Medicines and Healthcare products Regulatory Agency

24 April 2017

Update on Pharmacovigilance Projects

Purpose:
This paper provides the Board with an update on activities with a number of ongoing projects in the pharmacovigilance area.

Summary

There are a number of projects ongoing to strengthen the agency's pharmacovigilance activities. These include the Patient Safety and Vigilance Strategy (PSVS) that aims to better align the way vigilance is conducted on medicines and devices, PSVS is a key strategic priority for the agency. Alongside this VRMM are engaged in a broader set of activities to expand Yellow Card reporting from healthcare professionals and the public, and how we review signals using new tools to visualize data.
The overarching aim of all of the activities covered in this paper is to protect public health through a strong pharmacovigilance system that is embedded within the NHS and has open access to all.

Patient Safety and Vigilance Strategy
CET were updated on activities with the Patient Safety and Vigilance Strategy which is now in delivery phase. Good progress is being made, particularly on signal detection methodologies for medical devices using the same tools as for medicines. Work continues on aligning safety assessment methodologies and processes. A health summit with key stakeholders who send and receive safety communications is being planned to improve how we develop alerts and target health professionals.

Adverse Drug Reaction reporting
Adverse Drug Reaction (ADR) reporting continues to rise, in 2016 we received 42,791 ADR reports, and increase of 8% on 2015. Patient reporting rose by 23%. In January the Vision General Practice clinical system started to roll out electronic Yellow Card reporting, we continue to have discussions with the majority supplier EMIS around a similar roll-out in their systems. A business case is being developed to carry out a sustained campaign to raise awareness of, and encourage reporting to the Scheme. There will be a particular focus on patients and members of the public in this.

Harms from overdose (Poisons data)
Work is progressing with the National Poisons Information Service on obtaining a data feed from the UK Poisons Information Documents (UKPID) on cases where harm has occurred from an overdose of a medicinal product. After a period of negotiation including the signing a of non-disclosure agreement and contracting with a technical provider to analyse the data we have now received 2 years of data (2015/16) to initiate the pilot.

New Psychoactive Substances
We have been working with Public Health England to introduce a reporting system for these illicit drugs, formerly known as "legal highs". The system which has similar functionality to the Yellow Card web-form went live in March with a press release and other communications to raise awareness.

Integrating case reports with electronic health records
VRMM are working with CPRD to routinely and simply visualise drug/event pairs over time in the Clinical Practice Research Datalink. The intention is to support signal assessment by reviewing the occurrence of medical events before and after first prescription. A pilot exercise has taken place and the results were positive. A business case to explore how improvements to the tool could increase its value and to introduce this into our routine work is being developed.

Access for the public to information
Interactive Drug Analysis Profiles, i-DAPs went live in September 2016. These replaced the old Drug Analysis Prints with an interactive view of ADR data.

Strengthening Collaborations to Operate Pharmacovigilance in Europe
The SCOPE (Strengthening Collaborations to Operate Pharmacovigilance in Europe) Joint Action comes to completion at the end of April 2017. All deliverables have been published and a final stakeholder meeting was held to inform industry, patient organisations and health professionals of these. The deliverables will form part of the EU pharmacovigilance curriculum and will be housed the EMA EU Network Training Centre, this will help ensure the sustainability of the materials beyond SCOPE's lifetime.

Innovative Medicines Initiative project
The IMI (Innovative Medicines Initiative) WEB-RADR project completes in September 2017. The two workstreams are (i) mobile technologies for reporting and accessing ADR data and (ii) understanding the usefulness of social media data for pharmacovigilance. The recommendations from each workstream are being finalised. A further "exploitation" project is planned to ensure sustainability of the App beyond the lifetime of the project.

Resource implications:
All projects have been resourced within the VRMM Division with the exception of Patient Safety and Vigilance Strategy which is a cross agency project.
Technical providers have been funded through agreed business cases.
Public Health England are funding the work on new psychoactive substances.
SCOPE and WEB-RADR are funded through the European Commission/IMI

Timings:
N/A

Action required by The Board:
The Board is invited to comment on the updates provided.

Links:
VRMM

Author(s): Mick Foy

FOI/publication issues:
None

Can paper be published on INsite? (List any deletions required) Yes

CET sponsors: June Raine,

Update on Pharmacovigilance Projects

As a public health agency MHRA are committed to the continuous improvement of our safety surveillance systems. In pharmacovigilance there are a number of initiatives to improve not only the reporting of suspected adverse drug reactions via the Yellow Card Scheme but also and how we handle the large volumes of data we have and communicate with our external stakeholders. VRMM Division are engaged in a number of innovative projects to improve pharmacovigilance and patient safety. These cover not only how we conduct our activities within the agency but also how we engage with and share information with stakeholders.
The SCOPE Joint Action and WEB-RADR project seek to deliver lasting tools and guidance to other national pharmacovigilance centres and other involved in pharmacovigilance activities.

This paper provides the Board with an update on progress on eight of the main projects

Patient Safety and Vigilance Strategy

The Board have previously had updates on PSVS in September 2015 and February 2016. We are now in the delivery phase and the various deliverables were agreed at the March CET meeting (full paper attached at Annex 1). CET also agreed the resourcing of strategy and an amended programme management arrangement.
In summary the main deliverables are:

Project Team 1 – ADR reporting and Signal Management

Deliverable	Progress	Delivery Date
Delivery of mobile reporting for medicines (adverse reactions, counterfeits and defectives	We have started discussions with GDS about our overall strategy; this is to get early buy-in and collaborative working between ourselves and GDS as we move towards delivery. The initial plan to simply update the existing Yellow Card App is not the preferred option so a re-platforming of the Yellow Card system to mobile responsive pages whilst being the correct technical solution has added delay to the roll out. The delivery of mobile reporting for medical devices is being done as part of the Operational Transformation, with the ongoing Devices Transformation project, and therefore is out of scope for this work.	Q1 18/19 (indicative potential date, as there are still a number of decisions to be made which will impact the timelines)
Device Information Standard for Incident reporting	Work has started on the core elements of the standard. This will be discussed in the EU and international environments for wider adoption although the option to act independently for the UK is our fall-back position	Target delivery date as NHS Digital Standard Q1, 2018
Implement a formalised signal detection methodology for devices	Data security issues have been resolved and work is now progressing with regards to developing signal detection methodologies for Devices. These prototype methods will be tested against	CI investigations to be completed May 2017. Implementation into devices

	existing signals to evaluate their accuracy. A report from CI is expected in May 2017.	operations to be determined following report review
Investigate a common signal management process and tools for all healthcare product incident types	Will start once signal detection piece concludes and will be supplemented by the information from PT2's mapping exercise on handling of safety signals,	To be determined following review of CI report

Project Team 2 – risk benefit assessment

Deliverable	**Progress**	**Delivery Date**
Better use of CPRD for information on devices safety to support signal and risk assessment	Devices are focusing on three device groups to assess feasibility of using CPRD data for investigating and strengthening signals. The initial scoping suggests that CPRD data may contain codes that could provide useful additional overview information for procedures and associations with these (e.g. hip replacement in association with cancer) but will most likely not be able to provide information at the level of specific devices. We are still scoping the various code systems to better understand the limitations of using the data. To fully assess the feasibility of using the data, cross-linking of data sets will likely be needed. This will require formal project application and approvals. The feasibility study is still ongoing.	Q4 2017
Engagement with registries to support better data collection and information sharing	Initial data gathering exercise (to collate details of already established Device and VRMM registry contacts and to identify future potential contacts of value) completed. Prioritisation of most important registries to our work with a view to increased engagement is the next step.	Q1 2017
Devices specific PSUR	UK is leading a cross EU task Force to develop a devices specific PSUR. Ideally there will be an internationally agreed approach to implementation of the device PSUR however UK could implement a national approach if the EU implementation is considered too lengthy or disproportionate to risk	2018

Project Team 3 – safety messaging and risk communication

Deliverable	**Progress**	**Delivery Date**
Bring together customer services to create safety hub, pilot joint safety	Now a PSVS Delivery Manager appointed this will commence. Medicines and Devices will work together to prepare a	Q4 2017 Joint safety

update	joint safety update by June 2017.	update Q1 2017
Reduce the number of channels via which information is sent to HCPs	This is connected with the CAS and health summit work	Develop action plan in light of findings from the Health Summit - Q1 2017
Take over responsibility for sending DHPCs electronically	Plans for a 6 month pilot are being worked up to test whether DHPCs sent electronically by MHRA using Gov.Delivery would improve health professional engagement and action compared to DHPCs sent by industry by post, as they are now (further detail below)	Start pilot by Q1 2018
Intelligent point of care/prescribing system	This is a long-term project and not yet started.	TBC
Organise summit of health organisations that send safety messages to HCPs	MHRA is working with 13 partners to deliver the health summit pencilled in for 5 June 2017. Agenda being developed with partners (further detail below).	Q1 2017

ADR Reporting

The Board were given a detailed overview of ADR reporting in May 2016. Since then reporting volumes have continued to steadily grow as shown below in figure 1. It is encouraging to see the increase in direct reporting, particularly from patients.

In January the latest roll out of electronic reporting from a clinical system took place when the Vision General Practice system went live. Unlike the previous roll-out in the SystmOne GP system Vision updates require users to install the latest version, we will therefore see a slower increase in reporting than experienced in SystmOne. We have received 208 reports from Vision with numbers increasing month on month so far.

Figure 1 – ADR stats 2016

Yellow Card Reporting Stats

In 2016, there were 42,386 suspected ADR reports received by MHRA: an 8% (3,237 reports) compared to 2015. In 2016, there was a:

- 16% increase in direct YCs which make up 63% of all ADRs
- 13% increase in healthcare professional (HCP) YCs which make up 48% of all ADRs
- 23% increase in patient reports which make up 16% of all ADRs – a 300% (5,091 reports) increase since 2011
- 4% decrease in industry reporting which make up 37% of all ADRs

Between 2011 and 2016, direct reporting increased nearly 4 times as much as industry reporting (11,447 vs 3,052 ADR reports)

Year	Total (% change)	Direct (% increase)	HCP (% increase)	Patient (% increase)	Industry (% change)
2011	**25,691**	**13,105**	**12,589**	**1,6674**	**12,589**
2012	26,568 (3%)	13,787 (2%)	11,958 (5%)	1,829 (1%)	12790 (2%)
2013	31,528 (19%)	16,966 (8%)	14,113 (18%)	2,833 (5%)	14,573 (14%)
2014	31,554 (0%)	18,347 (58%)	14,542 (3%)	3,805 (34%)	13,170 (-10%)
2015	39,650 (26%)	23,426 (27%)	17,958 (23%)	5,471 (44%)	16,227 (23%)
2016	**42,791 (8%)**	**27,088 (16%)**	**20,333 (13%)**	**6,755 (23%)**	**15,641 (- 4%)**

The agency is keen to do more to raise awareness of the Yellow Card Scheme, particularly among patients therefore a business case to implement a new campaign is in development.

An issue we have received feedback on is the large number of medical terms a reporter is asked to select their reaction from. Currently the term list is from the entire MedDRA (Medical Dictionary for Regulatory Activities) dictionary. It can be off-putting to patients to select from this list as many of terms are not intuitive. We have therefore worked with the providers of MedDRA to develop a "patient friendly" set of terms. This has reduced the full term list from almost 76,500 terms to around 1,500 and using rash as an example from 221 terms to 15. We will pilot this term list to determine its usability compared with the previous list and whether the loss of specificity in some areas has a negative effect on signal detection.

Poisons data

The pharmacovigilance legislation[1] introduced in 2012 placed an increased focus on collecting Adverse Drug Reactions (ADRs) outside of a medicinal product's licensed terms of use including harms associated with overdose. A proposal was received from the National Poisons Information Service (NPIS) to collaborate in this area and investigate possible benefits from combining our data sources.

The NPIS is a national service commissioned by Public Health England (PHE) that provides expert advice to health professionals on all aspects of acute and chronic poisoning. The service includes a 24-hour national telephone support line from which all calls are answered by NPIS staff and logged on their database. The NPIS proposed to develop with MHRA an integrated Yellow Card reporting function for their staff to be able to report the cases received via their telephone enquiry service directly to MHRA's Yellow Card database. This is functionality we have already deployed with a number of other clinical systems including 2 GP software systems and 3 hospital based pharmacy systems.

In light of the different nature of data being collected by NPIS in comparison to typical ADRs associated with the therapeutic use of a medicinal product it was proposed and endorsed by CET that we would carry out a discovery project in advance of any integration of Yellow Card to explore UKPID data and carry out a retrospective analysis of the content of their cases. The purpose of this discovery project is to:

- Confirm the additional value of NPIS data above what we currently have in our ADR dataset
- Carry out a retrospective comparison of drug-event pairs between MHRA and UKPID cases to assess whether there would have been earlier signalling of identified safety concerns.
- Assess whether the addition of this data source would give us a better change to observe rare events that would be of specifically high signal detection value.
- If the data is valuable then provide recommendations on whether the data is sufficiently distinct to require separate signal detection process or can be managed according to existing signalling processes.
- Inform development of new reporting requirements in relation to overdose from both staff in the NPIS and broader Yellow Card guidelines for healthcare professionals reporting directly.

Since the endorsement of the discovery project in August 2016, we have been working with the NPIS to agree the terms of reference of the project and the details of handling the data to ensure confidentiality of any personally identifiable data. The MHRA has signed up to the Wales Accord Sharing Personal Information (WASPI) Framework. WASPI sets out a framework of principles and standards which organisations commit to as best practice for the

[1] Directive 2010/84/EU

sharing of data within the public sector. This includes agreements if using data processors, fair processing notices and ensuring adequate level of protection of the data with regards to storage and destruction of the data. MHRA and NPIS have developed a specific data disclosure agreement for the project specifying the method of data transfer, actions in case of data breaches and precise data fields that will be included in the transfer

We have engaged a supplier; Commonwealth Informatics to host NPIS and Yellow Card data on a separate server in order to compute the data and calculate the signal statistics.

It is expected that the transfer of NPIS data to the MHRA will take place in the week commencing the 11th of April 2017 with the aim for the analysis phase to start from the 1st of May 2017. The project team consisting of MHRA staff, NPIS staff and Commonwealth will meet on a fortnightly basis to discuss the data and agree further direction for the analysis. The discovery project will run for 4 months and a final report on the findings of the project will be delivered by September 2017.

New Psychoactive Substances

Since August 2015 the MHRA has been working with Public Health England on a project to explore the use of the Yellow Card reporting system as a means to capture reports from healthcare professionals on harms associated with the use of new psychoactive substances (NPS).

We were keen to collaborate with PHE on this project as it offered a number of benefits for MHRA's vigilance activities. The most important being access to an additional data pool in which to pick up adverse reactions relating to the use of NPS alongside licensed medicines, including possible interactions. Such data could potentially allow us to identify safety signals more quickly. It also expected that the project could expand the reach of Yellow Card to bring awareness about Yellow Card reporting to a new subset of healthcare professionals, particularly those working in drug treatment services who typically don't report many Yellow Cards.

Over the past 12 months we have been working with PHE to provide a copy of the Yellow Card website that gives PHE all of the functionality of Yellow Card but is tailored to ask a small number of additional questions around NPS. The website is called RIDR, which stands for Report Illicit Drug Reactions. It is PHE branded in order to be clear to healthcare professionals on PHE's public health responsibility with regards to issuing to any safety messages and determining actions that may be warranted based upon the reports received. It's a separate website, but there are links to Yellow Card; if you are a registered member of the Yellow Card website then you can use the same log in details. It offers familiarity for those who are already reporting through Yellow Card in terms of the steps to complete and the screens that they will see.

The website was launched on the 22nd of March 2017 with a press release[2]. Other efforts as part of the communication campaign include an article in Drug Safety Update, presentations to the national Medication Safety Officer network and at the Royal College of Emergency Medicines annual conference and the use of social media including an infographic that has been developed.

Since the launch we have received 12 reports, all of good quality, from a range of healthcare professionals which have reported serious reactions including blindness, seizures and fatal outcomes. Some of the reports are in conjunction with licensed medicines. We are currently analysing the data using our Empirica Signal statistical software and providing fortnightly reports on aggregated data to PHE and their Expert Clinical NPS Network. The project steering group meets on a quarterly basis and progress reports will also be shared CET.

[2] https://www.gov.uk/government/news/system-launched-to-help-tackle-harms-from-new-psychoactive-substances

Visualising CPRD data

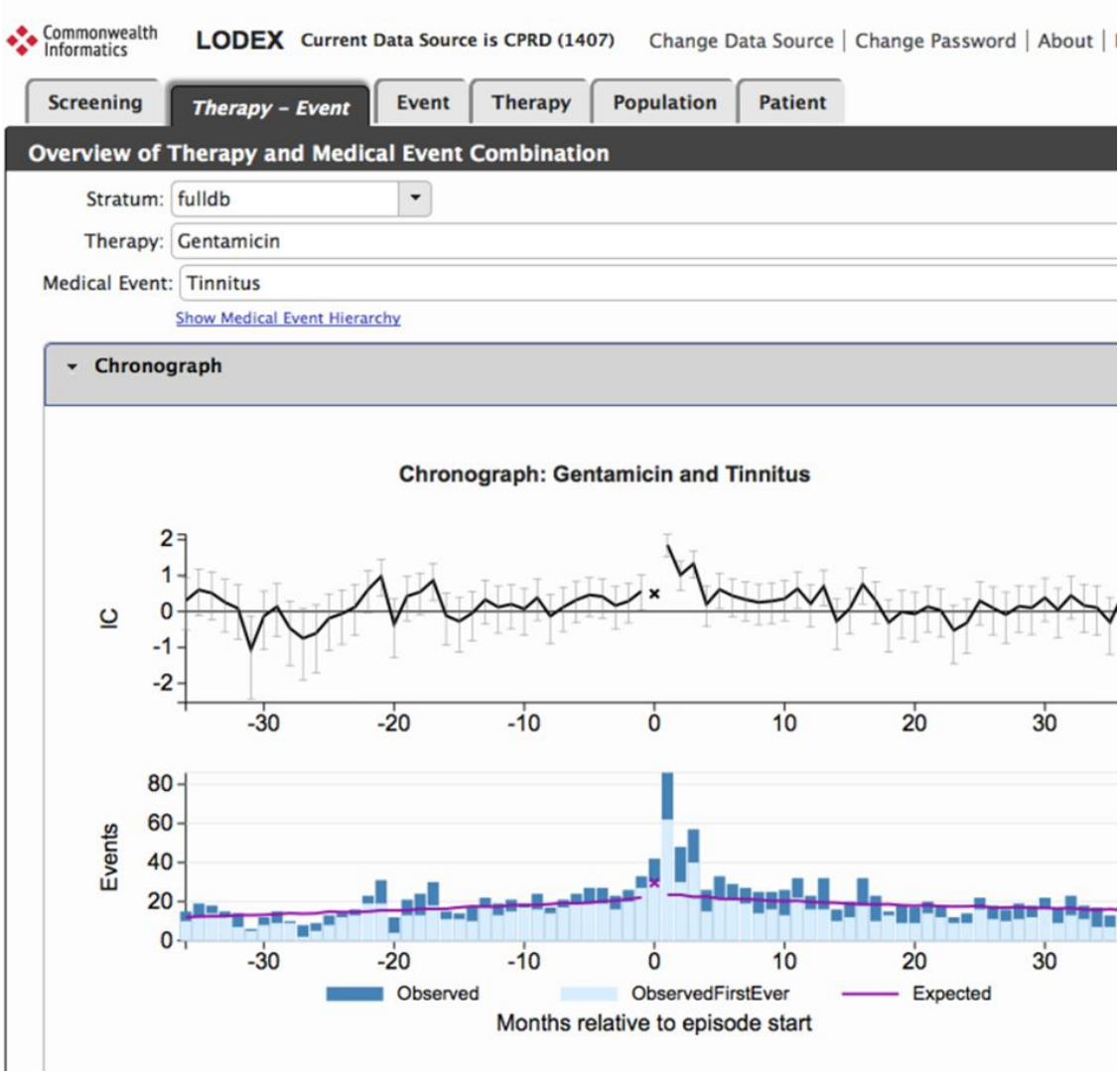
CPRD data has been extensively used directly by VRMM to explore potential safety signals and also to monitor outcomes following regulatory actions through the conduct of robust epidemiological studies. It has also been successfully used to strengthen vaccine pharmacovigilance by providing information on vaccine uptake and background risks in the target population enabling Yellow Cards to be placed easily into context and hence supporting proactive vigilance. This approach has increased the robustness of our assessment of signals related to vaccines arising from the Yellow Card scheme as well as helped to strengthen our communications regarding vaccine safety. It was identified there was a clear need to explore the value that CPRD data could offer to strengthen VRMM's routine signal detection processes for other medicines by supporting earlier and more scientifically robust decision making.

VRMM have worked with CPRD to explore the value of a tool called the Commonwealth Vigilance Workbench Longitudinal module software when applied to the Clinical Practice Research Datalink primary care data. This tool provides routine simple analyses of the CPRD data which are designed to aid assessment of safety signals arising from spontaneous data and other sources and is a reimplementation and extension of work led by the Uppsala Monitoring Centre. A pilot project was conducted by VRMM which explored both the potential extent of use of the tool as well as the potential added scientific value of using the CPRD data in this way through a review of a number of case studies.

Figure 2 shows an example of a chronograph displaying the data:

The pilot demonstrated that the primary care data in the CPRD could be potentially used, through the analyses provided in the software, to explore a substantial proportion of signals raised both by the Yellow Card scheme and from other sources. The case studies also demonstrated that the data was able to strengthen scientific decision making by extending our understanding of the characteristics of patients treated with different products or experiencing specific adverse events and exploring the temporal relationships between products and events raised in signals.
The findings of the pilot have been presented at recent International Conference on Pharmacoepidemiology & Drug Information Association conferences and a paper for submission to a peer-reviewed journal is being drafted. The pilot identified key areas for further development of the software, in terms of both the analyses it provides and the way it is implemented with CPRD data, to optimise its value and also a need for further exploration as to how its use could routinely complement VRMM signal management processes. Further consideration also needs to be given to ongoing developments with CPRD data and how these could impact. A proposal for a further pilot, embedded in current VRMM signal management processes, is being drafted with a plan to start within the next quarter subject to agreement.

Figure 2: Commonwealth Workbench Chronograph

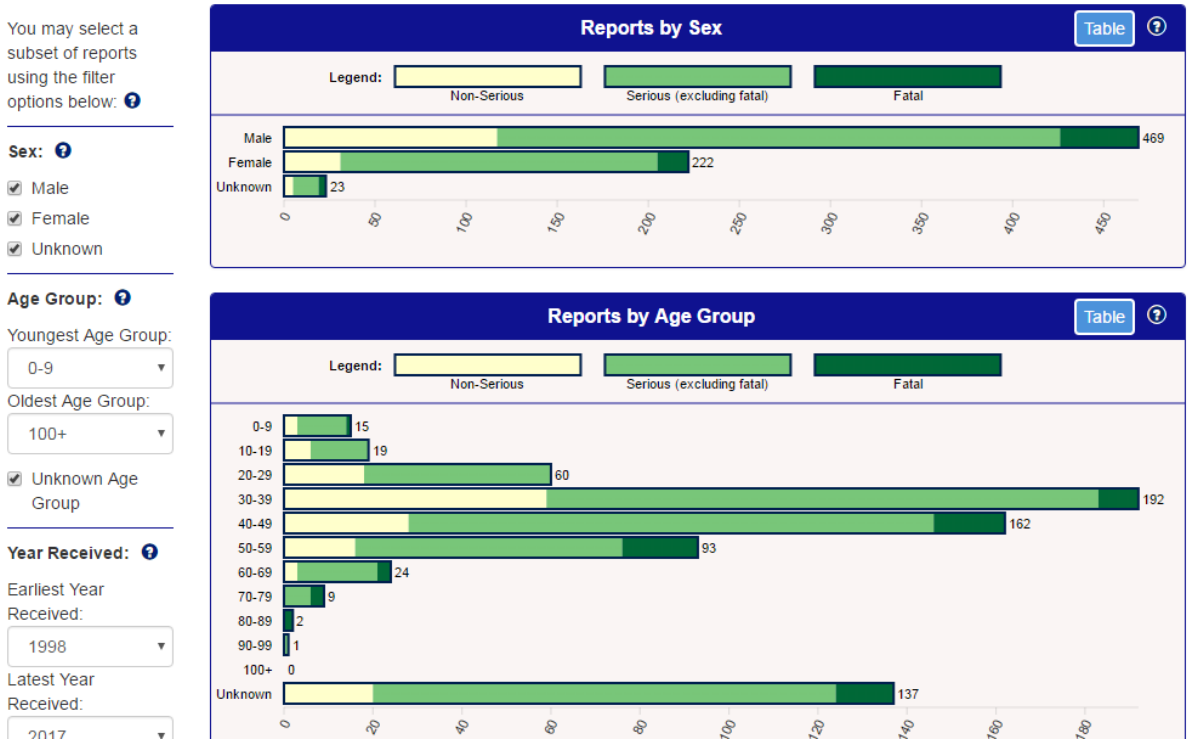


Access for the public to information

Interactive Drug Analysis Prints (iDAPs) were launched on the Yellow Card Website, replacing the previous static PDF reports during September 2016. iDAPs were designed in collaboration with key stakeholders during the Yellow Card 50th Anniversary celebrations with enhancements made based on user feedback. They provide an interactive overview of ADR reports received, enabling users to filter by a range of criteria to view data relevant to their individual setting. Figure 3 below shows an example iDAP.

Since launch there has been significant interest in iDAPs matched with increasing numbers of users with 10,000 to 12,000 page view per month during 2017. This comprises over 9,000 unique users, and over 40% returning to visit the page during the 3 month period. Interest in iDAPs from outside of the UK has also been noteworthy, with 51% of users being based abroad. This could be as a result of demonstrating the iDAPs at international meetings whilst little promotional activity has happened in the UK.

Figure 3 – iDAP



Strengthening Collaborations to Operate Pharmacovigilance in Europe

The SCOPE Joint Action has been running since October 2013 and is due to end at this month. The project was in response to the new requirements placed upon member states through the 2012 pharmacovigilance legislation and the need for member states to operate to a higher level.

The project has five main work packages looking at various aspects of pharmacovigilance: ADR reporting; signal management; risk communications; quality management systems; and lifecycle pharmacovigilance. The project has been managed by VRMM although each of the work packages above were a lead member state and various topic leads. In

After a period of information gathering and analysis a number of deliverables were identified and these have now all been produced.

Throughout the project there have been almost 9,500 days worked on the project by the 26 partners across Europe.

The final deliverables include 34 “Best Practice Guidance” documents supported by 14 e-learning modules and other digital poster and infographics.

These infographics were used in a coordinated digital campaign to raise awareness of the national ADR reporting.systems in November 2016. Twenty one countries took part in the week long campaign using social media channels to encourage patients and healthcare professionals to report ADRs. Overall reporting increased 13% as a result. In some countries there was a doubling of reports.

All the materials are now on the SCOPE website www.scopejointaction.eu and we have been working with the HMA through the European Medicines Agency on a Pharmacovigilance Curriculum. The SCOPE materials will be used to support pharmacovigilance training for member state assessors. The best practice guides and e-learning will be moved to the European Network Training Centre to be a permanent and maintained resource for continuous learning.

Another output from SCOPE is an accredited e-learning module for health professionals. Through the European Accreditation Council for CME (EACCME®) doctors will gain one CME credit on completion of the module which explains pharmacovigilance, ADRs and how to report.

Innovative Medicines Initiative project

The WEB-RADR (Recognising Adverse Drug Reactions) Innovative Medicines Initiative Project began in September 2014, and will complete in September 2017. The project developed to address the need to understand the potential impact on pharmacovigilance of mobile technology and the use of social media.

The project has two core technology work streams, delivering a mobile app platform and dashboard for social media data. These are supported by work packages focused towards user research and social media analytics. The technology work streams feed in to a scientific impact work stream to understand the value of the platforms, which in turn feeds into a policy work package which will recommend regulatory policy on use of mobile apps and social media to the EU network and beyond.

To date the mobile app has been rolled out in the UK, Netherlands and Croatia. A packaged version which will be available for other countries to adopt after the project is being tested in Burkina Faso and Zambia, which has been made possible through our work with the WHO. There has been significant interest in adoption of the platform and its underlying technology, and work ongoing to ensure sustainability of the tools beyond the life of the project.

The project has identified that social media data may supplement that gaining through traditional reporting routes, particularly in the area of misuse and abuse, but that in most areas it is less effective at identifying signals that spontaneously reported data. Policies are being developed to enable analysis of the data where appropriate, without mandating individual case reporting which evidence suggests would inhibit existing signal detection capability.

The project has opportunity to bid for an ‘Exploitation Call’ under the IMI2 framework, which is expected to launch in July 2017. The intention of the exploitation call framework is to extend the utility of the outputs of the original project, and delivery long term sustainability. The project intends to put forward a proposal which will include exploitation of the underlying app platform, and terminology mapping between regulatory and healthcare dictionaries. This will enable direct integration of the app outputs into the healthcare system, as well as wider epidemiological research opportunities.

Conclusions

The projects outlined above demonstrate how MHRA are taking active measures to protect the public health through a strengthened pharmacovigilance system. Improved ADR reporting, utilising new technologies, identifying new data streams, and making data publicly available in more interactive and user friendly ways helps to embed good pharmacovigilance practice into the healthcare system. The work we are leading and the tools and methodologies we are developing will benefit patients in the UK and beyond.

The Board are invited to comment on progress.

VRMM - April 2017

Annex 1 to MHRA 2017-OB-03

FOR THE CORPORATE EXECUTIVE TEAM

TITLE: Patient Safety and Vigilance Strategy (PSVS) - Now in delivery phase

Purpose:

This paper provides CET with

- the outputs of the three project work-streams which underpin the Patient Safety and Vigilance Strategy (PSVS),
- an update on the work around benefit risk following the CET position given in October 2016 that more work needed to be done in this area
- an update on the resources required to enable the strategy to deliver, specifically the new Programme Management function

Summary

This is the fourth paper on PSVS to the CET, the last being in October 2016, where the CET was presented with the project plans from the three Project Teams. The CET endorsed the Project Plans but also said that further work needed to be done in the area of risk benefit assessment. The CET also agreed to further resource to enable the strategy to deliver.

PSVS is now fully in the delivery phase of the project and progress is being made in a number of areas. Those to highlight up front are:

- Signal detection for devices. We are working with Commonwealth Informatics to develop methodologies for device signal generation and a report is expected in May
- Started discussions with GDS about our overall strategy for Yellow Card reporting for all incident types. This is to get early buy-in and collaborative working between ourselves and GDS as we move towards delivery
- Work starting on device information standard for incident reporting
- UK is leading a cross EU Task Force to develop a devices specific PSUR
- Feasibility study on use of CPRD data for devices near completion
- Working to deliver a joint medicines and devices safety update
- Working to develop a 6-month pilot to send DHPCs electronically by MHRA

- Preparing for a Health Summit of health organisations on 5 June

This paper provides a progress report from all areas including on additional resourcing the strategy to deliver according to project timelines.

Resource implications:
Resources have already been committed to the activities underway by the project teams. In October 2016 the CET agreed to additional resource to enable the strategy to deliver. Since then the Steering Group has agreed a model for the Programme Management function and Project Team 3 has recruited a delivery manager (0.6 G7). Project Team 1 has considered and decided against recruiting additional resource at this stage in the strategy. Additional resource in Project Team 2 is under consideration.

With regards to the Programme Management of the strategy, since the CET in October 2016 it has been agreed that the project team for the PSVS Will be led by Louise Loughlin

Timings:

The project plans indicate activities will continue into 2018

Action required by Corporate Executive Team:

CET are asked to note and comment on this update on the PSVS and in particular are asked to advise on next steps in relation to a common approach for risk benefit assessment following completion of the mapping exercise.

Links:

- VRMM
- Devices
- I,E&S
- IMD
- COMMS

Author(s): Mick Foy, Tony Sant, Amanda Bryan, PT Leads and input from wider co-ordination group

FOI/publication issues:

Can paper be published on INsite? (List any deletions required) Yes

CET sponsors: June Raine, John Wilkinson

Patient Safety and Vigilance Strategy

1. Introduction

1.1 In October 2016, the CET was presented with the project plans from the three Project Teams. CET endorsed the project plans, however, asked that further work be done in the area of risk benefit assessment. The CET also agreed to further resource to enable the strategy to deliver. This paper updates on progress in all three project teams, including on what has been done to develop proposals in the area of risk benefit assessment. The paper provides a timely update to CET given that the project is now moving from strategic planning into project delivery. Following agreement from CET in October 2016, the papers also updates on what has been done to secure additional resource to enable the project to deliver.

2. Background

2.1 CET is reminded of the agreed vision for the PSVS which has been communicated previously with both CET and the Board:

- Safer healthcare products through a world-leading system of proactive safety management, enabled by digital technologies.

- We will achieve this by working in partnership with the NHS, across the health and care system, and internationally, using and exploiting digital technologies

2.2 The strategic vision is underpinned by 5 strategic objectives set out at **Annex A**

2.3 A governance system (**Annex B**), with agreed terms of reference, has been established to support the development and implementation of the strategy. This includes a steering group, co-ordination group and the three project teams:

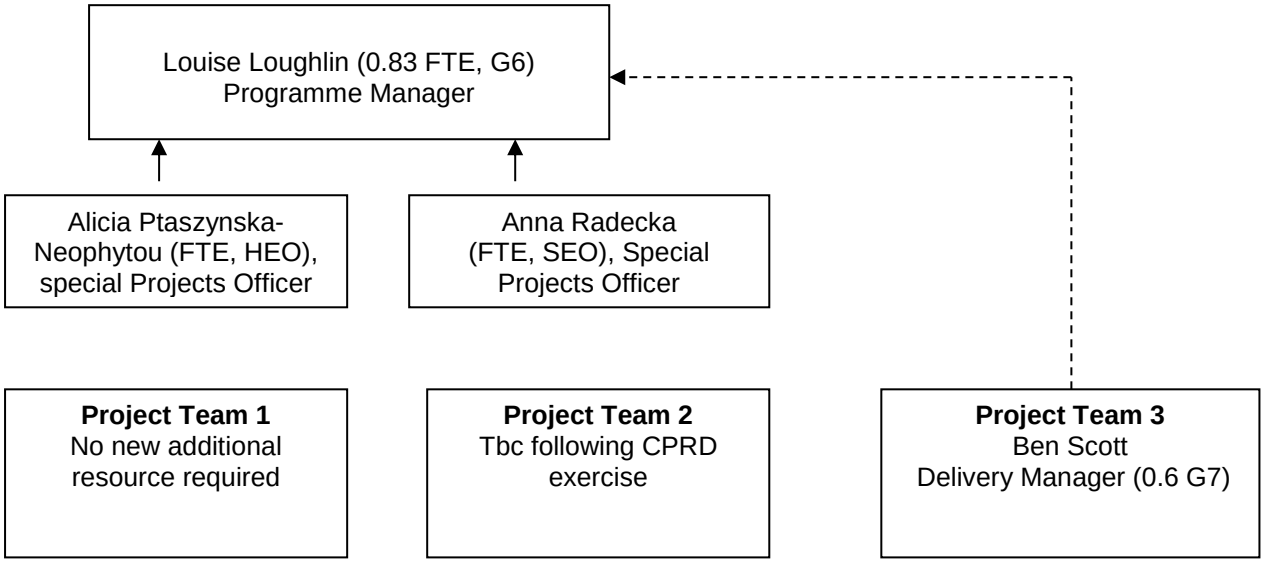
Project Team 1: Incident reporting and signal detection
Project Team 2: Risk benefit assessment
Project Team 3: Improving delivery, targeting and audit of safety messages and risk communication

3. Resourcing the strategy

3.1 At the CET meeting in October 2016 it was proposed that a FTE G6 Programme Manager was needed to fulfil the ambitions of the PSVS. Since then the Steering Group has agreed a slightly different model for the Programme Management function as it is not certain that a FTE G6 would be operating at full capacity at this stage in the strategy. Rather than recruiting a FTE G6 Programme Manager, a tried and tested team approach will be adopted. The Steering Group has agreed that a project team led by Louise Loughlin will take on the programme management for the PSVS. Louise Loughlin (0.83 FTE, G6) works for VRMM on a 0.5 FTE basis. Louise is supported by 1.0 FTE SEO and 1.0 FTE HEO. This approach will provide stability to the project management function through a collective ownership and shared

responsibilities. This will enable cover for leave and exceptionally busy periods to be managed well and staff turnover, which is always a high risk with a single point of responsibility will be mitigated. An additional and important benefit of this proposal is that it does not require the recruitment of new, additional staff but absorbs the PSVS work into an existing team that is being enhanced by a period of hand over from the existing PSVS project manager to bring continuity to the project. The handover from the existing project manager has being taking place since the end of January and has just completed.

3.2 In addition to the Programme Management function, a Delivery Manager (0.6 FTE G7) for Project Team 3 has been recruited and has been in post since 1 March 2017. Project Team 1 has considered additional resource to support their workstream and has decided against recruiting additional resource at this stage in the strategy as following a restructuring exercise in Devices some resource has been freed up to work on the PT1 activities. Additional resource in Project Team 2 is under consideration and will depend on the outcome of the study assessing the feasibility of using CPRD data for devices. A diagram setting out the resource model in place to deliver the strategy is set out below.



4. Summary of Project Team Deliverables and Timescales

Project Team 1 incident reporting and signal detection

4.1 **Project Team 1** is responsible for delivering **Strategic Objective 1** on effective capture of information and **Strategic Objective 2** on improving MHRA's signal detection capability. The deliverables for Project Team 1 are set out below together with an update on progress:

Deliverable	**Progress**	**Delivery Date**
Delivery of mobile reporting for medicines (adverse reactions, counterfeits and defectives	We have started discussions with GDS about our overall strategy; this is to get early buy-in and collaborative working between ourselves and GDS as we move towards delivery. The initial plan to simply update the existing Yellow Card App is not the preferred option so a re-platforming of the Yellow Card system to mobile responsive pages whilst being the correct technical solution has added delay to the roll out. The delivery of mobile reporting for medical devices is being done as part of the Operational Transformation, with the ongoing Devices Transformation project, and therefore is out of scope for this work.	Q1 18/19 (indicative potential date, as there are still a number of decisions to be made which will impact the timelines)
Device Information Standard for Incident reporting	Work has started on the core elements of the standard. This will be discussed in the EU and international environments for wider adoption although the option to act independently for the UK is our fall-back position	Target delivery date as NHS Digital Standard Q1, 2018
Implement a formalised signal detection methodology for devices	Data security issues have been resolved and work is now progressing with regards to developing signal detection methodologies for Devices. These prototype methods will be tested against existing signals to evaluate their accuracy. A report from CI is expected in May 2017.	CI investigations to be completed May 2017. Implementation into devices operations to be determined following report review
Investigate a common signal management	Will start once signal detection piece concludes and will be supplemented by	To be determined

process and tools for all healthcare product incident types	the information from PT2's mapping exercise on handling of safety signals,	following review of CI report

Project Team 2 – risk benefit assessment

4.2 **Project Team 2** is responsible for delivering **Strategic Objective 3** on looking at wider vigilance data pools and **Strategic Objective 4** on improving risk benefit assessment. The deliverables for Project Team 2 are set out below together with an update on progress:

Deliverable	**Progress**	**Delivery Date**
Better use of CPRD for information on devices safety to support signal and risk assessment	Devices are focusing on three device groups to assess feasibility of using CPRD data for investigating and strengthening signals. The initial scoping suggests that CPRD data may contain codes that could provide useful additional overview information for procedures and associations with these (e.g. hip replacement in association with cancer) but will most likely not be able to provide information at the level of specific devices. We are still scoping the various code systems to better understand the limitations of using the data. To fully assess the feasibility of using the data, cross-linking of data sets will likely be needed. This will require formal project application and approvals. The feasibility study is still ongoing.	Q4 2017
Engagement with registries to support better data collection and information sharing	Initial data gathering exercise (to collate details of already established Device and VRMM registry contacts and to identify future potential contacts of value) completed. Prioritisation of most important registries to our work with a view to increased engagement is the next step.	Q1 2017
Devices specific PSUR	UK is leading a cross EU task Force to develop a devices specific PSUR. Ideally there will be an internationally agreed approach to implementation of the device PSUR however UK could implement a national approach if the EU implementation is considered too	2018

	lengthy or disproportionate to risk	

Common approach to post marketing/authorisation risk assessment

4.3 In addition to these deliverables, at the last CET consideration in October 2016, the CET asked that more work was done to develop a common approach to risk assessment. In light of this a mapping exercise on how post-marketing/ post-authorisation safety signals are handled in Devices Division and in VRMM has been conducted. As part of this work Project Team 2 has looked at the tools used to support the signal/risk assessment process; the reports that are produced, who they are produced by and the sign-off process; and the criteria for seeking expert advice. For the Devices process, the Team also looked at the relative roles of the notified bodies (NBs) and MHRA in these processes and the mechanisms in place for sharing information on signals between the NBs and MHRA.

The results of this exercise are set out in **Annex D**

4.4 This mapping exercise has highlighted some key areas of commonality in approach: once a signal is identified, the next step for both Devices and VRMM is to gather additional data to strengthen and confirm the signal and to facilitate signal prioritisation (which use algorithms which are based on a number of factors including the strength of the signal and its potential public health impact), and also to agree what further data and assessment is necessary. For important new signals, this is followed by further data/evidence gathering, assessment of the additional data, seeking expert advice and taking regulatory action to minimise risk as appropriate.

4.5 One of the most obvious commonalities is the gathering of additional data to further investigate signals/risks, although the sources of this data may be different for medicines and devices. For medicines, health records databases (such as CPRD) are commonly used to further investigate safety signals but their use for devices is hampered by the lack of recording of device information in such databases. As above, the Project Team is continuing to investigate the feasibility of using CPRD for devices. Furthermore, preliminary work on compiling an index of MHRA contacts for external registries (for both medicines and devices) is complete and the project team will now prioritise registries to increase engagement with those that are the highest importance to both device and medicines vigilance.

4.6 In addition to the identified commonalities, a more detailed view of the two risk assessment processes has highlighted some key differences with regards to the following:

(i) ***Collective decision making*** –the approach to and stage in the process at which a collective evaluation of the strength of the signal is made and a decision is taken regarding what additional data is required and what further assessment is required (including need for expert advice);

(ii) **Data Assessment**-medicines produce an assessment report for every signal agreed by SMRM to be taken forward. Devices take a more bespoke approach according to factors such as trigger levels, device type and risk classification.

(iii) Formal criteria and approach to ***seeking expert advice;*** medicines have identified that an SOP is required to ensure consistency.

(iv) The format and consistency of outputs from the assessment process

(v) ***Transparency*** e.g. publication of expert committee discussions (meeting minutes) and public assessment reports;

(vi) ***Monitoring outcomes*** of regulatory action.

4.7 The Project Team proposes to consider whether a more common approach in these areas is appropriate and feasible and if the CET agrees will work to develop deliverables in this area by Q1 (June) 2017.

Project Team 3 – safety messaging and risk communication

4.8 **Project Team 3** is responsible for delivering Strategic Objective 5 on improving MHRA's ability to deliver and target safety and learning messages. The deliverables have been modified as some of the work such as the operation of the MSO/MDSO network and the CAS replacement were ongoing and not specifically the responsibility of PSVS.
The deliverables for Project Team 3 are set out below together with an update on progress:

Deliverable	**Progress**	**Delivery Date**
Bring together customer services to create safety hub, pilot joint safety update	Now a PSVS Delivery Manager appointed this will commence. Medicines and Devices will work together to prepare a joint safety update by June 2017.	Q4 2017 Joint safety update Q1 2017
Reduce the number of channels via which information is sent to HCPs	This is connected with the CAS and health summit work	Develop action plan in light of findings from the Health Summit - Q1 2017
Take over responsibility for sending DHPCs electronically	Plans for a 6 month pilot are being worked up to test whether DHPCs sent electronically by MHRA using Gov.Delivery would improve health professional engagement and action compared to DHPCs sent by industry by post, as they are now (further detail below).	Start pilot by Q1 2018
Intelligent point of care/prescribing system	This is a long-term project and not yet started.	TBC
Organise summit of	MHRA is working with 13 partners to	Q1 2017

health organisations that send safety messages to HCPs	deliver the health summit pencilled in for 5 June 2017. Agenda being developed with partners (further detail below).	

5. Engagement with the Healthcare System

5.1 As outlined above, one of Project Team 3's deliverables is to organise a health summit to discuss improving the impact of safety messaging in the healthcare sector. We recognise this is a system issue that cannot be tackled by one organisation alone. A desktop review of existing UK and European surveys carried out by MHRA showed that HCPs are overloaded with too many messages. This led to many messages being ignored with the potential that important public health information is not being read and acted on. The review concluded that, while MHRA could do more to streamline its safety messaging, this was a much wider problem in the healthcare system. As a starting point, we have identified 13 key partners who we have made contact with to explore the issues and their perspectives. Our goal is simple: by improving the healthcare messaging system we aim to make it easier for HCPs to keep informed about important clinical information, ultimately leading to improved patient safety. All the partners we have contacted have acknowledged this is a systemic problem in the healthcare sector, and have welcomed the opportunity to engage further to see what can be done to make improvements.

5.2 An exploratory meeting with our key partners was held on 20 February to prepare for a summit of stakeholders on 5 June 2017. It is estimated that the cost of the health summit and planning meetings for 2017/2018 will be around £15k. A summary of the meeting is attached at **Annex C**.

5.3 Linked to this is the deliverable to take over responsibility for sending direct healthcare professional communications (DHPCs) electronically. A DHPC is a communication intervention by which important safety information is delivered directly to individual healthcare professionals by a marketing authorisation holder (MAH) or a competent authority (CA), to inform them of the need to take certain actions or adapt their practices in relation to a medicinal product. DHPCs are not replies to enquiries from healthcare professionals, nor are they meant as educational material for routine risk minimisation activities. The PSVS Steering Group and Co-ordination Group have considered the options for a pilot to test whether electronic DHPCs (eDHPCs) sent by MHRA would improve health professional engagement and action, compared to DHPCs sent by industry by post, as they are now. Previous pilots/surveys, including SCOPE, have shown that messages from health organisations are better received by HCPs than messages from industry. Industry is also pushing to send DHPCs electronically.

5.4 The Steering Group has agreed in principle to start a 6 month pilot sending eDHPCs via Gov.Delivery by uploading CAS contact details into an email delivery system. The CAS system itself will not be used for the delivery of DHPCs in this pilot. Work is now underway to decide how best to take this work forward as the pilot would require a comprehensive methodology with clarity around what we are testing and its evaluation. This is best delivered through an independent research agency

working with MHRA and industry. If fully or part funded by the MHRA this will have resource implications in the region of £35K. Now the principle of running a pilot has been agreed, we will develop a specification and invite suppliers from the framework to tender for this work. The steering group will sign off the final methodology and costs before we contract a supplier.

5.5 While our ambition is to incorporate all medicines and devices safety messaging within the new CAS system, both VRMM and Devices have agreed that device Field Safety Notices (FSN) are out of scope of this DHPC pilot, primarily because FSN's are already sent out in electronic format, however, learnings from the pilot would be useful to devices further down the line.

6. Budget

There are budgetary implications for a number of the deliverables agreed in this PSVS delivery phase. These will be taken through the appropriate approval channels such as IMGB or Regulatory Group following advice from Finance.

7. Conclusion and questions for CET

7.1 This paper shows significant progress in a number of areas and informs the CET of the additional resource being allocated and the Programme Management function put in place to take forward the strategy.
CET is asked to note the progress made on the PSVS and in particular are asked to support:

i. the programme management model and resourcing decisions taken so far
ii. the content of the deliverables, progress and timelines

Additionally CET is asked if there are any further actions to be taken in relation to a common approach for post marketing/authorisation risk assessment.

Devices
VRMM

February 2017

Annex B

Strategic Objective 1 - Effective capture of information from incident reports and the wider scientific evidence base. This includes social media information and other technologies such as the YC App. The WEB-RADR project has presented opportunities for utilising new technologies and gaining an understanding of how social media can support vigilance activities. The YC app should be extended to devices and learnings from the social media investigations should be applied to all our activities.

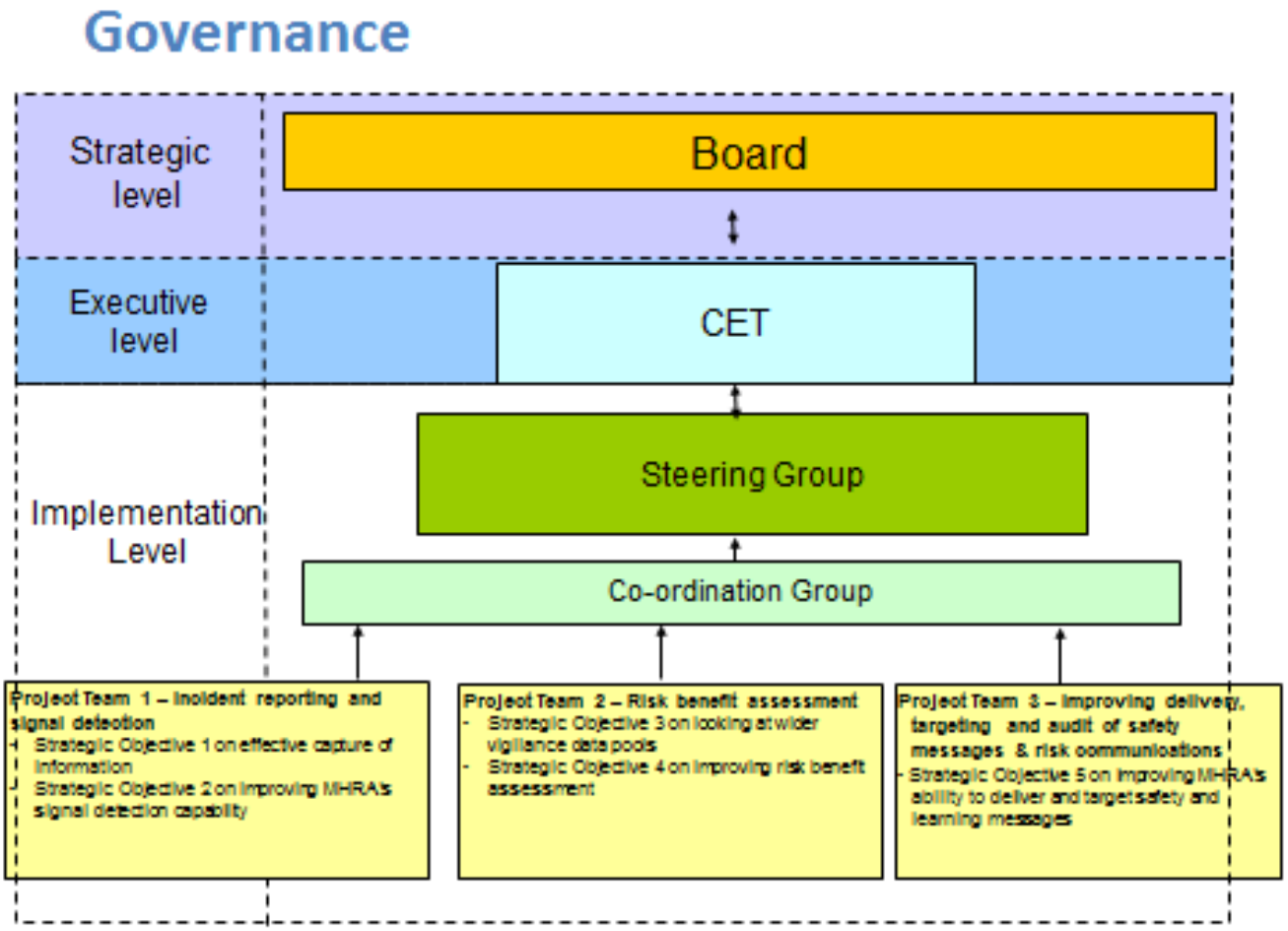
Strategic Objective 2 - Improving MHRA's signal detection capability. The signal detection tools we use continue to evolve, VRMM have a good track record in utilising new tools and methodologies to detect signals. We will look at how to further develop these tools and new text analytics and signal management tools in light of new data flows and at how best to apply these tools and methods to all MHRA areas.

Strategic Objective 3 - Improved access to wider vigilance data pools such as CPRD and national and international registries to support benefit risk assessment. Access to CPRD and other data sources is vital in supporting benefit/risk evaluation. We will look at how best to utilise such data for all vigilance activities.

Strategic Objective 4 - Improving benefit/risk assessment. We will review how risk management and risk minimisation measures in devices and medicines may benefit from a common approach. There are well established approaches, regulatory tools and templates in pharmacovigilance which may be applicable to devices particularly in light of the forthcoming devices regulations

Strategic Objective 5 - Improving MHRA's ability to deliver and target safety and learning messages. Led by Comms, we will review how we communicate safety messages, the channels we use, and how we measure the impact of our messages to those who need to be aware and deliver action and behaviour changes to improve UK patient safety.

Annex B


Governance
Strategic level
Board
Executive level
CET
Implementation Level
Steering Group
Co-ordination Group
Project Team 1 – Incident reporting and signal detection
- Strategic Objective 1 on effective capture of information
- Strategic Objective 2 on improving MHRA's signal detection capability
Project Team 2 – Risk benefit assessment
- Strategic Objective 3 on looking at wider vigilance data pools
- Strategic Objective 4 on improving risk benefit assessment
Project Team 3 – Improving delivery, targeting and audit of safety messages & risk communications
- Strategic Objective 5 on improving MHRA's ability to deliver and target safety and learning messages

Annex C

Patient Safety and Vigilance Strategy:

Project Team 3 –health summit planning meeting

Background and Introduction

The project team 3 delivery programme includes the development of a health summit with partners across the health and social care system to work towards improved targeting of patient safety messaging.

Methodology

This project has been developed through stakeholder engagement with key partners including NHS England, NHS Improvement, NHS Digital, devolved governments, GMC, CQC and DH. These organisations were selected because they distribute safety messages to healthcare professionals. Following initial telephone discussions partners were invited to complete a pre-planning questionnaire to explore key themes to be discussed at the planning meeting, these themes were consolidated into a summary document for partners to consider prior to the planning meeting.

The planning meeting 20 February

The planning meeting focused on small group facilitated discussion based on 4 themes for improvement as identified by partners' questionnaire feedback:

- Improved organisational systems
- Improved feedback
- Improved behaviour
- Improved channels

The planning meeting generated useful and productive discussions which pointed to the following themes:

- Better targeting of messages including filtering who receives messages and making the filtering process explicit to facilitate trust and confidence in the message
- Utilise plain English, active language to facilitate engagement with the message

- Explore the development of a common framework/template of suite of templates for safety messages
- Involve the end user in what we are trying to achieve –how does it feel to be on the receiving end of safety messages
- Co-ordinate safety messages across the system to enhance credibility and support local re-enforcement of messages. This may involve a suite of tools such as education, support and point of care information
- Measure impact e.g. epidemiology to identify changes in practice
- Build efficiency into the system/narrative – are there quantifiable cost savings to be made by being more efficient/target/responsive to safety messages?
- Utilisation of local champions to support safety messages e.g. lead pharmacists, medical device safety officers/medication safety officers

Actions and next steps

There was considerable enthusiasm for continued work this area. Further consideration needs to be given to the following:

- The interface between organisational action e.g. what do NHS Trusts need to do the individual practice of health professionals. This needs to be supported by a better understanding of the governance process which needs to be in place to ensure these actions occur and in a timely manner
- Agreement / consensus on how patient safety messages should be handled
- A national repository or communications system (which is UK wide) needs to be able to push out information but also needs to be accessible to all – including patients
- Confirm the aims and objectives of the summit as part of the planning meetings

In conclusion

Encouragingly, many of the issues raised at the meeting and through the questionnaire returns were also considered as part of project team 3's work and its subsequent recommendations.

The need for more scoping work was identified and further planning meetings should happen to develop principles around which the key partners could build consensus. The next one is scheduled for the end of March. Once achieved, we could consult wider on these principles at a health summit. There was agreement to try to stick to 5 June as the Summit date.

Annex D

Initial phase mapping

Medicines:

For medicines, once a signal is identified it is discussed at the ***weekly*** Signal Management Review Meeting (SMRM). The meeting will decide whether to confirm or refute the signal. If the signal is confirmed, the meeting will also decide whether further data are needed and the next steps for assessment of the signal. SMRM is conducted in-line with a detailed SOP and a signal assessment is presented at the meeting according to a specific template. These are rigorously adhered to in order to ensure consistency in the initial assessment and the decision making process. The SOP is so detailed as to stipulate which members of staff must be present; for example, the meeting cannot go ahead unless there is a medic present. This ensures that the necessary expertise and level of staff are actively involved in the decision making process for all signals. The decisions are captured in the minutes of the meeting which are stored in documentum (Sentinel). Details of signals confirmed by SMRM as requiring further assessment/action are entered in to Sentinel (Signal Assessment Case Folder) and EPITT (European Pharmacovigilance Issues Tracking Tool).

Devices:

In devices, assessment of signals goes through a daily 'pre-triage' assessment by junior device specialists using an algorithm based on device type and risk/ benefit details available at this time. In addition product specific technical groups and clinical review where there is a patient safety issue. The need for further investigation and information is agreed with the Team Manager and planned actions recorded on the adverse incident record. Device area groups may use risk assessment tools to further assess significance and seriousness of signal received

Second phase mapping

Medicines:

At this stage further data (as agreed by SMRM) is gathered for full assessment of the signal. Assessments are completed by pharmacovigilance scientists or Benefit Risk Unit assessors according to standard EU or UK templates. Assessments are signed off by the Unit Manager and Group Manager; EU-led assessments are also signed off by the PRAC delegate.

Devices:

For Devices the second phase also involves gathering of further data to assess the safety risks and to support actions that will mitigate the risks. The device specialist/assessor will discuss their assessment with the technical lead and Team Manager and record the outcomes in the adverse incident record. If appropriate a Safety Warning Decision Record Form will be submitted and agreed with the Technical Management Group (TMG). Where signals appear to be significant beyond the UK, communication with Europe via an EU enquiry form, and/or EU monthly vigilance teleconference may take place.

Expert Advice

	Devices	VRMM
Sources of (external) Expert Advice	**DEAC** & **3/4 standing EAGs** Meet quarterly and ad hoc as required. **Register of experts** – advice from individual experts is sought unless the issue needs expertise from more than one discipline or professional consensus is required in which case an *ad hoc* device-issue specific EAG may be convened.	**CHM & 11 standing EAGs** CHM, Pharmacovigilance EAG and some other others meet monthly. Others meet rarely although reports may be sent to members for written advice. Expert Advice in writing may also be sought if very urgent advice is required and cannot wait until the next scheduled meeting. Additional **list of experts** for very specialist issues or experts will be sought on *ad hoc* basis if no suitable expert on committees or list. PEAG membership includes clinical pharmacologists, GPs, nurse, pharmacist, epidemiologists, molecular toxicologist and lay reps.
Criteria for seeking advice	Clinical/specialist expertise is need when: - Potential for significant change to B/R balance - Potential for significant public health impact - Data does not support real safety concern but public reassurance required e.g. stress incontinence tape - niche technical/ medical/ scientific expertise required - Parliamentary interest - Disagreement amongst clinical profession - Signals for devices with 'history' e.g. Breast implants, metal on metal hip implants. .	No formal criteria or process but in general expert advice will be sought for the following: - Significant change to B/R balance - Potential for significant public health impact - Impact on clinical practice (e.g. new monitoring requirements – blood tests/MRI etc.) - Data does not support real safety concern but public reassurance required e.g. vaccines - Specialised/niche technical/ medical/ scientific expertise required - Coroner's Regulation 28 Reports - Fright factor (e.g. pregnancy, children)

		- Media interest - Parliamentary interest - Disagreement amongst EU Member States e.g. on level of risk or risk minimisation measures required - Disagreement with MAH (who may challenge scientific assessment) - Vexatious/persistent patient enquiries - Signals for medicines with 'history' e.g. NSAIDs, SSRI antidepressants, contraceptives, HRT, anti-epileptics; or AEs of special interest e.g. suicide, PML, neurodevelopmental delay.
Reports	Various reports produced both internally and externally (and reviewed internally or by an independent group where appropriate). Examples include: - Risk/file reviews (Device Specialists). - Clinical reviews (DCT). - Safety Warning Decision Form (assessed by TMG). - Manufacturer reports and risk assessments (reviewed by DS). - Commissioned Safety Testing or Data Research Project (produced externally; reviewed by DCT, DS, TMG, or an EAG as appropriate). - EAG reports for high risk cases. - EU Task Force reports for device specific cases.	BRMG assessors (with input as required from MHRA colleagues e.g. epidemiology, stats, non-clinical, NIBSC) conduct an assessment of data. The assessment report (based on standard templates), which includes a section detailing the advice sought, is presented to the committee.
Sign-off procedure for Committee Papers	Sign off procedure depends on the output: - SWDR (TMG and GM). - MDA / other safety advice publications and targeted letters (TMG, TM, GM).	All committee papers require sign off by the Unit Manager and Group Manager. Expert Committee Support will not send out reports to experts without an approval form signed by the UM

	- EAG reviews (DCT Director, DEAC). - Communication briefing (TM, Devices Director). - Vigilance guidance docs (GM).Ministerial briefings (Director/CEO	and GM. For EU led issues, the PRAC delegate will also be involved in the sign-off process.
Records	Records are documented on the Adverse Incident Tracking System (AITS) database.	All CHM/ EAG agendas, papers and minutes are stored centrally in Sentinel (Documentum)

VRMM has identified that the criteria for seeking expert advice are not formally documented currently. It was also noted that the current decision making process on whether expert advice is needed is often carried out between a BRMG assessor and their Unit Manager and therefore there is limited ***collective*** decision making (and therefore consistency within VRMM and across the division) about the need for expert advice, and no formal record of the decision making process. Consequently it is proposed that a VRMM SOP on criteria for seeking expert advice will be developed. In addition it is proposed that a formal, collective decision making process will be trialled within the weekly Signal Management Review Meeting. Decisions will be captured in the SMRM minutes.

Devices have a standard operating procedure for seeking expert opinion which outlines when to contact an expert, how to identify an appropriate expert from the register and record keeping. Devices also have a SOP for high profile incident management which includes sections on how to manage and document decisions reached.

Outcomes
The regulatory options available to Devices and VRMM are similar and range from no action to removal of the device or medicine from the market.

Documentation
The assessment planning process, assessment reports and the decision making process is well recorded in VRMM and this information is centrally accessible, ensuring a corporate memory exists. Importantly this also ensures that the data, decision making process and rationale underpinning any regulatory action (or why no regulatory action was taken) are readily accessible in the future.

For devices decisions on whom to consult and whether to take action, and final outcome of the investigation are justified and recorded in the relevant AITs (database) record.

Transparency
For medicines a summary minute of the UK CHM/EAG discussions and advice are publically available on the MHRA website. The European Medicines Agency also publishes the agenda and minutes for the EU Pharmacovigilance Risk Assessment Committee. VRMM and EMA also publish public assessment reports for significant risk assessments.

For devices AITS records are not publically available due to confidentiality constraints of the device directives. There is work going on within Europe at Medical Devices Vigilance working Group to increase transparency.

Interactions between MHRA & NB

Devices work closely with Notified Bodies in sharing information on medical devices. MHRA can request Information from notified bodies and ask them to look at specific manufacturer files and processes where they have concerns.

MHRA is also able to target their audit inspections of Notified bodies to concentrate on any areas where there are concerns. Manufacturers have a duty to report vigilance adverse to both us and the Notified body. Notified bodies must take relevant action which will range from monitoring the situation, to unannounced inspections of manufacturers, and ultimately withdrawal of certificates. Notified bodies keep MHRA informed of any safety concerns and suspension of any certificates.

Monitoring outcomes/impact of regulatory action

Medicines MAHs have a responsibility to evaluate the effectiveness of risk minimisation measures and quantify their impact on patient safety. As well as having approval of the approach taken and oversight of any epidemiological studies conducted by MAHs to do this, VRMM conduct their own research using, in particular, data from the Clinical Practice Research Datalink. The need for in-house monitoring following all regulatory actions communicated by VRMM is assessed with studies to examine prioritised issues then conducted.

For devices, the manufacturers also have a responsibility to monitor outcomes. The data within the CPRD that is suitable for monitoring changes in clinical practice and impact on patient safety following actions taken with regards to devices is extremely limited. Devices undertake such monitoring through their standard signal detection processes which capture data from a variety of sources.

Team will now start to prioritise registries and carefully consider how MHRA can incentivise and build relationships with registries with a view to sharing data.

Both Devices and VRMM regularly access important external expert advice on safety issues. In light of this it is also suggested that the Project Team further explores the potential to pilot seeking combined advice from devices and medicines experts for drug device combination products. Also, the Project Team will consider whether combining expertise from Devices and VRMM would benefit risk assessment and management for innovative products such as cellular therapies.