jones, Consultant Plastic Surgeon, St Helens and Knowsley NHS Trust

Given the time and effort involved, developers may be reluctant to engage with regulatory pathways. However, argued Mr Pritchard-Jones, it is possible to use regulatory systems as a framework for quality assurance.

Mr Pritchard-Jones has first-hand experience of such systems, having developed the Mersey Burns App and shepherded it through the MHRA approval process.²⁶ The app is designed to support the initial assessment of burns patients by non-specialist clinicians. As with all trauma, early critical assessment is essential – particularly during the first 'golden hour'.

Traditionally, the first stage of assessment involves completion of a so-called Lund and Browder chart, to indicate which areas of the body, and hence what percentage of the body surface, have been affected.²⁷ This is then used as a guide to fluid resuscitation. Both the initial assessment of body coverage and decisions on fluid resuscitation require clinicians to make a series of calculations – 19 in all.

The Mersey Burns App enables clinicians to illustrate graphically the areas of the body affected, with the software calculating the resulting surface area affected on the basis of factors such as sex and age, which are inputted by clinicians. The software also handles the calculations underlying fluid resuscitation. It provides a bundled report that is sent directly to specialists who will subsequently be handling the patient, enhancing continuity of care.

Mr Pritchard-Jones and his team have carried out various studies to validate the tool, using burns simulations. When tested, the software-generated answers closely matched those produced by traditional methods. In addition, the variation in the app-generated answers was much lower than those calculated with just pen and paper. It was also quicker to use and positively received by testers, including medical students.

²⁶ <http://www.merseyburns.com/>

²⁷ Hettiaratchy S & Papini R (2004). *Initial management of a major burn: II—assessment and resuscitation*. *BMJ*. **329**, 101-103.

These data formed part of the clinical data file submitted to the MHRA. Very careful attention had to be paid to the risk of malfunction, leading to the programming of a failsafe – the software checks its own function and will not operate if it detects a problem.

The app clearly fulfilled medical device criteria and, according to Mr Pritchard-Jones, the regulatory framework was an opportunity to be embraced. However, the app's financial model may not be typical – it was developed to support healthcare rather than as a commercial product, and relied on many people working in their spare time. It also benefited from a supportive NHS Trust which, importantly, picked up responsibility for liability (in exchange for intellectual property rights), without which development would have been highly problematic.

Case study – BlueStar: world's first FDA-approved mobile prescription therapy

Mr Ryan Sysko, Chief Executive Officer, Welldoc

A second example of software that has successfully navigated regulatory pathways, this time in the USA, was described by Mr Sysko, whose company has developed a software tool to support management of type 2 diabetes.

The company's product, BlueStar, is described as a 'mobile prescription therapy', emphasising the point that, conceptually, it can be considered equivalent to a drug treatment.²⁸

The clinical need it is addressing is the long-term management of type 2 diabetes, which calls for constant monitoring of blood glucose levels by patients and regular (generally quarterly) consultations with physicians. BlueStar has been developed to provide patients with more user-friendly feedback and self-management guidance to support their care outside of the physician's office. It also supplies physicians with analysed data to support more effective treatment decisions for patients during consultations.

Again clearly a medical device, the company sought and received FDA clearance, a process that took 3.5 years. However, in large part, this reflected the novelty of the application (and the company's lack of prior experience in seeking regulatory approval). The company was able to provide data from randomised controlled clinical trials demonstrating a beneficial impact on glycaemic control and a reduction in the number of hospitalisations.

Notably, the company was able to gain not only FDA clearance (primarily addressing safety) but also agreement for reimbursement from payers – in the USA, the key step in ensuring that a treatment will be used. Mr Sysko noted that the latter is an endorsement of the product's cost-effectiveness.

The product is treated like a pharmaceutical: it is prescribed by physicians and dispensed through a pharmacy, and the company provides training for physicians and patients as well as customer support. The American Diabetes Association recognised it as an entirely new class of product.

²⁸ <https://www.bluestardiabetes.com/>

Mr Sysko stressed that, although the clearance proposal had been lengthy, interactions with the FDA had been constructive, and that much of the delay related to the fact that they were breaking new ground. For example, there was a need to agree how regular software upgrades would be handled. Future applications, he suggested, could be handled more rapidly.

Session 2: Regulatory systems and standards for other software

Regulation and oversight for developing embedded medical software

Dr Chris Elliott FEng, Director, Léman Micro Devices SA

The second half of the meeting focused on whether health app development could learn lessons from software development in traditional engineering disciplines. Dr Elliott's presentation provided a bridge between morning and afternoon sessions, as he described a hybrid device – the Smartphone Vital Signs System – that integrates novel hardware, embedded software, a smartphone app and remote server software. Although clearly in the health app territory, this product has been developed through an approach rooted in conventional engineering principles.

The tool is designed to measure a range of physiological parameters such as heart rate and blood pressure, using a novel component that would be permanently attached to a smartphone when it is manufactured. It depends on software embedded in the smartphone and a downloadable app, as well as server-side software. Although intended for use by consumers, it is clearly a medical device – indeed, the hardware, app and embedded software are each classified as medical devices (the server software may be too), but it is possible that with the right electrical, software and contractual interfaces the phone itself would not be.

Dr Elliott pointed to the complex regulatory environment his company has to navigate – each country it would like to operate in has different systems. He also made the important point that, in this context, it was impossible to disentangle safety and efficacy. Since consumers may act upon the results they receive, safety can only be assured if they receive accurate information. The company will run a clinical trial to provide evidence of safety by demonstrating efficacy.²⁹

Because the device is intended for general consumers, regulators stress the importance of usability. Other key development parameters include security (ensuring the software cannot be hacked), function (stability of software, management of upgrades) and vigilance (mechanisms for reporting of problems).

Borrowing from engineering, the key principle in achieving these goals has been to identify and meet relevant standards – of which there are many, in addition to FDA guidance. Work to meet standards is embedded within a general quality management framework compliant with ISO13485.

²⁹ <http://clinicaltrials.gov/show/NCT02199457>

One particular challenge was the adoption of ‘agile’ software development – a more flexible and dynamic approach than conventional software development. This could present issues with accreditation. In practice, auditors have taken a supportive and flexible approach, recognising that the principles of standards have been achieved, even if the mechanisms have not been those traditionally applied.

Regulation and oversight for developing software for the nuclear industry

Professor Robin Bloomfield, Professor of System and Software Dependability, City University London

Given its enormous potential to cause harm, safety is paramount within the nuclear industry. Professor Bloomfield described the principles underpinning the design and assurance of ‘trustworthy’ computer systems within this industry.

Although the nuclear industry might seem very different from health apps, Professor Bloomfield pointed out that medical devices have the potential to cause harm, and have been associated with numerous avoidable deaths.

The regulatory regime in the nuclear industry places the onus on license holders to develop and document a safety strategy and plan. This is based on well-understood safety assessment principles, focusing in particular on a systematic approach to safety assessment and ‘defence in-depth’.³⁰ For software, there is a commitment to excellence in implementation and application of independent confidence-building measures such as static analysis and statistical testing. There is a fundamental responsibility to understand the risks and to put systems in place to mitigate or respond to any eventualities.

Professor Bloomfield emphasised the importance of assuring systems, for example by linking claims about performance to arguments and inferences, and thence to evidence. ‘Challenge and response’ cycles can also be an important way to test and enhance systems, and build confidence that systems are operating optimally.

These safety assessment principles defined by the regulator permeate the whole industry. These principles are not prescriptive and do not specify exactly what should be done, but provide a critical framework for clarifying what issues should be thought about, and how they should be thought about.

Regulation and oversight for developing automotive software

Dr Michael Ellims, Director, Sybernetic Ltd

Many lives depend on safety in the automotive industry. As Dr Ellims pointed out, minimising the numbers of people killed on the world’s roads each year is a central aim of the industry, manifest in a strong global regulatory framework.

³⁰ ‘Defence in-depth’ is an information assurance concept in which multiple layers of security controls are placed throughout an IT system.

The regulatory framework applies to mass production vehicles, and is in place to ensure that manufacturers are consistently able to produce vehicles to the same quality standards. Manufacturers aim to achieve 'type approval' for each model, which covers conformity of production facilities, approval of test facilities and conformance to regulation. Type approval is bestowed by competent national authorities; in the UK's case, the Vehicle Certification Agency.

Extensive global regulatory guidelines apply to the automotive industry, including 133 United Nations Economic Commission for Europe (UNECE) regulations (dating back to 1958) and 15 United Nations Global Technical Regulations (UN GTR) regulations from 1998. Software regulation is part of multiple regulations, particularly a series of annexes related to the safety of complex vehicle control systems. Although they are short, Dr Ellims suggested that considerable work was needed to satisfy the conditions of these annexes. They require that manufacturers have a clear safety concept, and have considered what happens to vehicles under both non-fault and fault conditions. The key principle, he suggested, was that manufacturers had a deep understanding of their systems and how they were operating, and hence had carried out a safety analysis and had been able to verify it.

Although the framework has its drawbacks, including the fact that it applies to entire vehicles and does not require 'deep dives' to test software, Dr Ellims suggested it was effective. Indeed, he added, company's internal systems were often even more strict than international regulations mandated. In part, this reflects the importance to the brand of being perceived as safe, plus the enormous costs associated with recall of vehicles to correct errors.

***Overview of the conclusions of the US National Academies Report, Software for Dependable Systems: Sufficient Evidence?*²³**

Dr Martyn Thomas FREng, Non-Executive Director, Health and Safety Executive

Software engineering, Dr Thomas suggested, showed one key difference from other engineering disciplines – it was less effective at learning lessons from the past. This shortcoming was the impetus for an important publication produced by the US National Academies, *Software for Dependable Systems: Sufficient Evidence?*, which aims to provide a coherent intellectual framework for software engineering projects.³¹

In order to develop 'certifiably dependable software', Dr Thomas suggested that three conditions must be met: explicit claims should be articulated; the evidence for those claims should be provided; and expertise must be demonstrated to support the reliability of evidence.

In reality, absolute dependability under all circumstances cannot be guaranteed, so it is important to clarify what the limits of dependability are – under what circumstances can developers be sure their software will operate and what confidence do they have in these

³¹ National Research Council of the National Academies (2007). *Software for Dependable Systems: Sufficient Evidence?* The National Academies Press. Washington, DC.
<http://www.nap.edu/catalog/11923/software-for-dependable-systems-sufficient-evidence>

predictions? What assumptions have been made? It may also be necessary to make different predictions for different aspects of operation, such as security and performance.

Evidence is essential for substantiating claims. Most evidence is generated by testing, but the range of situations that can be assessed in this way can be limited. A more comprehensive approach is to generate evidence by analysis, and standard tools are available to analyse systems that have been developed according to rigorous software engineering methods.

The third strand, expertise, is also critical. Software engineers must have an intimate understanding of the domain they are working in, but also of the wider systems in which it is embedded; indeed, software must work dependably with other software, hardware and, crucially, the users. There is much merit in keeping systems as simple as possible and adhering to standard practices unless there is a very good reason not to.

In conclusion, Dr Thomas hoped that following the principles outlined in the National Academies' publication would improve the quality of software engineering and ensure more lessons from the past were learned. The outcomes would be beneficial to software engineers in the long run, as debugging programs is a major cost in software development.



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