SCOPE Work Package 4
ADR Collection

Raising Awareness of National Adverse Drug Reaction Reporting Systems: Case Studies by Country

SCOPE

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Acknowledgments

Author

Mitul Jadeja, MHRA, UK

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Purpose of document

The document is a compilation of case studies showcasing examples of good practice shared by various National Competent Authorities (NCAs) within each Member State (MS). This information is in alphabetical order by MS and should be used in conjunction with the SCOPE guidance documents on raising awareness levels of national ADR reporting systems.

Examples are aligned to the numerous suggestions in the SCOPE guidance document and supporting e-learning module on raising awareness levels of ADR reporting. There are also examples of: how success is measured for campaigns; case studies of regional monitoring centre (RMC); and campaign case studies provided by an NCA or national Pharmacovigilance Centre within a particular MS. This means that the suggestions may be different and varied between NCAs.

Bulgaria

Benchmarking – a formal assessment of awareness levels

Three surveys were conducted from 1995-2012. In:

1. 1995 a survey focused on the knowledge about national ADR reporting system was performed among 300 general practitioners by specialists from the Pharmacology cathedra of Medical Faculty Sofia.
2. 1998 a specialist from the Bulgarian Drug Agency (BDA) performed a survey on the main causes of low ADR reporting activities among 244 medical doctors, appointed as chief of clinical wards in hospitals (provincial towns).
3. 2012 a survey among 550 pharmacists and 120 medical doctors (GPs and specialists) was performed by specialists from the Pharmacy Faculty Sofia to assess their awareness of their role in the national PV system.

The last questionnaire consisted of general questions concerning not only estimating levels of reporting but also attitude of the HCPs towards treatment with generics and information regarding medicinal products such as advertising. Within the questionnaire respondents were asked about low reporting rates of suspected ADRs in Bulgaria. The survey indicated the following perceptions:

- 26% (64 respondents) did not know where to report
- 53% (130) were not sure whether the ADR was a result of the treatment with the current medicinal product
- 62% (43) had concerns that the ADR presented was due to treatment error
- 7.8% (19) considered that the medicinal products which are authorised for treatment do not cause any ADRs
- 11% (28) considered low reporting rates to be a result of other unidentified reasons.

Above percentages exceed 100% due to multiple answers from responders.

From a survey conducted in 1995, 187 (62.3%) out of 300 HCPs responded:

- 9% stated a barrier to reporting was the lack of information on how to report
- 37% stated that authorised medicinal products have a guaranteed safety profile
- 18% stated that they are overwhelmed with work and this was the barrier to reporting.

The most recent survey conducted by an external body illustrates that 19% of the doctors are not aware of the system for suspected ADR reporting. Although Bulgaria does not have any official document for awareness level raising strategy the NCA states it follows a systematic approach. Specific information to raise awareness is mainly conducted through publishing on the BDA website but also includes:

- Yearly updated guidelines for HCPs on how to report. It includes sections on: the legal responsibilities of HCPs, the history of reporting system; the importance of PV in medical practice; what happens with suspected ADR reports; addressing confidentiality issues; who can report and how to report. The information also includes completed examples of suspected ADR reporting forms.
- Regular press releases about safety issues
- A corresponding section for patients including education about PV, how to report and press releases on safety concerns
- Paper publishing of, the 'Adverse Drug Reaction bulletin' at least twice annually (also available on the BDA web site)
- Electronic reporting forms for HCPs and patients, and list of additional monitored products
- A dedicated telephone line for all PV related questions that is advertised on the reporting site
- A local scientific journal: 'Science pharmacology' which regularly publishes articles on PV
- The creation of a national PV committee for the BDA.

A poster presentation and dispelling ADR reporting myths

During a campaign, a poster was presented by the Bulgarian Drug Agency (BDA) at an annual clinical pharmacology congress containing the following messages:

- 30% of ADRs are preventable
- ADRs as causes of hospitalisation and mortality
- The main causes for withdrawals of products are ADRs.

The tree illustrates the analogy and philosophy BDA promotes. The root is evidence based medicine which drives regulatory changes (the trunk). The branches are therapeutic groups for example combined hormonal contraceptives and safety topics are the leaves, for example, venothrombotic risk and cancer of breast or endometrium. For each identified risk there is a message of warning for the HCP that illustrates the role of safety information within prescribing practice.

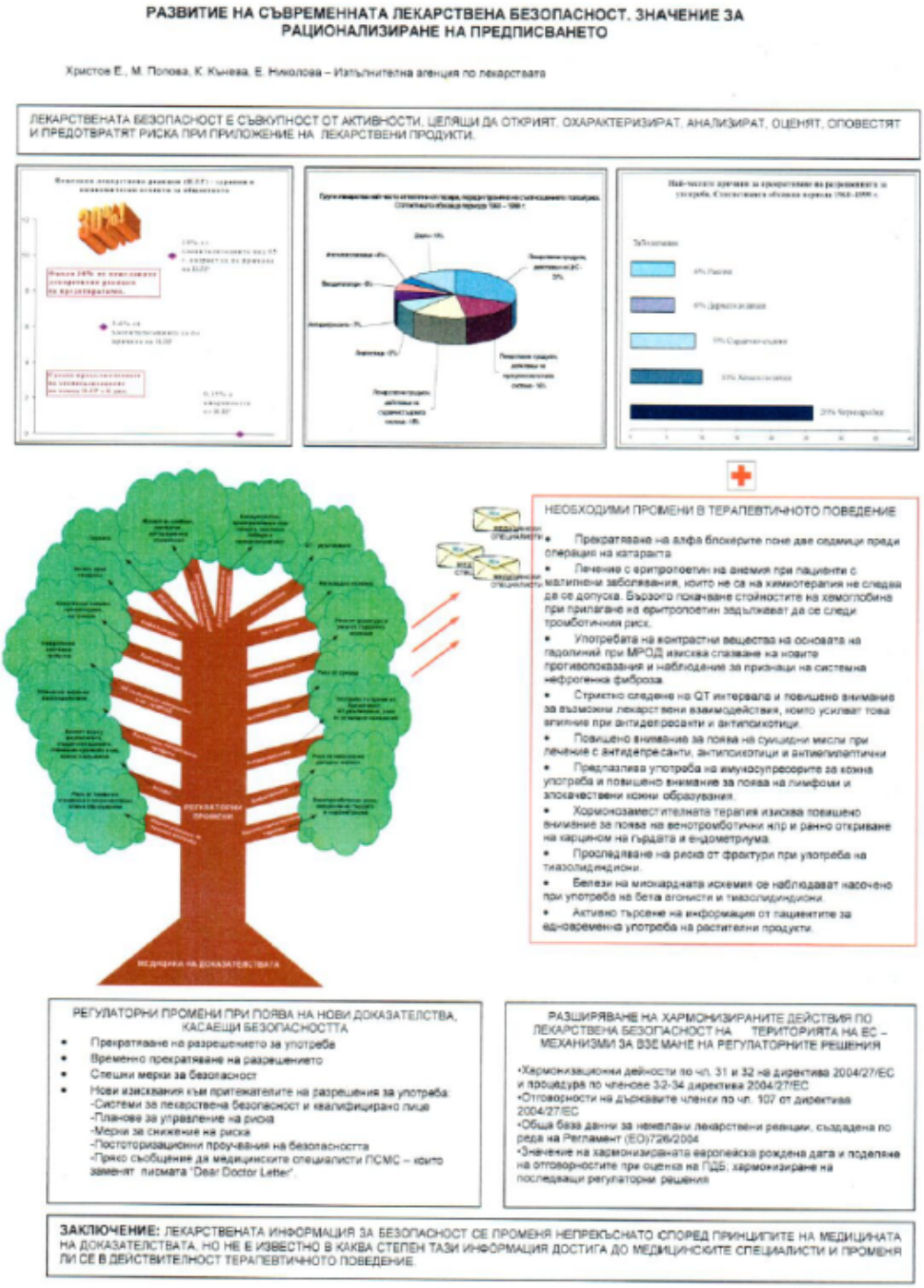


Figure 1. Poster presented at annual congress of clinical pharmacology

Another example used by BDA through a publication is about dispelling 10 myths and unsubstantiated arguments around the reporting of suspected ADRs. This approach is also used for pharmacy students via a presentation annually for those specially interested in suspected ADRs. NCAs may wish to consider adapting and tailoring this to suit their needs.

Table 1. Ten unsubstantiated arguments and myths about ADR reporting, and the response to dispel the argument (adapted from BDA article and presentation for SCOPE WP4.3)

Ten arguments and myths about suspected ADRs	
Argument/myth	**Answer**
1. I am not sure that the reaction is related to the medicinal product use.	It does not matter if you are uncertain whether a reaction is associated with the medicine being taken. Even if you only have a 'suspicion' that this is the case, then you should report. Please do not be put off from reporting simply because you are not certain about cause and effect.
2. There are many data about the patient that are not known to me.	Please do not be put off reporting if you do not have the full patient information. A report is considered valid if it contains the minimum 4 pieces of information: a) A patient identifier (minimum one piece of information is needed e.g. initials, patient identification number, date of birth, age, age group or gender etc.) b) A suspected drug c) A suspected adverse drug reaction d) Reporter details If in doubt, please report.
3. I am not sure that providing such information, about the patient, is legal.	Patient names and date of birth are not included on reports. Information is kept confidential and patient identity is not disclosed during reporting. Only patient initials, age or gender are needed to report a suspected ADR.
4. I wouldn't like to be held responsible for inappropriate treatment based on the provided data.	ADR reports are not used for monitoring professional commitments. BDA specific – it is important to avoid any misuse of reporting. Reports received are only considered as valid after confirming it with the reporter.
5. I don't want to have any trouble with the manufacturer of the medicine.	Pharmaceutical companies (Marketing authorisation holders) are interested in collecting the data on suspected ADRs. They are legally required to do this as part of their PV activities. A lack of safety reports is considered as an unfulfilled commitment to patient safety.
6. The medicine is new and therefore reliable, so I don't think it's possible to have any severe ADRs.	All medicines are carefully monitored after they are placed on the EU market. If a medicine displays a black triangle, this means that it is being monitored even more intensively than other medicines. This is generally because there is less information available on it than other medicines, for example because it is new to the market, or there is limited safety information on its long-term use.

Ten arguments and myths about suspected ADRs	
Argument/myth	**Answer**
7. I have strong clinical experience with the medicine so any reaction that presents itself can't be associated with the medicine.	There are many very rare and serious ADRs which may not be seen by every HCP in their practice. Sometimes ADRs can occur after months or years of taking a medicine, and therefore it is very important to report suspected ADRs.
8. I do not have an ADR reporting form.	Reports can be made by [NCAs can insert their methods to report a suspected ADR]
9. I don't have enough time to report all suspected ADRs.	It is considered a HCPs professional responsibility to report suspected ADRs. Please report: • All suspected ADRs to drugs that display a black triangle (▼) • For established drugs and vaccines report all suspected ADRs that you consider to be serious. They should be reported even if the effect is well recognised. Serious reactions are those which are: • Fatal • Life-threatening • Disabling • Incapacitating • Have resulted in, or prolonged, hospitalisation • Considered medically significant by you • A cause of congenital abnormalities
10. I don't believe that reporting has any benefit to me or my patients.	All medicines have the potential to cause ADRs. Reporting allows an early warning system for the identification of previously unrecognised suspected ADRs. It also provides valuable information on recognised ADRs, allowing medicines regulators to identify and refine the understanding of risk factors that may affect the clinical management of patients. The value of the reporting suspected ADRs has been demonstrated many times and it has helped to identify numerous important safety issues that were not known about before being reported.

Croatia

Strategy on raising awareness of national ADR reporting system

The strategic plan has been made on an annual basis so far by the Croatia's medicines Agency, 'HALMED'. HALMED conducts numerous activities aimed at raising awareness of ADR reporting among different groups of their stakeholders. Activities have included the development and distribution of leaflets on ADR reporting, conducting a public education campaign, providing technical solutions for facilitating the process of suspected ADR reporting i.e. introduction of UMC's online application for patient ADR reporting, workshops for HCPs, collaboration with patients and their organisations, media campaigns, printing booklets and leaflets, and participating in congresses.

From year 2014 onward, their strategic plan was prepared for a 5-year period covering 2014-2018. The raising awareness related elements are enveloped within the general strategic plan which include:

- Section 2.3; Values – subheading: 'we are patient and public health oriented'- The patient and their needs are always the focus of HALMED's interest, bearing in mind that only high quality work, as well as prompt reactions contributes to public health well-being.
- Section 2.9; Networking and communication – identification and engagement with all of HALMED's stakeholders to build a stronger and more advanced system to answer to all the demands of their stakeholders in a more efficient manner.
- Section 3.1.1, 3.3.1 and 3.3.3.

Section 3 of the HALMED document describes each of its strategic goals in detail. It is a well thought out method of approaching objectives. For each, HALMED outlines a specific objective, its strategy, action steps, prerequisites, responsibility, evaluation of indicators and time. Specific to raising awareness of ADR reporting systems the following are highlighted:

Goal #1 – to contribute to the safety and quality of medicines and medical devices through effective risk management and market surveillance

- Section 3.1.1 – Objective #1.1; To ensure the continued and high quality monitoring of adverse reactions/events concerning medicinal products and medical devices in the territory of the Republic of Croatia

- Action step
  - Develop a training programme to support the increase in patient and healthcare professionals reporting adverse reactions for medicines and adverse events for medical devices by enhancing public awareness on the importance of reporting.
  - Support scientific efforts in the field of pharmacovigilance and rational pharmacotherapy with the inclusion of information on pharmacogenomics.
  - Collaborate with healthcare professional bodies, patient associations and academia in education training programmes.
- Prerequisite
  - Preparedness and willingness for collaboration on the part of national and international institutions and bodies, as well as healthcare professionals and patient associations.
  - Sufficient and well educated and trained staff.
  - Allocation of financial resources.
  - Adequate IT tools.
- Responsibility
  - The Head of the Department is responsible for implementation
- Evaluation of indicators
  - Increased levels of adverse reaction reports, including serious adverse reaction reports with higher quality information received from patients and healthcare professionals.
  - HALMED has developed strong links with other national and regional institutions and patient associations involved in patient safety and works closely with them to maximise patient safety.
  - With the help of an on-line tool, adverse reaction reporting by healthcare professionals is increased and report quality is improved.
  - HALMED is recognised as a relevant and useful source of information on safe medicines by healthcare professionals and patients.
- Time
  - All the actions regarding this objective will start in the year 2014 and are supposed to be finished by the end of 2018.

Although there is no specific ADR reporting mention, HAMLED indicate that the following sections form the baseline for increasing awareness level activities and increasing ADR reporting from patients:

Goal #3 To deliver transparent, pertinent and well-timed communications to patients, public and healthcare professionals

- Section 3.3.1 – Objective #3.1; Prompt public oriented communication on safety, efficacy and quality issues
- Section 3.3.3 – Objective #3.3; Patient associations, healthcare professional organisations and public engagement strengthening in the activities of HALMED.
- Strategy for the objective
  - The Public Relations Office will develop suitable communication tools that will enable patient associations, healthcare professional organisations and the public to be more deeply involved in the activities of HALMED in relation to safety, efficacy and quality issues of medicinal products and medical devices.
- Action steps
  - Review patient and public engagement models of other regulatory and state agencies and implement a plan for the more profound involvement of patients in regulatory activities of HALMED.
  - Improve collaboration with patient associations and healthcare professional organisations.
  - Strengthen the possibilities of public involvement through new media.
- Prerequisites
  - Well-established cooperation with national patient associations and other national organisations with a specific interest in medicinal products and medical devices.
- Responsibility
  - PR will be responsible for the implementation of Objective 3.3.
- Evaluation of indicators
  - Public and patient representatives are engaged in the activities of HALMED and their knowledge, experience and views are taken into account in decisions and communications.
- Time
  - All the actions regarding this objective will start in the year 2014 and are supposed to be finished by the end of 2018.

Strategy guidance document Annex 1 – HALMED Strategic Plan 2014-2018

Suggestion 4 – consider developing a mobile application for ADR reporting

On 18 May 2016, HALMED launched its app to report suspected ADRs for HCPs and the patients. HALMED organised a media conference to launch the app in Croatia and was picked up by a TV channel and media[1].

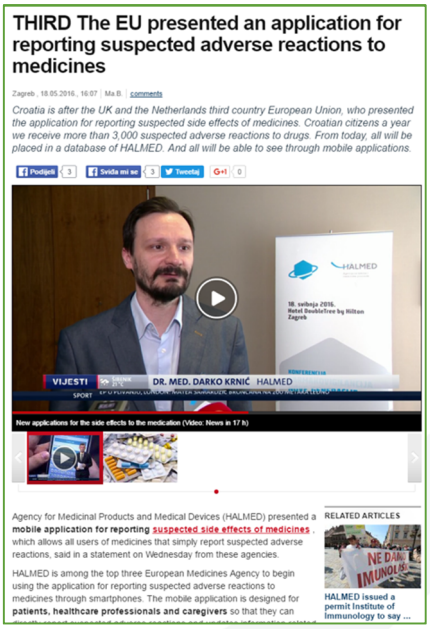


Figure 2. HALMED raising awareness of its new mobile app for suspected ADR reporting publicised via national media and video

Suggestion 5 – consider creating a QR code to link to the national ADR reporting site for promotion

As part of HALMED's 2013 public campaign, QR codes were integrated into adverts published in daily newspapers and specialised magazines, as well as in information leaflets distributed to pharmacies, to encourage ADR reporting, reading the PILs and accessing the information on the safe use of medicines. HALMED used QR codes in two ways for promotion.

Promotional materials used to highlight the importance of PIL reading included a man having trouble assembling a piece of furniture without instructions. The wording and image suggested on the poster inferred that one shouldn't assemble furniture without instructions and, likewise, that one shouldn't take a medicinal product without reading the PIL. The advert was published in daily newspapers and specialised magazines. The posters highlighted what the PIL is and why it should be read. HALMED's contact details were also included along with QR code directing patients to the patients section on HALMED's website.

[1] http://dnevnik.hr/vijesti/hrvatska/halmed-lani-25-posto-vise-prijava-nuspojava---385020.html accessed 26 May 2016

Figure 3. Advertisement aimed at promoting importance of PIL reading

Figure 4. Advertisement aimed at promoting importance of ADR reporting

A similar poster was used to also raise awareness about importance of ADR reporting aimed at women. The poster included a housewife with burned T-shirt, suggesting that, similar to housewife not taking a burned T-shirt lightly, one should, more importantly, pay close attention to suspected ADRs and report them. Adverts were published in daily newspapers and specialised magazines with messages of how to report suspected ADRs to HALMED alongside the QR code which led patients directly to online application for ADR reporting (https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=HR).

The same approach was used for promotional information leaflets on how to report suspected ADRs which were distributed in the pharmacies throughout the country as part of the campaign. The detailed information on the other side of the leaflet covered the importance and procedures for reporting, what happens to a report and addressing reporter confidentiality.

Figure 5. Information leaflets on how to report ADRs were distributed in the pharmacies throughout the country as part of the campaign

Suggestion 7 – have downloadable ADR reporting forms and materials for raising awareness

Figure 6. An example of information on the HALMED website, including sections for patient and HCPS, downloadable links and information about medicines.

Suggestion 8 – develop case studies showing the importance of reporting

Case studies are used mainly for presentations with HCPs at congresses or during post graduate education. The use of high impact images within a PowerPoint slide is a common approach, which aims to resonate with the reporter to leave a lasting impression about the importance of ADR reporting.

An example that works very well in Croatia is the thalidomide story, used to represent lack of awareness and the impact of underreporting. The slide deck shows the history of thalidomide with at least 13 images of children affected by phocomelia and 2 adult photos.

Another is the example of a patient that experienced rib fracture as a result of severe coughing after taking multiple ACE-inhibitors, which is used to educate HCPs on the importance of reporting drug interactions.

HALMED tries to present the most recent and striking example images from case reports. DHCPs are a good basis for finding real life examples from HALMEDs database or from literature cases. Some examples include: cases of gastrointestinal and serious skin reaction reactions with piroxicam; the risk of osteonecrosis of the jaw with bisphosphonates; and potentially life-threatening side effects after accidental exposure to transdermal patches containing fentanyl.

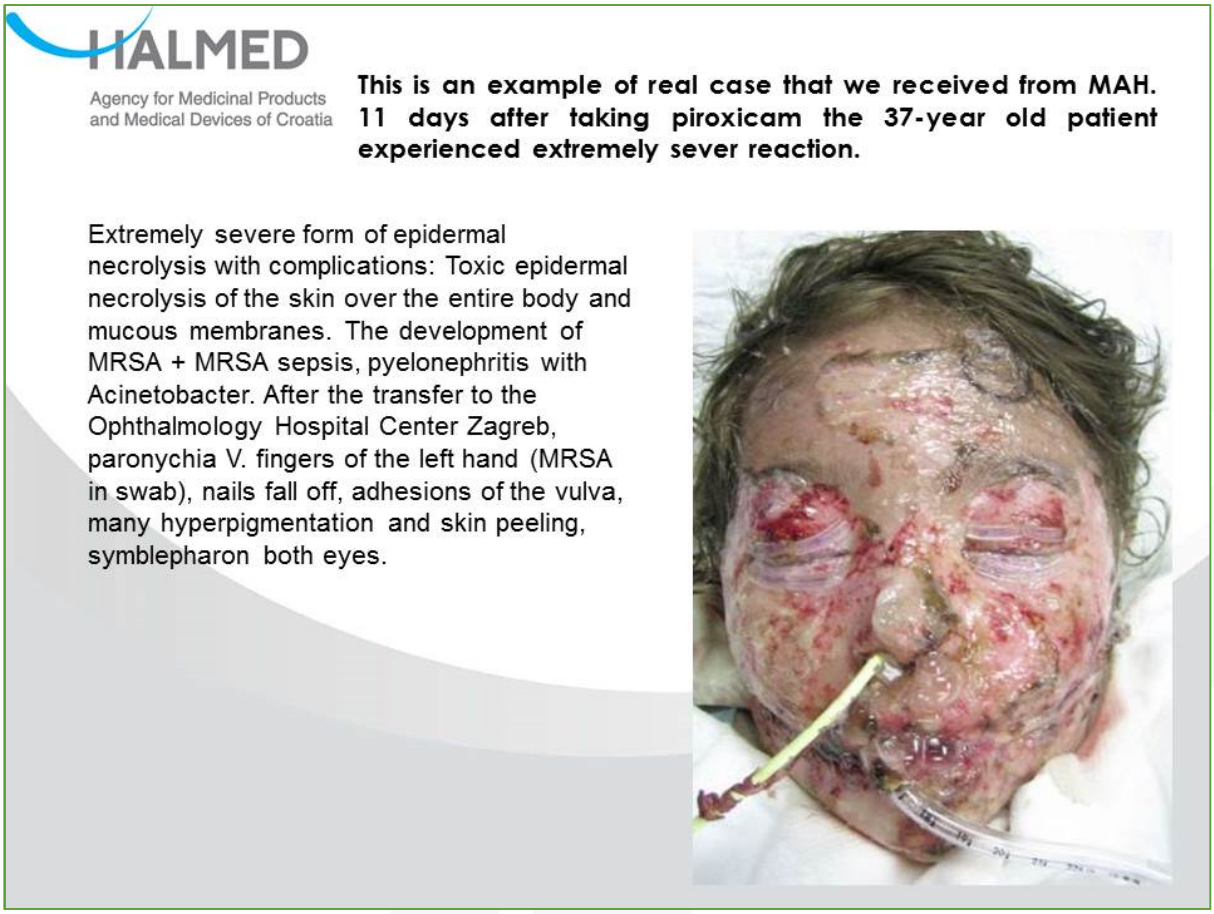


Figure 7. An example PowerPoint presentation from HALMED that showcases a case study of suspected toxic epidermal necrolysis (TEN)

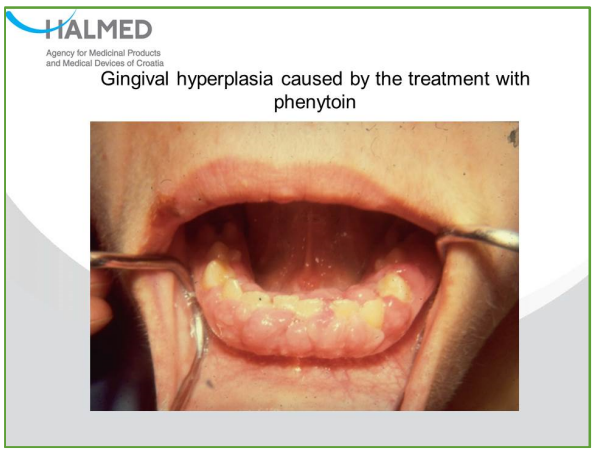


Figure 8. Second vivid example; gingival hyperplasia – used to show the importance of reporting suspected ADRs

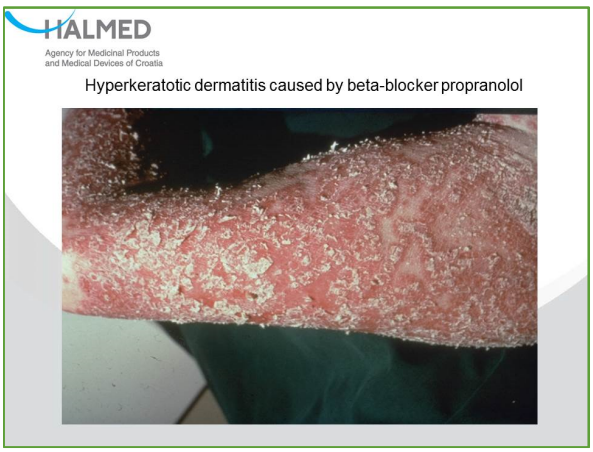


Figure 9. Third vivid example; hyperkeratotic dermatitis – used to show the importance of reporting suspected ADRs

Alongside such case studies a presentation describes the entire PV process, from collecting reports to signal detection. It also gives the final impact on the patient, any regulatory action from PV and the effect to the health system. The presentation brings together pieces of as many aspects as possible to provide an overview of PV, especially the importance of reporting suspected ADRs.

Suggestion 9 – develop an e-learning module on ADR reporting for HCPs or use the SCOPE package

Updated at least annually, or when required, a learning package has been developed in co-operation with a working group of PV staff within the pharmaceutical industry. It gives a general basic knowledge and the legal background of PV. It also describes interesting case reports to facilitate a better understanding about reporting and also to raise the awareness of different topics such as ADRs associated with bisphosphonates.

Suggestion 11 – educate reporters locally – consider using regional centres

As part of HALMED's educational strategy, it aims to encourage and facilitate suspected ADR reporting. Its activities include a series of regular workshops for HCPs and Qualified Persons responsible for PV. HALMED staff use such workshops to educate these target groups on the national PV system and how to report suspected ADRs. At the time of the 4.3 survey report HALMED had organised a total of 90 workshops. These workshops have been attended by nearly 1,600 HCPs and MAH representatives.

Suggestion 15 – recognise and reward reporting – CPE points for medics and pharmacists

In this respect, HALMED mainly focuses its efforts with medical doctors and pharmacists. There are three main ways in which HALMED rewards reporters:

- Continuous professional education (CPE) points for medical doctors and pharmacists who report suspected ADRs

  HALMED has obtained the authority to issue CPE accreditation from the Croatian Medical Chamber and Croatian Chamber of Pharmacists for suspected ADR reports from doctors and pharmacists. Reporters receive an individual response from HALMED containing with specific scientific information relating to their suspected ADR report. This is considered a form of CPE and therefore accredited. HALMED maintains a database of ADR reporters to assign the correct number of CPE points to each reporter.

- Workshops for medical doctors and pharmacists about ADR reporting, which are also accredited with CPE points

  Workshops are organised at no cost for doctors and pharmacists upon request from a hospital and participants are also accredited with CPE points. Usually there are several workshops per year and the common topics include the concepts of basic PV, a description of the national ADR reporting system, how to report, the importance of reporting, and any specific issues requested by the hospital. For example, an overview of ADRs from a specific therapeutic class or ADRs relating to specific organ system. Based on the feedback from reporters and workshop participants, CPE credits are considered to be an effective way of motivating doctors and pharmacists to report in Croatia.

- Rewards for pharmacists who report the highest number of ADRs in the previous calendar year

  Rewards are given annually to the top three pharmacists that report the most suspected ADRs within the last calendar year. Rewards include professional books, Croatian Pharmacopoeia subscription or education – for example participation at congresses or conferences within a pharmaceutical area. Rewards are presented at the annual conference of the Croatian Pharmaceutical Society and seem to be well recognised and popular among pharmacists, based upon the feedback from participants at the conference. The Annual Conference of Croatian Pharmaceutical Society is usually well attended and is used as a good medium to engage reporters and motivate them to report.

HALMED considers the support of Croatian Chamber of Pharmacists and Croatian Pharmaceutical Society as key for raising awareness and motivating pharmacists to report.

It is believed that the actions described above have contributed to an increase in pharmacy reporting. Other activities might also have contributed, such as HALMED's public education campaign on the importance of suspected ADR reporting and reading the PIL. Although the campaign that was conducted at the end of 2013 was directed primarily at the patients, it was at a national level and is thought to have contributed to the increase in reporting.

Based on this success, HALMED has plans to establish similar collaborations with other HCP bodies and their respective societies, with a particular focus on motivating medical doctors to increase suspected ADR reporting.

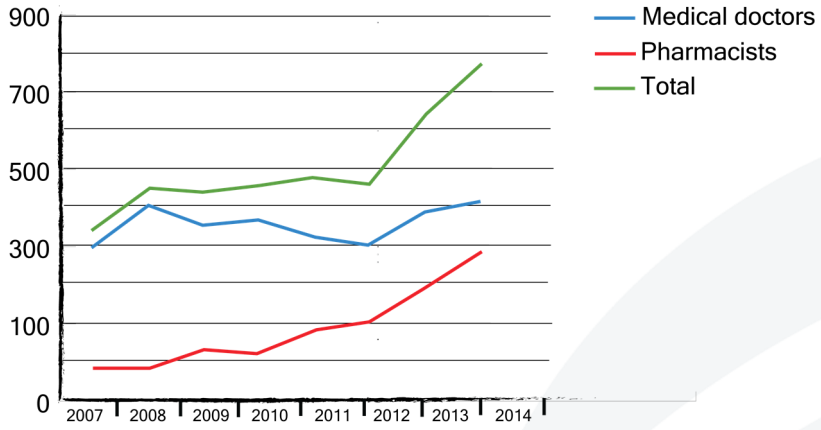


Figure 10. Number of HCP reporters for the period from 2007 to 2014

The graph above shows the total number of suspected ADR reports increasing between 2007 and 2014, especially since 2012; due to the increased number of suspected ADR reports received from pharmacists.

Information on NCA's websites

The main channel for distributing information on reporting for HALMED is through its website[2]. It includes several sections dedicated to the process and importance of suspected ADR reporting. Guidance documents for reporting are also available such as guidelines for patients within the 'For Patients' section, and it can also be reached via a central banner featured on the homepage. The guidelines for HCPs like most NCAs are found within the 'Pharmacovigilance section'. There are also specific sections for finding new safety information, and professional and scientific events.

Information on reporting requirements for MAHs is also available in the same section, in a Q&A format.

[2] http://www.halmed.hr/en/Farmakovigilancija/ Accessed 5 April 2016

Instructions for reporting are adapted in line with the group of reporters they are directed to, and explain the reporting requirements in detail. In addition, there is a special section of the website dedicated to 40 years of spontaneous ADR reporting in Croatia. The section contains a number of informative texts aimed at making users and patients more familiar with the importance and procedures of suspected ADR reporting as well as with the system of monitoring the safe use of medicines in Croatia.

Radio

Through HALMED's 2013 public education campaign radio advertisements were developed to promote suspected ADR reporting. Two examples of the radio advertisement scenarios aired during the campaign are provided below:

Radio advertisement on the importance of ADR reporting

[humming sound of lawn mower] This new lawn mower is working so smoothly, it's precise; its blade is so sharp… [small explosion sound] What?! Smoke?! It's getting out of control! [loud noise] Not the roses!!!

Sometimes the things that function perfectly can also have unwanted effects; even the medicines. If you notice a side effect while using the medicine, report it as soon as possible.

You can report side effects to medicines and find additional information on safe use of medicines at www.halmed.hr.

HALMED – the Agency for Medicinal Products and Medical Devices.

Radio advertisement on the importance of reading the patient information leaflet

[sound of hammering and drilling] If it is not assembled according to the instructions, a nicely connected piece of furniture will not remain stable for too long. [sound of the closet falling apart]

And if you take a medicine without reading a patient information leaflet first, it might not work properly, either. Before taking your medicine, always read the patient information leaflet and use the medicine according to the instructions provided therein.

You can find additional information on safe use of medicines at www.halmed.hr.

HALMED – the Agency for Medicinal Products and Medical Devices.

Theatre production – a focus on paediatrics

In February 2015 HALMED introduced an innovative collaboration with a children's theatre (called Mala scena) to promote the importance of ADR reporting. It was aimed at children, the young and adults.

The play was called: 'No, Not You! Or on Differentness' and is about the stigma associated with those affected by epilepsy and ways to cope with the condition. The play is primarily intended for school children and young people attending the theatre. Leaflets are distributed to spectators at every performance. These are educational, which enables the continuation of dialogue after the play with details of relevant information on suspected ADRs and reporting.

It is the first play in Croatia to motivate children and their parents to think about epilepsy and side effects. A more detailed description of the play can be found here.

Figure 11.Three images from theatre production through which HALMED promoted reporting

Photographs of the play can be accessed by clicking here.

Campaign case study: Patients

Run for nearly two months, from 5 September 2013 to 31 October 2013, HALMED's public education campaign promoted the importance of ADR reporting and Patient Information Leaflet (PIL) reading. Although directed primarily at patients, the campaign also increased the number of suspected ADR reports from HCPs and contributed to a more comprehensive media approach to issues related to medicines safety.

During the first month of the campaign, billboards were set up by the main roads and highways across the country with striking images and memorable messages. Similar advertisements were repeated at regular intervals in different daily newspapers, as well as on selected radio stations, while on-line banners were also selectively placed on news portals and on the websites of several patient organisations as a result of collaborative working with other organisations.

The second part of the campaign included pop up stands set up in pharmacies nationally. They were supplied with information leaflets on how to report ADRs. Simultaneously, posters encouraging patient reporting were sent where patients would see them in a trusted healthcare environment. For example, in patient waiting rooms at GP surgeries, paediatric, dental and gynaecological waiting areas in healthcare centres. The poster is also available on the HALMED website.

The language used in the promotional materials was intended to be user-friendly and have analogies to real life situations. This enabled messages to be perceived more intensely and clearly by the wider target group (patients from socio-demographic groups). Visual images included a housewife with a burned T-shirt compared to a medicine causing a side effect, while the importance of PIL reading was illustrated through a man having trouble assembling a piece of furniture without instructions. When setting up the most appropriate messages, and ways of presenting them, a consideration was that women are more common reporters than men, thus the messages were primarily directed towards women.

Figure 12 – English translation of the analogy of real life situations to make messages about medicines to be perceived more clearly by a wider target groups

Figure 13 – the same image on a billboard in Croatia

QR codes were also included within some promotional materials which linked directly to the online reporting site.

Figure 14. A similar concept about men – stressing the importance of reading the PIL for a medicine illustrated by a man having troubles assembling a piece of furniture without instructions

Figure 15. Example leaflet that was distributed to pharmacies for patients. It describes how to report ADRs

HALED's website is used as one of the main platforms for promoting the key campaign messages. The website section, For Patients, can be accessed from the home page. It offers a direct link to the suspected ADR reporting site and is also promoted as a source of information for patients to access within the banners used in the campaign. Similar information was also included within HALMED's newsletter.

The campaign was supported by PR activities that included holding a press conference and sending a press release to the media at the launch. A number of different media statements and interviews were also organised to increase awareness of the campaign and promote suspected ADR reporting. The campaign also served as a platform for new collaboration opportunities. This included engaging specialised health magazines and various patient organisations to place adverts, publish articles and information on their respective web pages, and receiving direct feedback.

Other campaign materials can be found here.

Online reporting promotion

Since the introduction of the Uppsala Monitoring Centre's online patient ADR reporting tool in August 2012 which HALMED adopted, the number of patient reports were low and static. Numbers only started to increase once HALMED proactively began to promote the fact that Croatia was the first country in the world to implement and start using the reporting tool. Nearly three times as many reports were received compared to the year before (45 to only 16 reports in 2011). This was made possible via a press release and news item on the HALMED website. The news was subsequently covered by many different media sources.

A direct link to reporting tool is available on the HALMED website; it is positioned within the PV and 'For Patients' sections, and it is additionally made visible via the central banner on the homepage. Furthermore, HALMED has worked with relevant health related websites (e.g. www.cybermed.hr), patient organisation websites (e.g. www.rijetke-bolesti.hr) and learned societies websites (e.g. www.farmaceut.org) to link to it.

Measuring success

HALMED measures awareness activities through systematic monitoring of media coverage, tracking the changes in number of suspected ADR reports, tracking the number of enquiries related to medicines safety, and the use of web analytic tools (e.g. number of website visitors and visits etc).

HALMED's previous positive experience of a campaign confirmed the correlation between the media coverage and changes in patient reporting rate. This was taken into account and the same impact was observed by HALMED in its next campaign in 2013. The number of ADR reports before and after the campaign were compared: Prior to the campaign between 1 January and 4 September 2013, 59 patient reports were received. Within two months of the ongoing campaign 49 patient reports were received. This marked around a 3.5 fold increase in the number of patient reports per month in comparison to the pre-campaign period. Although small in number, compared to the year before, there was an overall 300% increase in number of patient ADR reports in 2013. More than half of these reports were received via the online application for patient reporting. The campaign results were subsequently presented in Uppsala Reports 66, July 2014 edition[3] since it was using the UMC's patient application tool.

The increased rate of patient ADR reporting is sustained. HALMED attributes this to the successful campaign as it achieved a more permanent position and impact on patient reporting of suspected ADRs in Croatia.

[3] http://www.who-umc.org/graphics/28198.pdf - Uppsala Reports 66, July 2015, pg14

In 2014 there were a total of 187 suspected ADR reports received directly from patients – the highest number it had received at the time of submitting this information. The numbers of patient reports still accounts for the same proportion in the total number of spontaneous suspected ADR reports received by HALMED at 6%. This is because the campaign also resulted in an increase in direct suspected ADRs received by HCPs. Total numbers of suspected ADR reports increased by 25% (621 reports) in 2014 compared to 2013. The number of patient related enquiries reported also greatly increased as a result of the campaign.

HALMED indicated that the campaign not only brought about an increase in the number and quality of patient and HCP reports of suspected ADRs but also contributed to a more comprehensive, informed and balanced media approach in the coverage of issues related to medicinal product safety. This was observed by the systematic monitoring of press articles performed daily by HALMED's Public Relations Office. Extensive media coverage during the campaign was observed using the same method.

Finally, using the Google Analytics tool, HALMED monitored and analysed the number of web page visitors its website. This included all the web pages used within the campaign through the use of QR codes and general URLs directing patients and HCPs to awareness raising material and safety information about suspected ADRs. There was a noticeable increase in number of web views and unique viewers during the second, more intense part of the campaign, as well as in the immediate period following the campaign. Such numbers remain sustained.

Czech Republic

Videos, postcards and posters

The second campaign run by SUKL commenced in January 2014 until March 2015. It was aimed at doctors, but also extends to patients, the general public and pharmacists.

SUKL developed postcards for doctors and pharmacists. Using visual humour in the form of a cartoon, it was a good way of raising awareness. The accompanying letter included information about suspected ADR reporting. The postcard also drew attention to SUKL's website for reporting and to the PV Newsletter on the back of the postcard.

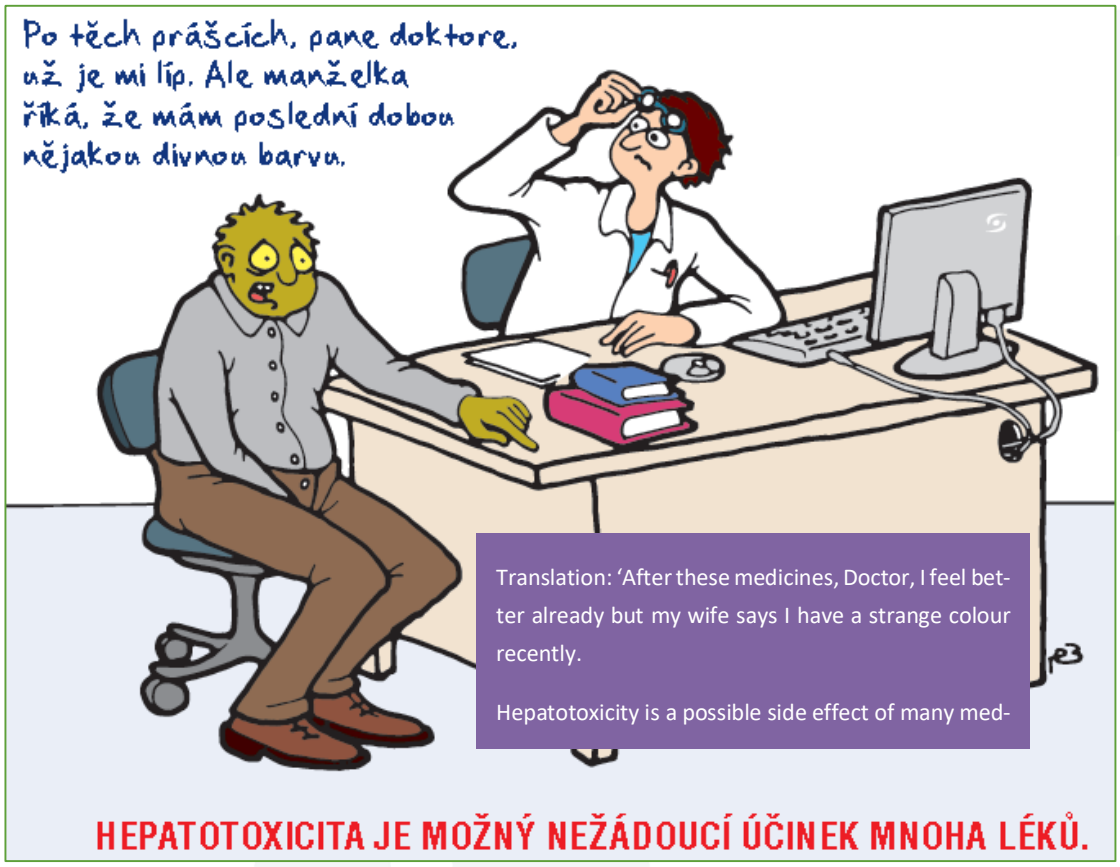


Figure 16. A postcard distributed to doctors and pharmacists which highlights serious side effects and where to report them

The SUKL PV department publishes a newsletter[4] 4 times a year with new safety information about medicines. SUKL now also publish a number interesting cases reported to the Agency in each newsletter, intended to raise reader's awareness about reporting suspected ADRs.

[4] http://www.sukl.cz/sukl/nezadouci-ucinky-leciv-informacni-zpravodaj - SUKL's PV newsletter; accessed 10 June 2016

Other information materials are available on SUKL's website dedicated to patients[5] SUKL have developed interesting promotional materials. Although not specifically for suspected ADRs they are linked by reporting to the NCA, which captures such information through its reporting scheme. The materials are more specialised counterfeit products and buying medicines online.

'Nebezpecneleky' translates to 'dangerous medicines' and 3 videos have been developed to highlight the importance of medicines safety. These are supported by a website, posters and Facebook for the campaign:

- http://www.nebezpecneleky.cz/silak ('silak' translates to 'strong man')
- http://www.nebezpecneleky.cz/hubena ('hubena' translates to 'lust')
- http://www.nebezpecneleky.cz/stydlin ('stydlin' translates to 'shame-face')

Figure 17. Three posters highlighting dangers of counterfeit medicines, purchasing online medicines and encouraging reporting

[5] www.olecich.cz – patient dedicated website in CZ, accessed 10 June 2016

Figure 18. Posters distributed to pharmacies – further reinforcement of dangers of buying online medicines and the effects they can have – the right thing and the wrongs things to do; raising awareness about SUKL

This campaign was supported digitally through twitter and via a Facebook page: https://www.facebook.com/Nebezpe%C4%8Dn%C3%A9-l%C3%A9ky-118391661523844/

As a result of these campaigns SUKL is facing the rapid increase of the patient reports.

Further plans for SUKL relating to strategy and promotion include:

- Continuing the education of HCPs to become familiar with why and how to report suspected ADRs.
- Development of a plan for TV or a radio broadcast
- An e-learning set for HCPs
- Plans for medical students to make them familiar with the suspected ADR reporting system prior to leaving University to begin their clinical practice.

Campaign case study: Physicians

The State Institute for Drug Control ('SUKL') conducted their first campaign in October 2009 to December 2010 targeting physicians and their associated bodies. The campaign was focused on GPs and paediatricians to increase awareness of ADR reporting as they usually are the first to come across suspected ADRs.

Promotion occurred through workshops and seminars. A series of seminars for paediatricians were held in 6 towns, and awareness was raised through expert conferences and articles in selected health journals. A short patient video was also developed that was displayed on TV monitors in GP and hospital waiting rooms. Hundreds of campaign materials of posters and small stickers were distributed to health centres and practices. This helped to increase the number of suspected ADR reports from these reporter groups.

Translation:

'Suspected adverse Drug Reaction in a patient?'

Report it!

Everything you need can be found at:

http://www.sukl.cz/nahlasit-nezadouci-ucinek

(SUKL contact information)

Figure 19. Small stickers sent to physicians during the SUKL campaign

Figure 20. The URL in the sticker points to a more detailed PV page on SUKL website

Translation:

You have suspected an adverse drug reaction in a patient?

Have you come across a serious ADR?

(serious criteria listed)

Have you come across an unexpected side effect with a medicine?

• recognised side effects are described in the PIL or SPC

Have you ever come across a severe situation that impacts the health of the patient?

• misuse of overdose • use outside the approved indication • Inefficiency of medicine

…Report a suspected ADR State Institute for Drug Control

Everything needed for a report can be found at: http://www.sukl.cz/nahlasit-nezadouci-ucinek

Please report anything you consider unusual or different. When reporting the suspected ADR, you need not be convinced that the adverse effect was caused by a drug!

Thank you for helping to ensure the safety of medicines!

(SUKL contact information follows)

Figure 21. A more traditional campaign poster to raise awareness with HCPs and increase reporting

Denmark

Suggestion 15 – recognise and reward reporting

Competition for medics

The Danish Medicines Agency ('DKMA') ran a competition in 2015[6] as part of their campaign for increasing suspected ADR reports from doctors and medical students. Winners of the National Board of Health competition: 'make medicines safer – report side effects', were given prizes in the form of tokens e.g. for academic books that were awarded to six individuals from four universities including the University of Copenhagen, Aarhus University, and Aalborg University.

Suggestion 21 – publish ADR trending data to encourage promotion and research

Using a press news item, the DKMA published an article announcing an increase in the numbers of suspected ADRs it received in 2015. This news item also contained a hyperlink to its annual report that was published on its website.

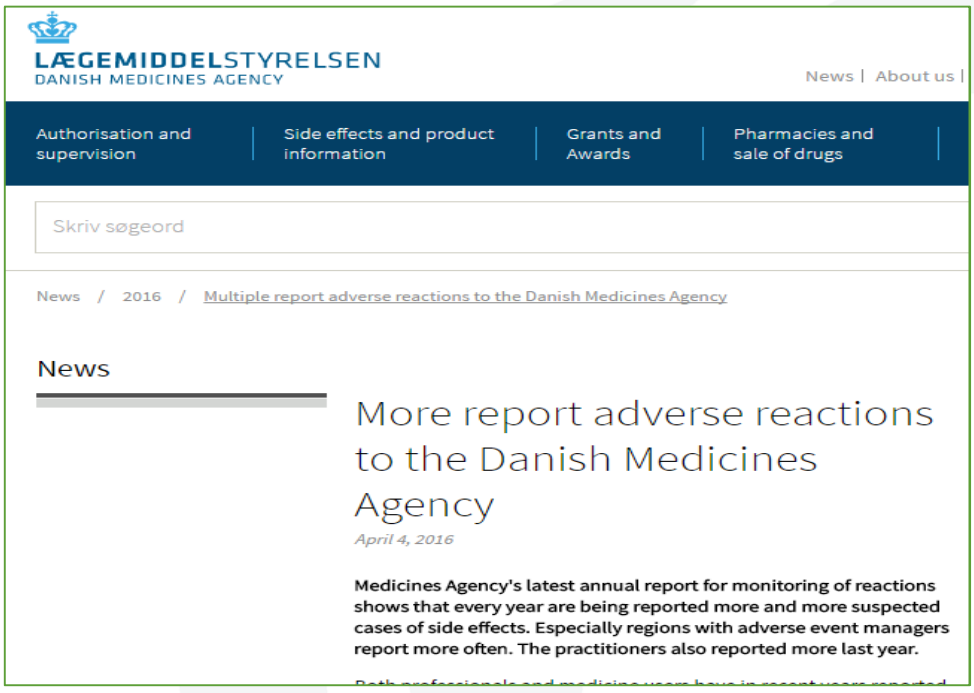


Figure 22. Danish Medicines Agency publish annual trending ADR data via news item[7]

[6] http://laegemiddelstyrelsen.dk/da/om/kampagner/goer-medicin-mere-sikker-meld-bivirkninger/konkurrence accessed on 24 March 2015

[7] http://laegemiddelstyrelsen.dk/da/nyheder/2016/flere-indberetter-bivirkninger-til-laegemiddelstyrelsen; Accessed 13 April 2016

Suggestion 24 – explore and maximise any promotional opportunities for joint collaborations and partnerships; aim to promote through low/no cost outward facing communication channels

Collaboration with NHS and affiliations around surveillance programmes.

Learning website with videos

Through collaboration with other organisations, the DKMA has developed a learning website, presenting videos on the importance of reporting suspected ADRs: www.meldenbivirkning.dk. Users are guided through the process of creating a report via another video, and have the opportunity to test themselves and their knowledge of side effects. Finally, users can get answers to some frequently asked questions.

Figure 23. Screenshot of the video showing different staff from the DKMA and other prominent champions explaining the importance of reporting side effects; http://greatdanefilm.dk/web/laeger/20102011bivirkning/

Figure 24. Screenshot of the video of a Danish hospital doctor showing how easy it is to report a side effect; http://greatdanefilm.dk/web/laeger/20102011bivirkning/

This learning website aimed at HCPs also describes the work flow of what happens to an ADR report when sent to the NCA through interactive illustration, some FAQs, and related links.

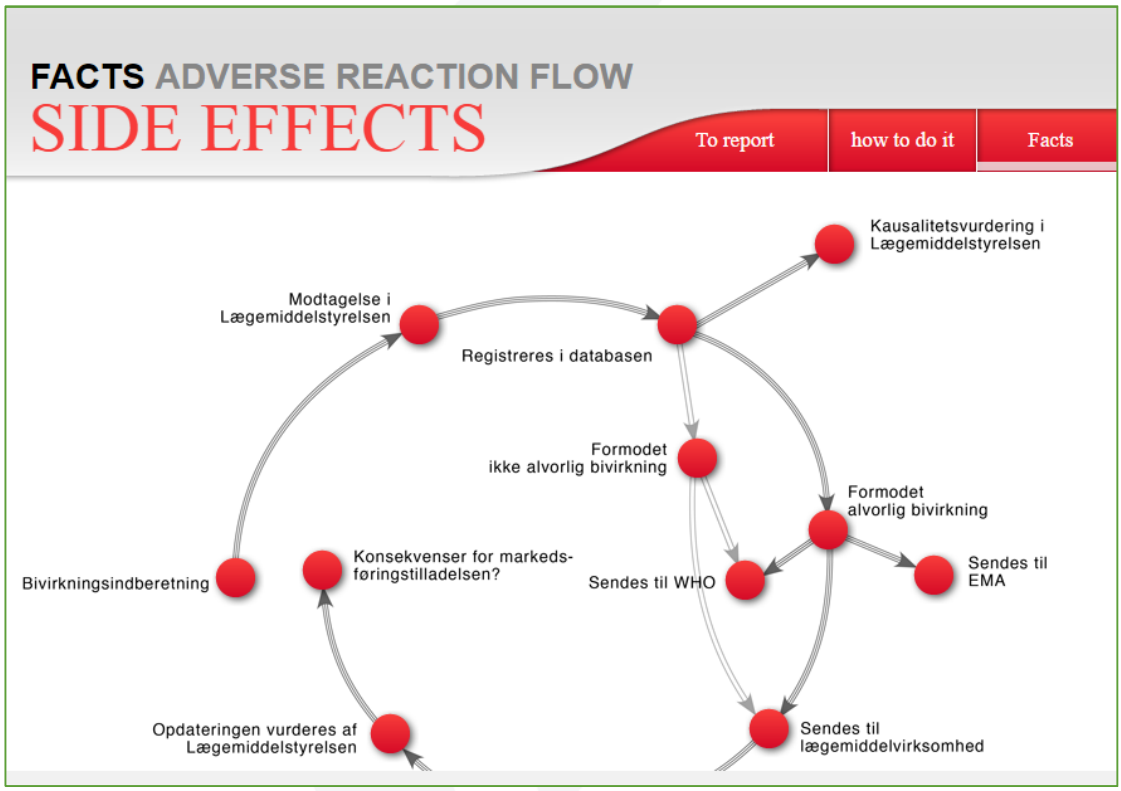


Figure 25. ADR workflow on the learning site (only in Danish)

Campaign case study: Doctors in general practice and medical students

The 'Make medicine safer' campaign in collaboration with the Board of Health targeted doctors in October 2015. Messages included the importance of reporting suspected ADRs to help make medicines safer. The campaign also was also aimed at medical students to explain reporting guidelines and the importance of reporting. The campaign was launched to reverse a declining trend in the number of reports from the GPs. The decline coincided with the number of reports generally increasing. The campaign was part of the DKMA's Action Plan III for enhanced PV in 2014-2015.

A preliminary survey with GPs via a small-scale telephone questionnaire was conducted to ascertain current knowledge and experience of reporting. Participants were found an external communication bureau and via networks. Results showed the barriers GPs face are a lack the time and belief that reporting is too burdensome. In addition, the survey found doctors lack general knowledge about reporting suspected ADRs, guidelines to report and what the suspected ADR reports are used for.

The overall campaign message was that 'reporting is taking responsibility for patient safety'.

Campaign efforts – in the early phase, the GP scientific college was invited to collaborate providing scientific input and feedback prior to developing campaign material. Later in the process, the college distributed material and published an article in their scientific magazine.

In order to maximise effects, a three-tier approach was used:

1. **GPs** – a smaller part of the project using leaflets and a small card with information to report ADRs for consultation rooms.

2. **Training** – DKMA collaborated with the Danish Health Authority's Education & Registration Division, which arranges mandatory courses for post-graduate medical students. They inputted into known as SOL courses (Sundhedsvæsenets Organisation og Ledelse) to add information about suspected ADR reporting. Since June 2015, the DKMA also provides lectures in pharmaceutical safety on 3 courses on a permanent basis. The courses are held twice a month and co-hosted by a staff member from the DKMA's PV Division and a regional ADR manager/clinical pharmacologist. Presentations are well received by the participants and scores highly in evaluations after each course session.

3. **Medical students** – materials were developed for use by the teachers in pharmacology at all 4 Danish universities and included reporting guidelines, cases and exercises. Materials were tested first before distribution.

Adverts were placed in various professional magazines read by the medical students and on social media platforms. A short film, explaining the rules and ADR reporting in general was developed. The film was, among other materials, used as part of a competition to win a vouchers for medical books which helped to raise awareness of the campaign.

A small increase in the number of suspected ADR reports from GPs was seen in 2015 from 8% in 2014 to 11%. It is likely that the increase in the number of ADR reports from GPs is attributable to the campaign. More information on the campaign is on the DKMA's website: http://laegemiddelstyrelsen.dk/da/om/kampagner/goer-medicin-mere-sikker-meld-bivirkninger

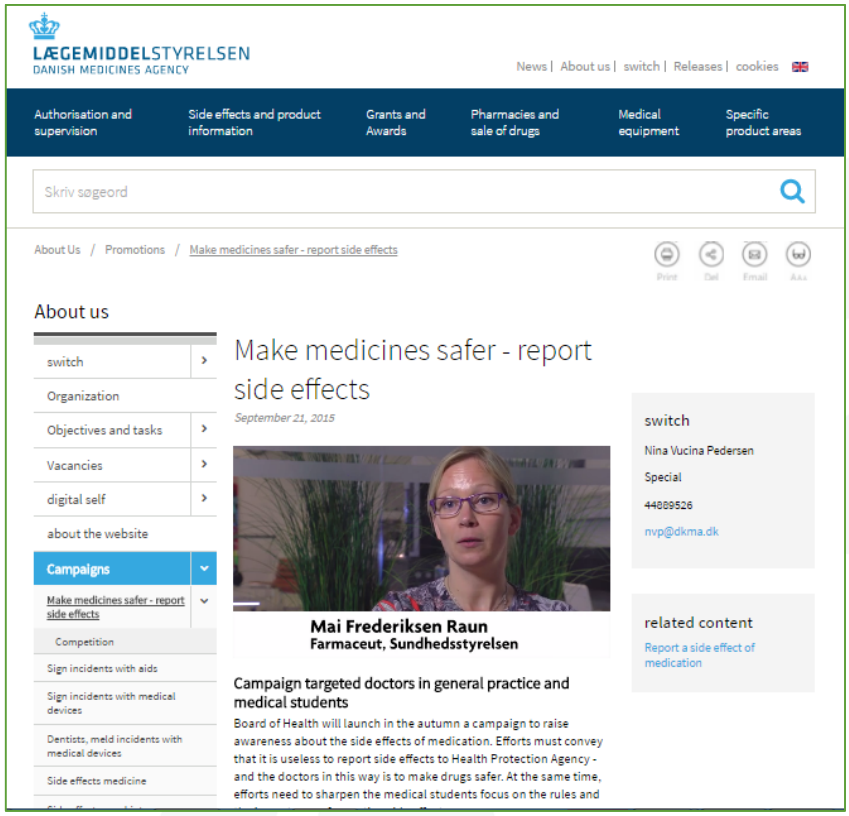


Figure 26. Screenshot for campaign page launched by DMA September 2015

Materials produced for the targeted campaign are accessible through the following links:

- Advertisement: Side effects in your patients (Pdf)
- Brief: Make medicine safer (pdf)
- Booklet: Making medicines safer (pdf)
- Education of medical students: Reporting of adverse reactions (PowerPoint)

Campaign case study: Psychiatrists, psychiatric patients and their relatives

Building on a previous campaign aimed at hospital doctors in 2010 this campaign ran from March to October 2014 to raise awareness on reporting side effects in psychiatry and increase low reporting. Hospital doctors, their respective patients and relatives of patients were targeted. Messages included the professional duty for doctors to report, and for patients and their relatives to know that they too can report side effects online: www.meldenbivirkning.dk. The campaign efforts also aimed to dispel reporting myths whilst giving doctors and patients knowledge of how to react when faced with a suspected ADR, including how to report a suspicion.

Materials produced for the targeted campaign are accessible through the following links (in Danish):

- Information leaflet for hospital doctors and district psychiatry – report side effects in psychiatry (pdf)
- Leaflet for patients and relatives in psychiatry (pdf)
- Educational material for psychiatrists (PowerPoint presentation)
- Educational material for doctors (doc)

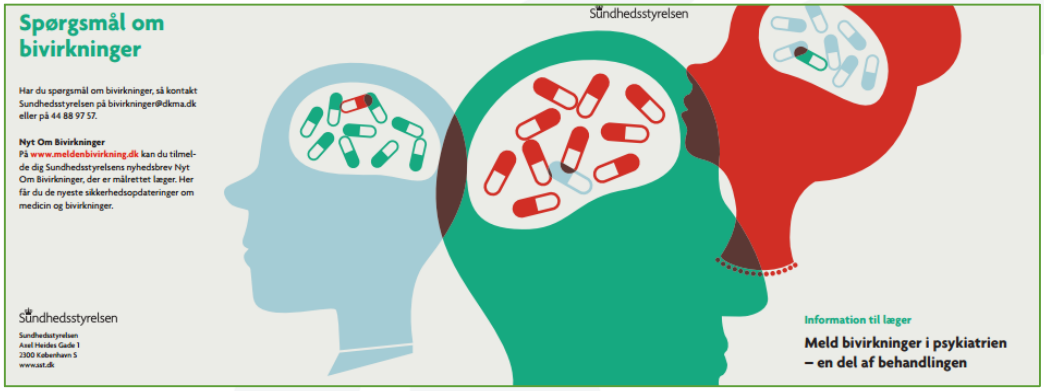


Figure 27. Page within the leaflet encouraging hospital doctors to report

Figure 28. Page of the patient leaflet which shows a screenshot of the reporting site

The PowerPoint presentation aims to:

- Teach the individual doctors to assess whether an ADR must be reported or not
- Show how a suspected ADR must be reported via www.meldenbivirkning.dk
- Show how the Board of Health uses the suspected ADR reports
- Draw attention to the safety newsletter 'Danish Pharmacovigilance'
- Put reporting culture on the agenda.

In addition to just providing PowerPoint, there is also a guidance document to support the presentation covering areas such as:

- Why and when an ADR should be reported?
- Special challenges in psychiatry
- Cases examples of reports
- Where to find safety information
- Where to pay extra attention to ADRs
- How to report
- Feedback
- Sertraline case study
- More information – newsletter for HCPs
- Follow-up lessons
- Contacts

All campaign material was tested by psychiatry team in Southern Denmark. More information on this campaign can be accessed here: http://laegemiddelstyrelsen.dk/da/om/kampagner/meld-bivirkninger-i-psykiatrien-en-del-af-behandlingen

Campaign case study: Nurses and carers

This 2012 campaign, was aimed at helping nurses be better equipped for responding to suspected ADRs, escalate any problems and initiating reporting. The campaign message was also a call to action to nurses and carers – to get them to flag up potential side effects so that patients could be seen by a doctor and any suspected ADRs could be reported.

The reason for the campaign was because senior citizens were often found to have problems with their medication (e.g. due to high doses, polypharmacy and interactions, and resulting ADRs). According to the Association of Danish Pharmacies approximately 75% of residents in nursing homes and 15% of all citizens over 75 years living in their own homes, have serious problems with their medication.

In early 2012, nursing staff were sent material from the DKMA via their employers on how to respond to suspected ADRs. In addition, the DKMA prepared teaching materials for use at departmental meetings to talk about set side effects.

The campaign included a curriculum update for caregivers through their workplace and were supplied with materials from the National Board of Health on how to respond to ADRs.

Campaign material for the nursing staff included:

- Educational material for use at departmental meetings (ppt file)
- Instructions for teaching material (pdf file)
- Film: Side effects of medications
- Movies: Spread the word!
- Film: Talk to your doctor!
- Booklet on adverse reactions to medicines (pdf file)

Other materials produced for the targeted campaign have included (in Danish):

- Text of municipal intranet (pdf file)
- Educational material for use at departmental meetings (ppt file)
- Instructions for teaching material (pdf file)
- Cover letter (pdf file)
- Flyer for public health workers (pdf file)
- Booklet for nurses and healthcare assistants (pdf file)
- Letter to social managers (pdf file)

Press Kit:

- Press Release: New efforts to create more knowledge and greater focus on the side effects of medicine in the care sector (pdf file)

Measuring success

From the DKMA's campaign entitled: 'make medicines safer – report side effects'[8] a specific report was created evaluating the campaign. This report can be seen in the Annex 7 document, 'How awareness levels are raised for ADR reporting systems through campaigns, RMCs and how they are measured', which has been translated into English using Google Translate.

[8] https://laegemiddelstyrelsen.dk/da/om/kampagner/goer-medicin-mere-sikker-meld-bivirkninger accessed 18 April 2016

Estonia

Measuring success

The State Agency of Medicines indicated monitoring the number of suspected ADR's per year as a measure including the quality of reports without further specification.

France

Suggestion 22 – use social media channels regularly

Figure 29. ANSM's Twitter page: https://twitter.com/ansm

ANSM has made use of social media through publishing recent suspected ADR trending data on Twitter making use of a picture of a pie chart which shows a breakdown of reporters. This is supported with a URL linking to further information in the ANSM bulletin.

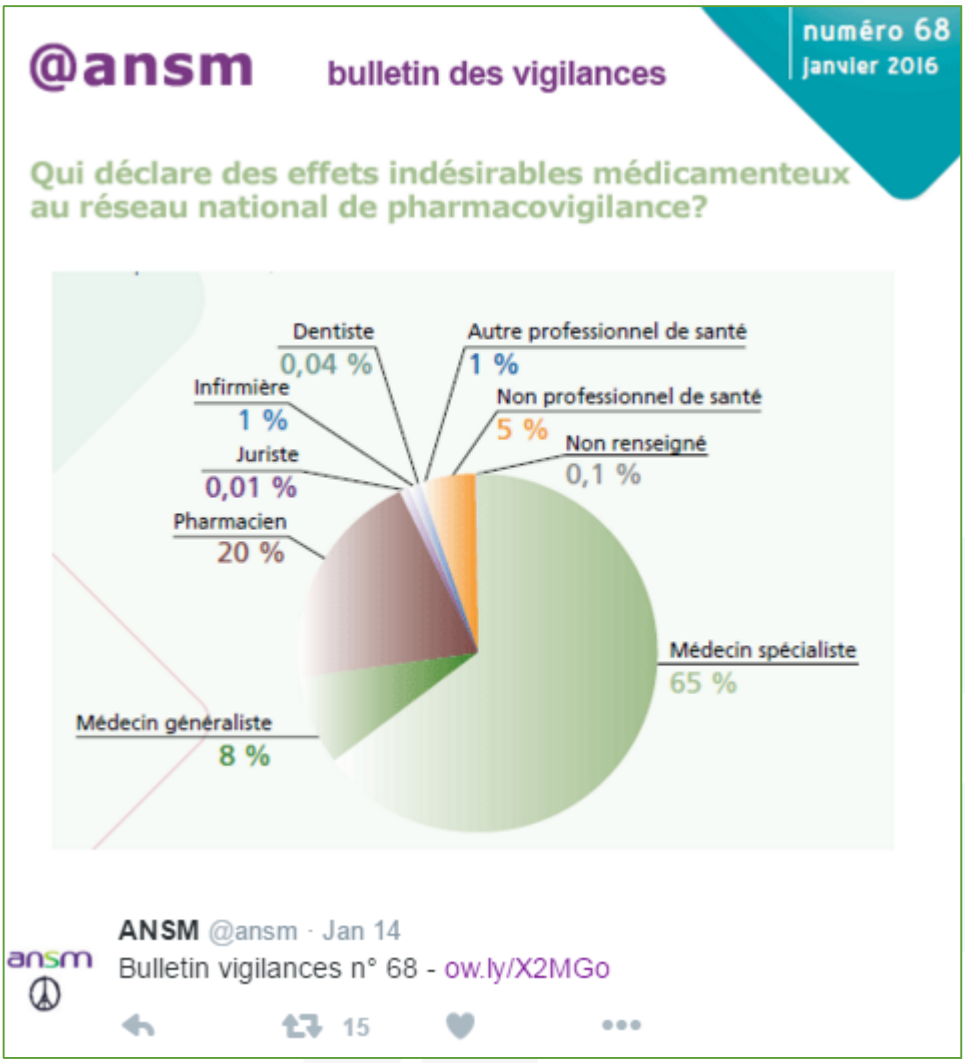


Figure 30. ANSM publishes ADR trending information using Twitter: 'Who reports the most ADRs to the national PV system?' With a link[9] to a more detailed information in ANSM bulletin[10]

ANSM also makes good use of Twitter to promote awareness raising activity involving patient associations and a workshop that was held over a number of days. Different photos were tweeted on different days using URLs and photos of the event.

[9] http://ansm.sante.fr/var/ansm_site/storage/ANSM_BV_68.pdf#page=14

[10] https://twitter.com/ansm?lang=en-gb accessed 5 April 2016

Figure 31. ANSM's further use of Twitter about a workshop on patient reporting '#ANSM: 3rd Day of Information and Discussion with the patient associations'

Campaign case study: Patients

ANSM ran a patient campaign from November 2013 to January 2014. This tied into the launch of their online electronic reporting form, which was announced using a press release to patient organisations and via ANSM's website. Social media was also used to reach the public through Twitter. This was further coordinated with patient organisations requesting them to retweet messages to maximise reach of the message.

ANSM actively meets with diverse patient organisations and their representatives on specific issues to help communicate and encourage ADRs reporting. Information Day meetings are held with such organisations to discuss the reporting of suspected ADRs by patients. At these meetings, patient organisations are requested to inform and educate patients within their own networks on how to report ADRs based upon information available on ANSM's website. Similar themed workshops are also organised at ANSM's Regional Centres.

ANSM encourages many patient organisations to run projects aimed at educating patients to report suspected ADRs. The following are two example YouTube videos from ANSM's work with the French haemophilia association: https://www.youtube.com/watch?v=FbhXPSSPYRo

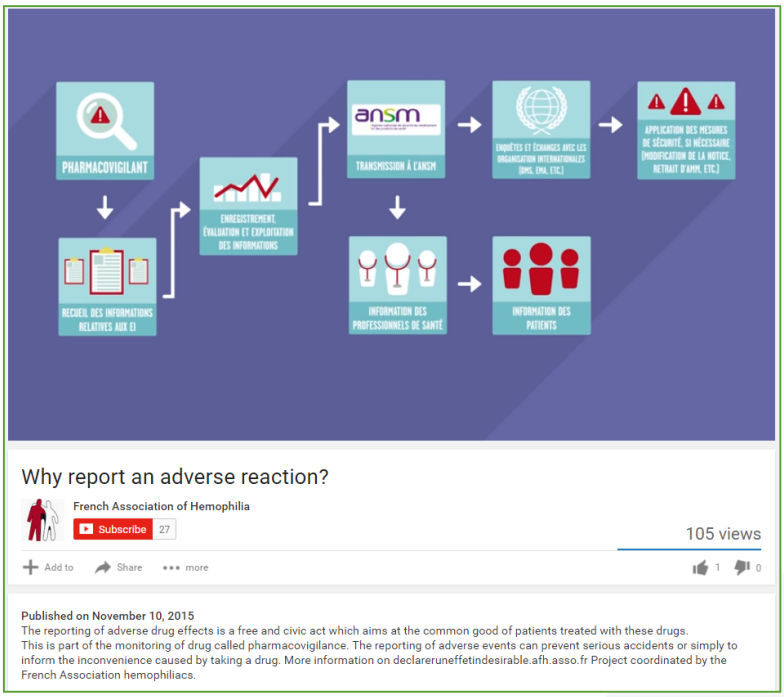


Figure 32. Why report an ADR video (in French): https://www.youtube.com/watch?v=cRLHFKuNQEc

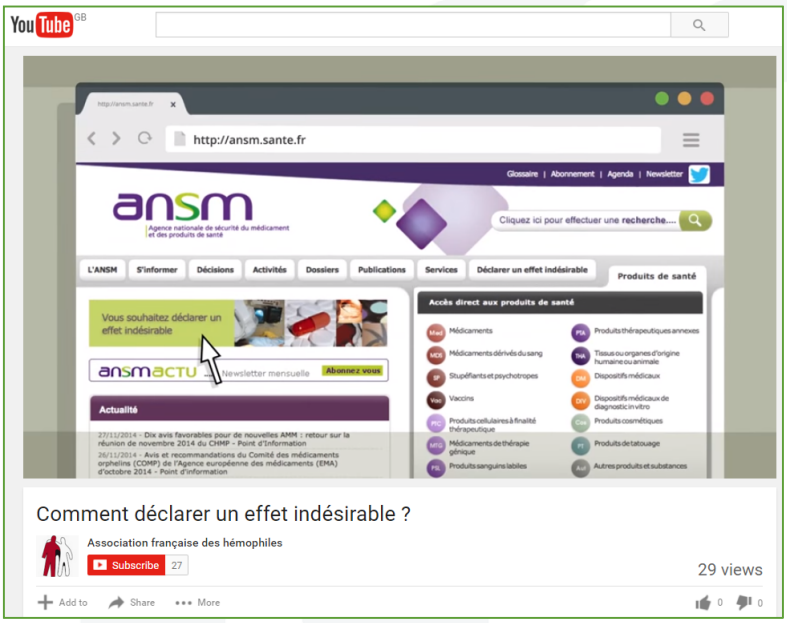


Figure 33. How to report a side effect (in French)

At EU level ANSM works together with EMA and representatives of European patients' associations (Eurordis for example) involved in actions to encourage patient reporting.

Patients' associations are informed, consulted and asked to communicate the information to their members. Parallel work to support patients' information around this document is ongoing. For the fifth consecutive year, ANSM calls for projects addressing patient organisations and other users of the health system. This annual call for projects intends to stimulate community initiatives focused on the proper use and reducing risks associated with health products.

Campaign case study: Paediatric medication errors

ANSM received many cases of medication error for oral administration of paediatric medicines around November 2013, including some serious ADRs in children ranging from 2 to 11 years old. Similar looking devices such as dosing pipettes and syringes were being used interchangeably to administer different medicines. This often was for a medicine that required a different dose. As graduations vary from one device to another using it for another medicine can lead to higher doses being administered rather than the recommended dose.

ANSM took this to its expert medication error working group which led to an awareness raising campaign aimed at patients and their families in 2013. The campaign took the form of a mini-poster reminding people of the 4 key rules to minimise the risk of errors. Next steps of the campaign involved recommendations to pharmaceutical companies with the aim of improving the safety of dosing devices and designs of medical devices brought to market.[11]

Measuring success

ANSM's patient reporting campaign was specified within its Agency business targets for the year. In addition to this there was transparency of subsequent suspected ADR trending numbers within ANSM's annual report to reflect the campaign.

[11] http://ansm.sante.fr/var/ansm_site/storage/original/application/bc8a2c87edccbad836f8da9eec45418b.pdf accessed 14 April 2016

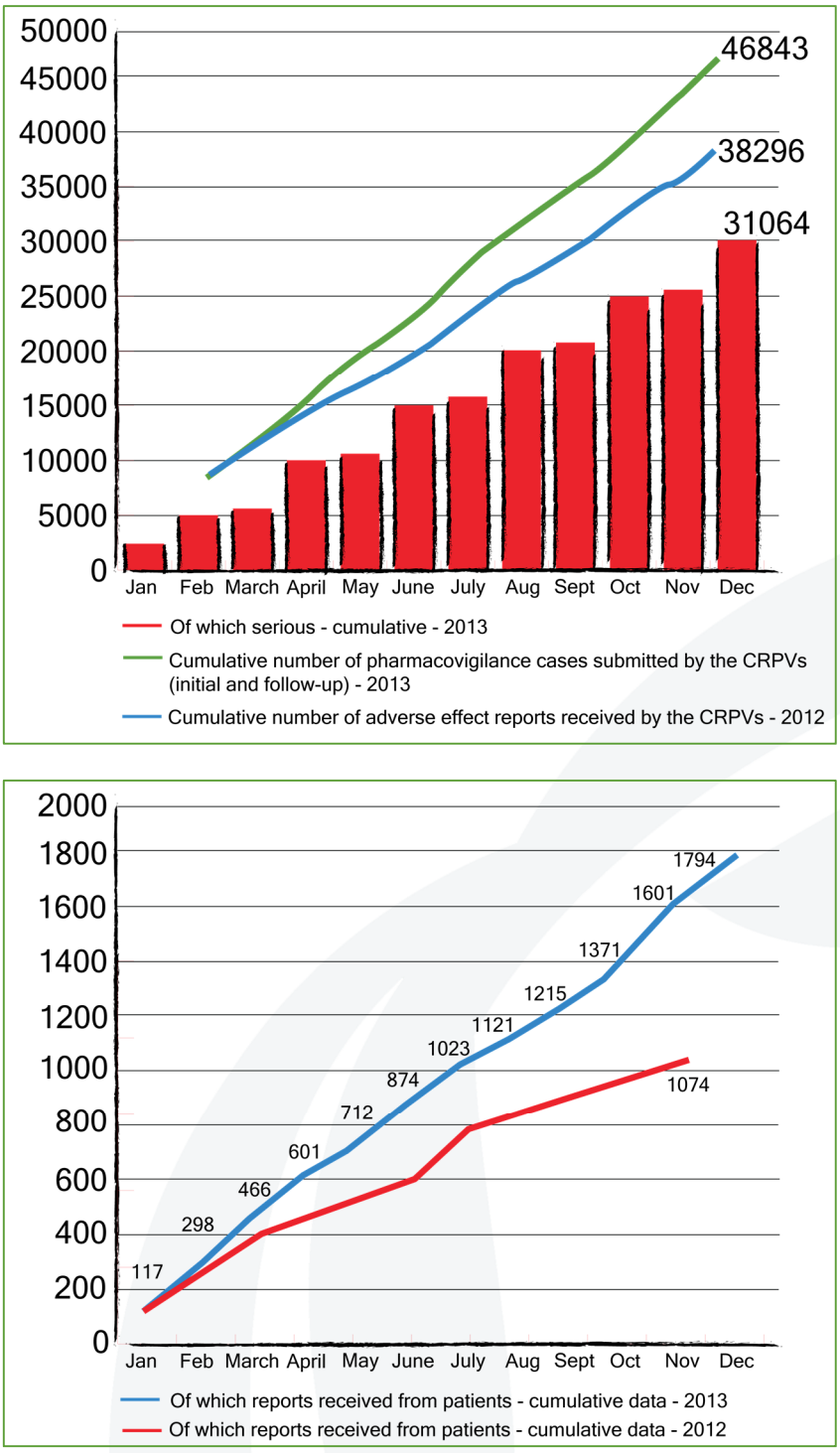


Figure 34. Patient reporting analysis shows 2 graphs within ANSM's 2013 annual report mentioning the awareness campaign

Regional Monitoring Centres in France

The 31 Regional Pharmacovigilance Centres (CRPV) in France lead their own awareness and information activities independently to promote local suspected ADR reporting. Other institutions such as regional health agencies coordinate such work with the CRPVs.

Among their responsibilities for collecting suspected ADR reports, CRPVs are also responsible for educating HCPs, patients and their organisations about suspected ADRs. Patients and HCPs are encouraged to contact their local CRPVs about medicines information.

Their contact details and many of the individual CRPV website links are posted on ANSMs website[12].

CPRV websites host information about local events, the legalities of reporting, links to reporting, relevant information on PV and regulation, safety newsletters, and other useful links to ANSM, EMA etc. Two such examples are:

- http://www.pharmacovigilance-limoges.fr/
- http://www.pharmacovigilance-fcomte.fr/1/accueil.html

[12] http://ansm.sante.fr/Declarer-un-effet-indesirable/Pharmacovigilance/Centres-regionaux-de-pharmacovigilance/(offset)/4 ; French Regional Centres accessed 12 June 2016

Greece

Strategy on raising awareness of national ADR reporting system

The 'National Organization for Medicines' has a strategy on promotion of pharmacovigilance, which includes:

- Updating their web portal with information on ADR reporting
- Having a mobile phone application for reporting
- Conducting a campaign on ADR reporting (television advert)
- Increasing participation at conferences (HCP and patient organizations)
- Increasing the number of workshops with HCPs
- Newsletter, mailings and promotional material updates.

Due to resource constraints resources have been moved away from the Adverse Reactions Department.

Measuring success

An increase in patient reporting was measured by the National Organization for Medicines (NOM) which was attributed to the implementation of new legislation in 2012 and their most recent campaign in 2013.

The Greek campaign measured the effectiveness their awareness activities through workshops, lectures, and conferences. Low participation by HCPs was noted at conferences.

In addition, engaging with HCPs allowed an insight into their behaviours. HCPs do not take the time to read RMP and DHPCs educational materials that contain a request for reporting. This has led to an ongoing study regarding the measurement of RMP educational materials in collaboration with academia.

Hungary

Interactive presentation

Below is an open access link to a video presentation used by the Agency to promote additional monitoring. An online software used was to create the presentation called 'Prezi'. The presentation is now in the public domain allowing it to be copied, shared digitally, embedded into websites and liked.

The full presentation can be accessed here: https://prezi.com/mmpgops2jmq5/additional-monitoring-communication-campaign-in-hungary/

Figure 35. An example Prezi interactive presentation used by Hungary in their additional monitoring campaign

Iceland

Suggestion 24 – explore and maximise any promotional opportunities for joint collaborations and partnerships; aim to promote through low/no cost outward facing communication channels

IMA has collaborated with Frumtök, the Icelandic Association of the Pharmaceutical Industry, with regard to the distribution of educational materials/DHPCs to HCPs, and materials which always include prompts to report ADRs. IMA has also collaborated with the hospitals (including the University Hospital) and the national health systems in order to enable HCPs to report ADRs through the electronic system used to prescribe medicines to patients. There were collaborations with hospitals during an awareness campaign in late August 2011 to January 2012, where lectures were given in most hospitals around the country.

Measuring success

The number of suspected ADR reports that IMA receives are monitored due to raising awareness activities over the years such as its campaign from August 2011 to January 2012. The awareness campaign in 2011 resulted in a 119% increase of reports to IMA, from 250 reports in 2011 to 547 in 2012. Activity outputs measured included the number of: presentations for HCPs students and patients, form distribution in pharmacies and lectures to HCPs in their healthcare institutions. Challenges noted included the difficulty in getting active participation from patient organisations and following up surveys.

Ireland

Benchmarking – a formal assessment of awareness levels

Using a questionnaire aimed at HCPs, the 'HPRA' researched how information on medicines is accessed, including their views of the NCA, prior to their rebranding from IMB to HPRA in July 2014, and the frequency of reporting an ADR to the NCA.

Suggestion 7 – have downloadable ADR reporting forms and materials for raising awareness

HPRA's website also contains information around side effects, pharmacovigilance and downloadable forms and leaflets:

- For patients: http://www.hpra.ie/homepage/medicines/safety-information/reporting-suspected-side-effects
- Example patient leaflet: http://www.hpra.ie/docs/default-source/publications-forms/information-leaflets/medicines-and-side-effects_web.pdf?sfvrsn=6
- For HCPs: https://www.hpra.ie/homepage/medicines/safety-information/identifying-and-understanding-risks/healthcare-professional-and-pharmacovigilance

Suggestion 9 – develop an e-learning module on ADR reporting for HCPs or use the SCOPE package

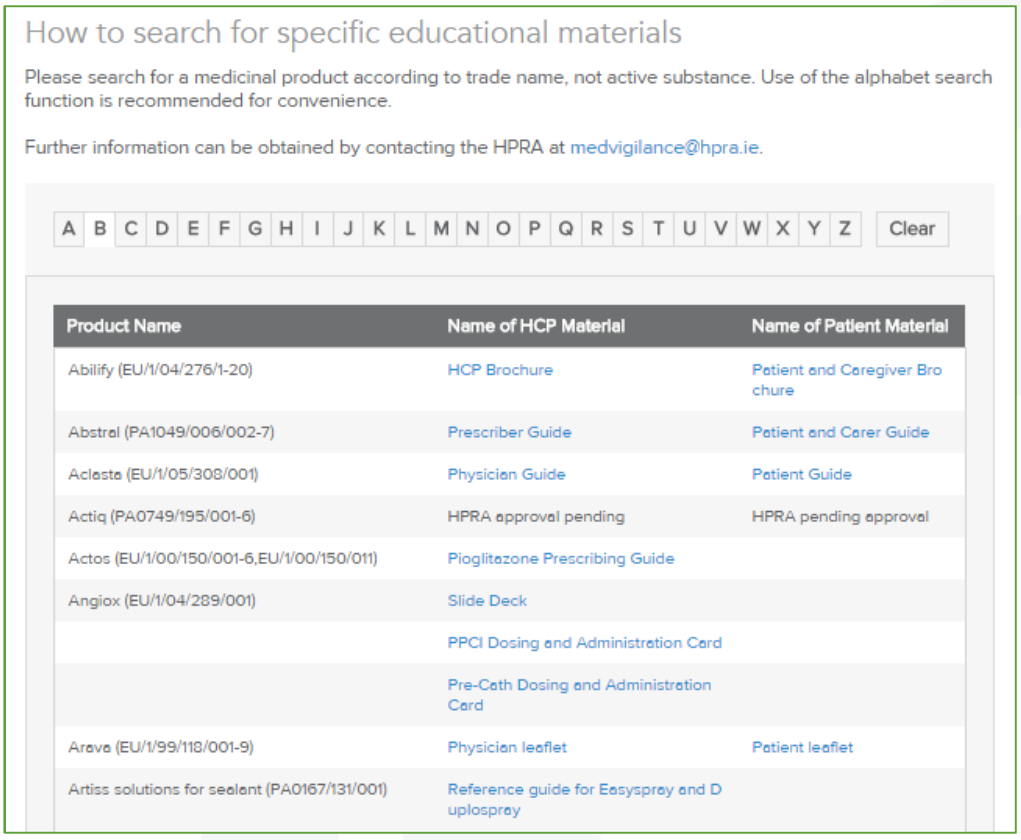
The Irish Academy of Continuing Medical Education (iaCME) is an independent provider of accredited CPD for healthcare professionals using e-learning and web based technologies. It was established and developed to meet current CPD requirements and is operated by Irish HCPs who have extensive experience in the area of medicines regulation and quality management, as well as CPD. Their mission is "To enhance professional competence and patient care by providing a world class on-line CPD source".

As part of the CPD services provided by iaCME in conjunction with HPRA, they have developed a module on ADR reporting, which includes a screencast in the training materials that follows the entry of details in the HPRA online ADR report form.

iaCME has also developed a series of CPD[13] modules based on the information and advice for HCPs included in the HPRA's Drug Safety Newsletter (DSN). The DSN can be used for practice-based CPD to enhance knowledge in relation to the safety of medicines and to support healthcare professionals in applying learning from the newsletter to their individual practices. This resource is offered free of charge to HCPs and may be accessed via a dedicated link on the HPRA website. A new module is produced for each DSN. These are published approximately 6-7 times a year following review and evaluation of the draft module by HPRA.

On successful completion of a module, a downloadable personalised certificate is provided to users reflecting the CPD activity and acting as a record, customised for each specific edition of the newsletter.

HPRA have also developed a resource of educational materials which is on their website[14].



How to search for specific educational materials

Please search for a medicinal product according to trade name, not active substance. Use of the alphabet search function is recommended for convenience.

Further information can be obtained by contacting the HPRA at medvigilance@hpra.ie.

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z Clear

Product Name	Name of HCP Material	Name of Patient Material
Abilify (EU/1/04/276/1-20)	HCP Brochure	Patient and Caregiver Brochure
Abstral (PA1049/006/002-7)	Prescriber Guide	Patient and Carer Guide
Aclasta (EU/1/05/308/001)	Physician Guide	Patient Guide
Actiq (PA0749/195/001-6)	HPRA approval pending	HPRA pending approval
Actos (EU/1/00/150/001-6,EU/1/00/150/011)	Pioglitazone Prescribing Guide	
Angiox (EU/1/04/289/001)	Slide Deck	
	PPCI Dosing and Administration Card	
	Pre-Cath Dosing and Administration Card	
Arava (EU/1/99/118/001-9)	Physician leaflet	Patient leaflet
Artiss solutions for sealant (PA0167/131/001)	Reference guide for Easyspray and Duplospray	

Figure 36. HPRA website showing educational materials for HCPs and patients

[13] https://www.hpra.ie/docs/default-source/Safety-Notices/april-mims-2013final.pdf?sfvrsn=0 : Use of *ia*CME for CPD purposes

[14] https://www.hpra.ie/homepage/medicines/safety-information/educational-material HPRA educational materials for medicines – accessed 14 March 2016.

These educational materials are downloadable and may be intended for HCPs, patients and carers. For example, educational materials may outline what a doctor needs to consider before prescribing a medicine for their patient, or what specific monitoring (e.g. regular blood tests) is required while their patient is on that medicine. Likewise, educational materials may help in reminding patients about important safety information that they need to be aware of before and during treatment with a medicine, so that they use the medicine safely and effectively. They may also provide advice to patients on when to seek medical advice. Examples of educational materials for HCPs include HCP guides, dosing and administration guides, prescriber checklists and monitoring charts. Examples of educational materials directed at patients include patient alert cards, patient guides and patient reminder cards.

Educational materials are produced and distributed by the MAH of the medicinal product and are specific to that medicinal product. They are not required for all medicines but rather are provided if it is considered that they will aid in optimising the safe and effective use of the product. The need for educational materials is agreed with the HPRA and be may be decided at the time of approval of the medicinal product or at a later time in the lifecycle of the product.

Only educational materials which have been reviewed and approved by the HPRA are listed on the HPRA website. The materials are published with the agreement of the MAH responsible for producing them.

Suggestion 24: explore and maximise any promotional opportunities for joint collaborations and partnerships; aim to promote through low/no cost outward facing communication channels

Interaction with professional bodies is as required e.g. generic substitution bill, falsified medicines directive, distribution of HPRA publications to members. There are on-going interactions with patient organisations to raise awareness.

HPRA have developed good working relationships with most of the relevant HCP organisations including the regulatory and professional bodies for registered doctors, GPs (ICGP), pharmacists (PSI), nurses and midwives (NMBI), and dentists (IDA).

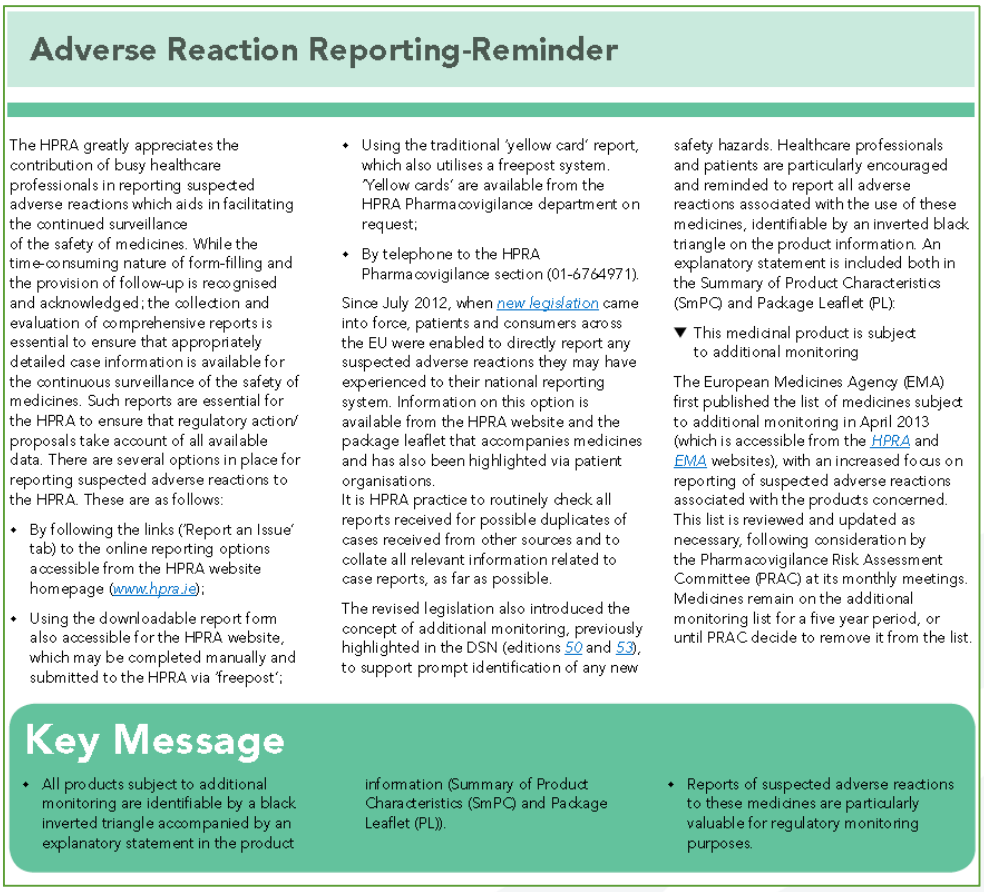
Such organisations disseminate HPRA's Drug Safety Newsletters (DSNs) to their respective members approximately 6-7 times per annum. Regular articles reminding HCPs to report suspected ADRs are included within the DSN with the different reporting options available highlighted.

The HPRA also meets with national patient organisations in relation to product specific issues, as well as overall reporting and monitoring activities.

A range of materials to raise awareness with patients are distributed to patient organisations and are also on display in many GP surgeries in Ireland. Such materials are also downloadable on the HPRA website and cover a range of topics from 'Medicines and Side Effects' to 'How to take Medicines safely'. The 'Medicines and Side Effects' leaflet specifically informs patients about what an ADR is and how to report. DSNs are also distributed to patient organisations when relevant.

Figure 37.Three illustrations of the range of leaflets HPRA has available which are disseminated with collaborative organisations: 'How to take Medicines safely', 'Medicines and Side Effects'[15]

[15] http://www.hpra.ie/docs/default-source/publications-forms/information-leaflets/medicines-and-side-effects_web.pdf?sfvrsn=2 HPRA leaflet on medicines and their side effects: Accessed 11 April 2016



Adverse Reaction Reporting-Reminder

The HPRA greatly appreciates the contribution of busy healthcare professionals in reporting suspected adverse reactions which aids in facilitating the continued surveillance of the safety of medicines. While the time-consuming nature of form-filling and the provision of follow-up is recognised and acknowledged; the collection and evaluation of comprehensive reports is essential to ensure that appropriately detailed case information is available for the continuous surveillance of the safety of medicines. Such reports are essential for the HPRA to ensure that regulatory action/ proposals take account of all available data. There are several options in place for reporting suspected adverse reactions to the HPRA. These are as follows:

- By following the links ('Report an Issue' tab) to the online reporting options accessible from the HPRA website homepage (www.hpra.ie);
- Using the downloadable report form also accessible for the HPRA website, which may be completed manually and submitted to the HPRA via 'freepost';
- Using the traditional 'yellow card' report, which also utilises a freepost system. 'Yellow cards' are available from the HPRA Pharmacovigilance department on request;
- By telephone to the HPRA Pharmacovigilance section (01-6764971).

Since July 2012, when new legislation came into force, patients and consumers across the EU were enabled to directly report any suspected adverse reactions they may have experienced to their national reporting system. Information on this option is available from the HPRA website and the package leaflet that accompanies medicines and has also been highlighted via patient organisations.
It is HPRA practice to routinely check all reports received for possible duplicates of cases received from other sources and to collate all relevant information related to case reports, as far as possible.

The revised legislation also introduced the concept of additional monitoring, previously highlighted in the DSN (editions 50 and 53), to support prompt identification of any new safety hazards. Healthcare professionals and patients are particularly encouraged and reminded to report all adverse reactions associated with the use of these medicines, identifiable by an inverted black triangle on the product information. An explanatory statement is included both in the Summary of Product Characteristics (SmPC) and Package Leaflet (PL):

▼ This medicinal product is subject to additional monitoring

The European Medicines Agency (EMA) first published the list of medicines subject to additional monitoring in April 2013 (which is accessible from the HPRA and EMA websites), with an increased focus on reporting of suspected adverse reactions associated with the products concerned. This list is reviewed and updated as necessary, following consideration by the Pharmacovigilance Risk Assessment Committee (PRAC) at its monthly meetings. Medicines remain on the additional monitoring list for a five year period, or until PRAC decide to remove it from the list.

Key Message

- All products subject to additional monitoring are identifiable by a black inverted triangle accompanied by an explanatory statement in the product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)).
- Reports of suspected adverse reactions to these medicines are particularly valuable for regulatory monitoring purposes.

Figure 38. Illustration of HPRA drug safety newsletter article reminding HCPs about reporting

Congress and a special award

The HPRA has had a stand at the annual, national 'BT Young Scientist & Technology Exhibition' in Dublin for the last seven years. It is a popular event, which attracts over 50,000 people making it one of the largest of its kind in the world. The event aims to bring science, technology, maths and engineering alive in schools across Ireland, and help people realise their relevance to every-day life, to career choice, and to the future prosperity of the Irish economy.

HPRA use this as an opportunity to develop an understanding among students and other members of the public of the work of the Agency and its role in protecting public health, including the reporting of suspected ADRs. The stand focuses on building awareness of the HPRA and brand, providing an opportunity for attendees to participate in a small scientific experiment. Staff members participate at the stand over the three days of the exhibition and the HPRA sponsors a 'Special Award' each year, presented to the project considered to contribute most to promoting the safe use of health products. It is an important way of discussing side effects and reporting with young children.

Campaign case study: Patients

Although in the SCOPE survey, HPRA did not indicate that it has conducted a public campaign, however, it does meet with patient organisations in relation to product specific issues, as well as overall reporting, monitoring activities and safety recommendations. The HPRA Communications department has produced a range of information leaflets for patients which have been distributed to patient organisations and are also on display in many GP surgeries in Ireland. These leaflets, are also accessible from the HPRA website[16] and cover a range of topics from 'Medicines and Side Effects' to 'How to take Medicines safely'. The 'Medicines and Side Effects' leaflet specifically informs patients about what an ADR is and how to report them. Drug Safety Notices are also distributed to patient organisations when relevant. More information can be found on the HPRA website and examples of these forms are already covered within the strategy guidance document.

Figure 39. An HPRA 5 page leaflet for patients about medicines and side effects - includes a number of FAQs

[16] http://www.hpra.ie/homepage/medicines/safety-information/reporting-suspected-side-effects HPRA leaflets available online; accessed 14 April 2016

Italy

Regional Monitoring Centres in Italy

The Italian Medicines Agency (AIFA) indicated it had 16 RMCs within the SCOPE WP4.3 Survey. Italy has 21 state regions and autonomous provinces. The Italian PV System, coordinated by AIFA, consists of a local structure responsible for pharmacovigilance (LRP), regional pharmacovigilance centres (RPCs) and Italian regions.[17] An interactive map of Italian RPCs is available on the AIFA website and also contains contact information of local staff within each region for easy access by HCPs: http://www.agenziafarmaco.gov.it/it/responsabili

Regional structures cooperate with AIFA to disseminate safety information about suspected ADRs and provide training on PV to HCPs. In common with other EU countries, the state regions may utilise the RPCs to support such activities.

In 2007, there was a change in law which facilitated a programme of active PV[18],[19] in regional states. This helped RPCs who are responsible for proposing specific PV projects, which are approved and agreed with AIFA.[20] Two of the five areas for project proposals are: 1) the study of suspected ADRs, and 2) drug information and training directed at HCPs to stimulate spontaneous suspected ADR reporting.

Hence, specific regional projects facilitate educational and promotional ADR campaigns. This is the reason why 41 campaigns were indicated by AIFA in the WP4.3 survey. Such projects have contributed to the increasing trend in the number of suspected ADRs received annually by AIFA. AIFA also indicated that the quality of the data in their national PV database has improved as a result. Projects have encouraged a deeper understanding of the safer use of medicines in clinical practice according to the guidelines and according to the principles of the Evidence Based Medicine.

[17] Pimpinella G, Tartaglia L. Pharmacovigilance and the Italian Medicines Agency. J Pharmacol Pharmacother 2013;4, Suppl S1:4-6; http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3853667/, accessed 21 April 2016

[18] Programme for Funding Active Pharmacovigilance Projects in the Italian Regions F. Trotta, L. Tartaglia, A. Alessandro, M.L. Casini, S. Capponi and F. Ferrazin Italian Medicines Agency (AIFA), Roma, Italy Drug Saf 2012; 35 (10): 877-970

[19] Rapporto sul programma di farmacovigilanza attiva finanziato attraverso i fondi regionali disponibili anni 2008-2009 http://www.agenziafarmaco.gov.it/it/content/fondi-regionali-di-farmacovigilanza-0

[20] http://www.agenziafarmaco.gov.it/it/content/fondi-regionali-di-farmacovigilanza-0; regional funds accessed 10 April 16

Many projects have been developed by RCPs, using different methods and tools for example:

- Raising awareness about PV with pharmacists
- Promotion of paediatric suspected ADR reporting in collaboration with Mother and Child Services, the paediatricians of the OU Paediatrics and the Paediatric and Neonatal Intensive Care Units
- A regional PV course for HCPs
- General promotion of PV and appropriate use of medications.

Even if a project was not specifically aimed at increasing awareness of suspected ADRs, it still had an effect of raising awareness about the profile of suspected ADRs and reporting because of the participants. For example, one of the projects was an information program for GPs and through them, to patients. It focused on the appropriate use of medicines and cost, in line with regional strategies of clinical governance. This project still had elements about side effects and raised awareness.

The effect of RPCs is evident from the substantial increase in suspected ADR reports received by AIFA since 2007.

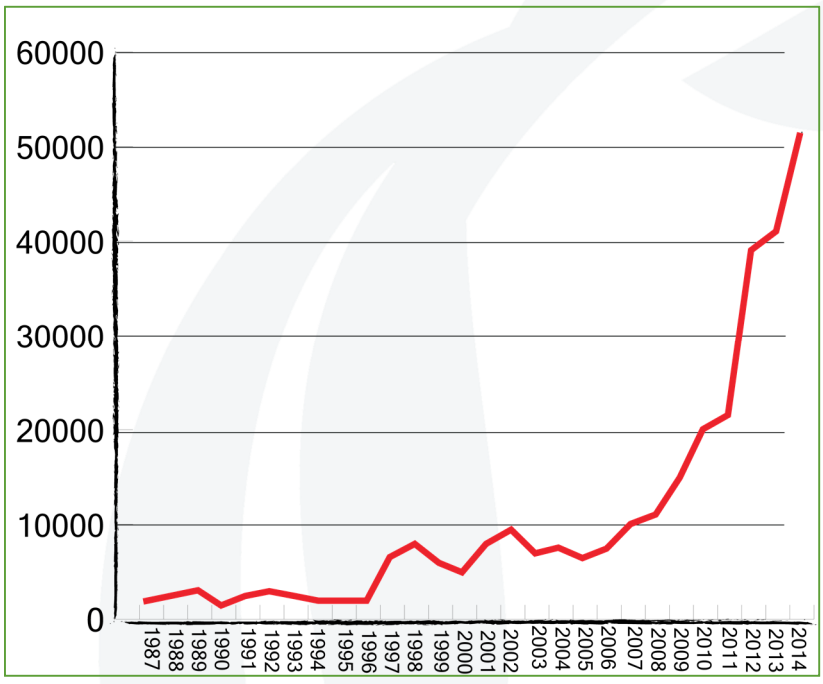


Figure 40. The number of Italian suspected ADRs over time; a rapid increase due to project work of RMCs

Campaign material and collateral used in the different RPCs are not shared actively, as AIFA just receives the project protocols.

The following are example campaigns and project initiatives showing good practice from Italian RPCs.

Campaign case study: Patient and pharmacy

In 2010, in the region Veneto, a campaign was launched through community pharmacy to promote the reporting of suspected ADRs by patients. The project, promoted and coordinated by the Service University Hospital of Verona pharmacology department, collaborated with the RPC of Federfarma Veneto and AIFA. It involved about 200 pharmacists working in 118 pharmacies, both public and private, and distributed promotional material to different provinces within Veneto.

The objectives of this project were to:

- Evaluate the ability of patients to identify and report suspected ADRs
- Increase communication between the pharmacist and patients in the overall management of a medicine, starting with PV information
- Evaluate the effectiveness of a model so it can be reproduced in other regions.

The study, lasting four months, took the form of a training project for pharmacists. This was accredited by Commission ECM of the Veneto region. Each pharmacist had a goal to interview 400 interviews, but were asked to interview at least 24 patients within a week. The patients had to be aged over 18 years old and had to have taken at least one medicine within the last month.

A special card was recorded by the pharmacist or the patient. It included any problems suspected to be related to the medicine, with an indication of the medicine suspected to be responsible. The patient then delivered the card to the pharmacist, or it was sent directly by mail, fax or via the internet to the RPC of Verona.

Within 4 months 46,794 interviews took place (62% with women) who had used a medicine in the last month. 9.5% of interviews had a card returned. For patients who had reported a suspected ADR to medications on the card this was submitted as an ADR report. 52% (2,312 reports) of these returned the card directly to the pharmacist. The data is very relevant as less than 5% of the doctors and other HCPs actively participate in reporting suspected ADRs in Italy. Most of the cards were associated with minor reactions and the quality of the cards were good. The results led AIFA to extend this project to other Italian regions.

IL PUNTO

N. 64 - MAGGIO 2011

Segnalazione spontanea: metti un Centro regionale nel motore!

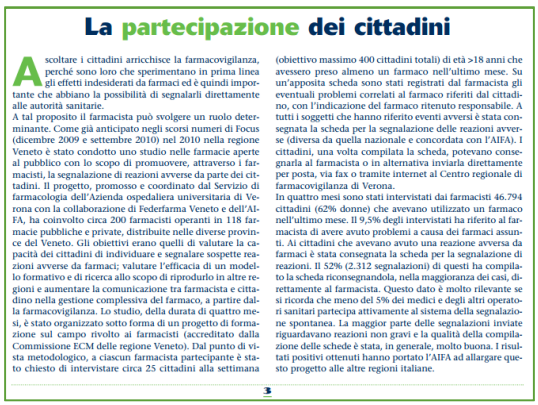
Continua la crescita delle segnalazioni di reazioni avverse in Italia, con un incremento nel 2010 del 39% rispetto al 2009. L'Italia si avvicina così agli standard stabiliti dall'OMS.

Figura 1. Andamento del numero di segnalazioni in Italia

Bastano pochi numeri a illustrare la situazione della segnalazione spontanea di reazioni avverse in Italia nel 2010. Le segnalazioni sono state circa 20.200 con un incremento del 39% rispetto al 2009. L'aumento è stato costante negli ultimi cinque anni, con un incremento annuo medio del 30% (vedi figura 1).
Il tasso di segnalazione è stato nel 2010 di oltre 330 segnalazioni per milione di abitanti, valore ormai vicino a Paesi con elevato tasso di segnalazione quali il Regno Unito, la Francia e la Germania. La situazione è quindi molto positiva, con un andamento che ben promette anche nel corso del 2011: nel primo trimestre di quest'anno infatti l'aumento registrato è del 19% rispetto allo stesso periodo del 2010.
A differenza dell'anno scorso, però, la crescita si è concentrata in alcune regioni: Veneto e Lazio hanno più che raddoppiato le loro schede; in Lombardia, Abruzzo e Campania l'incremento è stato del 50% circa. La Lombardia è la regione con il maggior numero di segnalazioni (oltre 8.500 segnalazioni) e con il più alto tasso di segnalazione (quasi 900 schede per milione di abitanti), seguita dal Veneto, dalla Toscana e dalla Basilicata (vedi figura 2).
L'anno scorso nell'indicare i motivi di una situazione così positiva si avanzavano alcune considerazioni che possono essere ripetute identiche quest'anno: "buon coordinamento e finanziamento delle attività di farmacovigilanza da parte dell'Agenzia italiana del farmaco, inserimento e operatività dei Centri regionali di farmacovigilanza, impegno nelle attività di formazione/incentivazione dei segnalatori e nella raccolta dei dati da parte dei responsabili di farmacovigilanza delle ASL" (*Focus*, giugno 2010).
Senza nulla togliere alle altre componenti, vorremmo sottolineare l'importanza dei Centri regionali di farmacovigilanza. Quando nel maggio 2007 commentavamo su *Focus* la "silente riforma" del sistema di segnalazione spontanea scrivevamo che "da sempre abbiamo auspicato la creazione di Centri regionali e il loro inserimento nel sistema nazionale di farmacovigilanza. Siamo quindi convinti che la riforma avrà effetti positivi: oltre al miglioramento nella qualità e nell'analisi dei dati potrebbe portare anche a un aumento del tasso di segnalazione" (*Focus*, maggio 2007). Eravamo buoni pro-

Figura 2. Tasso di segnalazioni nel 2010 per Regione

2



La partecipazione dei cittadini

Ascoltare i cittadini arricchisce la farmacovigilanza, perché sono loro che sperimentano in prima linea gli effetti indesiderati da farmaci ed è quindi importante che abbiano la possibilità di segnalarli direttamente alle autorità sanitarie.
A tal proposito il farmacista può svolgere un ruolo determinante. Come già anticipato negli scorsi numeri di Focus (dicembre 2009 e settembre 2010) nel 2010 nella regione Veneto è stato condotto uno studio nelle farmacie aperte al pubblico con lo scopo di promuovere, attraverso i farmacisti, la segnalazione di reazioni avverse da parte dei cittadini. Il progetto, promosso e coordinato dal Servizio di farmacologia dell'Azienda ospedaliera universitaria di Verona con la collaborazione di Federfarma Veneto e dell'AIFA, ha coinvolto circa 200 farmacisti operanti in 118 farmacie pubbliche e private, distribuite nelle diverse province del Veneto. Gli obiettivi erano quelli di valutare la capacità dei cittadini di individuare e segnalare sospette reazioni avverse da farmaci; valutare l'efficacia di un modello formativo e di ricerca allo scopo di riprodurlo in altre regioni e aumentare la comunicazione tra farmacista e cittadino nella gestione complessiva del farmaco, a partire dalla farmacovigilanza. Lo studio, della durata di quattro mesi, è stato organizzato sotto forma di un progetto di formazione sul campo rivolto ai farmacisti (accreditato dalla Commissione ECM delle regione Veneto). Dal punto di vista metodologico, a ciascun farmacista partecipante è stato chiesto di intervistare circa 25 cittadini alla settimana (obiettivo massimo 400 cittadini totali) di età >18 anni che avessero preso almeno un farmaco nell'ultimo mese. Su un'apposita scheda sono stati registrati dal farmacista gli eventuali problemi correlati al farmaco riferiti dal cittadino, con l'indicazione del farmaco ritenuto responsabile. A tutti i soggetti che hanno riferito eventi avversi è stata consegnata la scheda per la segnalazione delle reazioni avverse (diversa da quella nazionale e concordata con l'AIFA). I cittadini, una volta compilata la scheda, potevano consegnarla al farmacista o in alternativa inviarla direttamente per posta, via fax o tramite internet al Centro regionale di farmacovigilanza di Verona.
In quattro mesi sono stati intervistati dai farmacisti 46.794 cittadini (62% donne) che avevano utilizzato un farmaco nell'ultimo mese. Il 9,5% degli intervistati ha riferito al farmacista di avere avuto problemi a causa dei farmaci assunti. Ai cittadini che avevano avuto una reazione avversa da farmaci è stata consegnata la scheda per la segnalazione di reazioni. Il 52% (2.312 segnalazioni) di questi ha compilato la scheda riconsegnandola, nella maggioranza dei casi, direttamente al farmacista. Questo dato è molto rilevante se si ricorda che meno del 5% dei medici e degli altri operatori sanitari partecipa attivamente al sistema della segnalazione spontanea. La maggior parte delle segnalazioni inviate riguardavano reazioni non gravi e la qualità della compilazione delle schede è stata, in generale, molto buona. I risultati positivi ottenuti hanno portato l'AIFA ad allargare questo progetto alle altre regioni italiane.

3

Figure 41. Two articles describing: the increase in suspected ADRs as a direct result of RMCs initiatives in Italy; the example of the Venetian RMC campaign[21]

[21] http://www.farmacovigilanza.eu/sites/default/files/FF_n.2-2011_B.pdf Accessed 21 April 2016

Google Translation:

A REGIONAL PV PROJECT

Pharmacists can support reporting of ADRs from patients

The patient ADR reporting form

N.B. Both sections are more detailed but simple to complete (description of event and drug)

Patients can deliver reports in Pharmacy, send them via Fax (number), by mail or report via internet

Figure 42. An example poster from the RPC campaign aimed at patient in pharmacists

Campaign case study: Venetian RPC Vigilance network: 'Vigirete'

'Vigirete' translates to 'Vigilance network'. It consists of a regional network of pharmacies operating in direct communication with the RPC and HCPs concerning medicines, their patients, and PV. It started as a pilot project in the Veneto region in October 2014, promoted by the RPC Veneto and Federfarma Veneto, sponsored by the regional Italian professional body for pharmacists. Since 2015, this has expanded to become a multi-regional project, coordinated by the RPC of Veneto, approved by AIFA. The participating regions include: Basilicata, Campania, Lazio, Liguria, Marche, Puglia and Veneto.

Figure 43. The logo and brand of the campaign initiative

The network aims to:

- Create an integrated network of pharmacies operating with PV in mind
- Strengthen the interaction and relationship between pharmacists and patients, especially with regard to the overall management of a medicine and optimising any communications on the safe use of medicines
- Guarantee patients the support and assistance of a qualified pharmacist to be available for any problems arising from the use of a medicine
- Improve and increase public information on spontaneous suspected ADR reporting and its importance
- Educate and raise awareness amongst pharmacists about the reporting of suspected ADRs in pharmacies.

For patients, the Vigirete campaign included[22]:

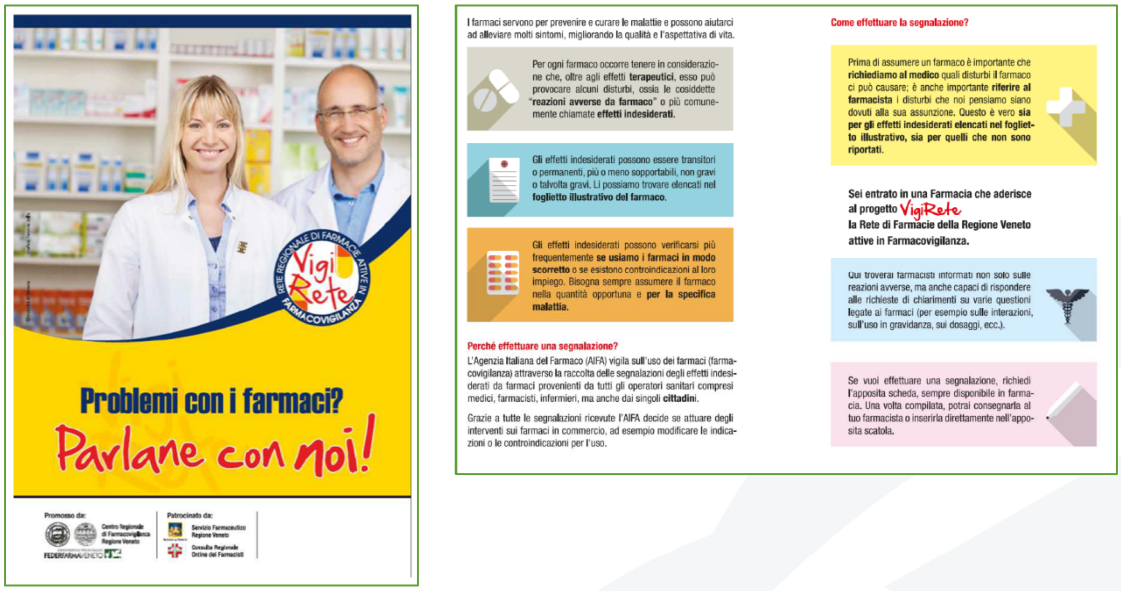
- Easy identification of the pharmacies that were part of the network
- Promotional materials in pharmacies
- Posters to stimulate ADR reporting
- A brochure on the objectives of the network and on spontaneous suspected ADR reporting
- Accessible patient ADR reporting forms
- A box for collecting completed forms
- Information on efficacy and ADRs
- A video explaining the Vigirete on YouTube.

For pharmacists the campaign included:

- A brochure explaining the goals and opportunities available as being part of the network
- Free access (after registration) to the web-based platform www.vigirete.it
- Information on the most important and frequent ADRs related to the most used medicines
- Information on the most important interactions involving particularly OTC medicines
- Free access to two web-based courses on PV and spontaneous ADR reporting

[22] Setting up a patient reporting system the Italian experience, Ugo Moretti, PV Centre, Veneto Region; http://www.lareb.nl/getmedia/abbb2d63-c0ba-4fef-9de0-cd9fc15f9f48/Moretti.pdf - presentation at Lareb conference on patient reporting, April 2015 - accessed 21 April 2016

- A document and material on how to communicate with patients on specific important issues (e.g. use of generics, black triangle, etc.)
- PV news
- A forum for discussion
- The link to reporting suspected ADRs.



Google translation:

Do you have problems with a medicine?

Speak with us

(Contact details for reporting listed)

[This was also a separate poster]

Messages within the leaflet included:

information about taking medicines and side effects being listed within patient information leaflets, why it's important to report, how and where to report, what is done with a suspected ADR report and potential regulatory action, reporting regardless of causality, the vigilance network, speaking to a pharmacist to report any suspected side effects or if one had any questions.

Figure 44. Example leaflets issued in pharmacists from the campaign

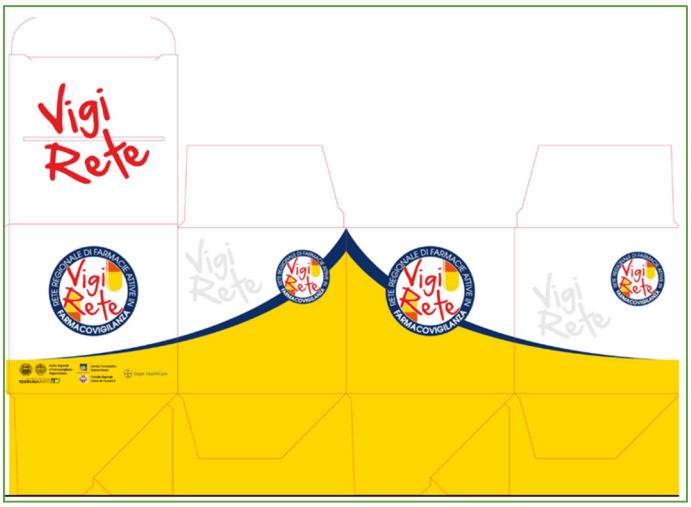
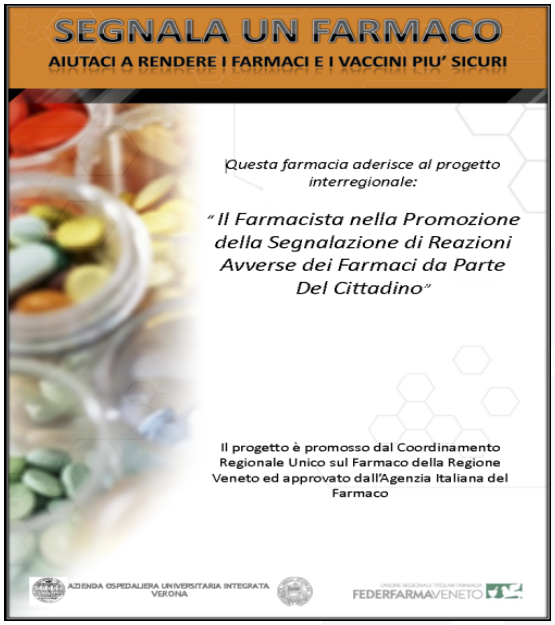


Figure 45. An example template of the box sent to pharmacies to enter any completed patient ADR reports



Google translation:

This pharmacy is part of the inter-regional project:

"This Pharmacist is promoting the reporting of suspected ADRs by patients"

The project is sponsored by the Regional Co-ordination Act on Drugs of the Veneto Region and approved by the Italian Medicines Agency

Figure 46. A traditional poster for pharmacists used to promoting suspected ADR reporting in Veneto region

Figure 47. An example of 2 sided bite-sized information cards for patients that highlight the effectiveness of the campaign – an increase of 2,100 reports and a thank you for their contribution to PV system

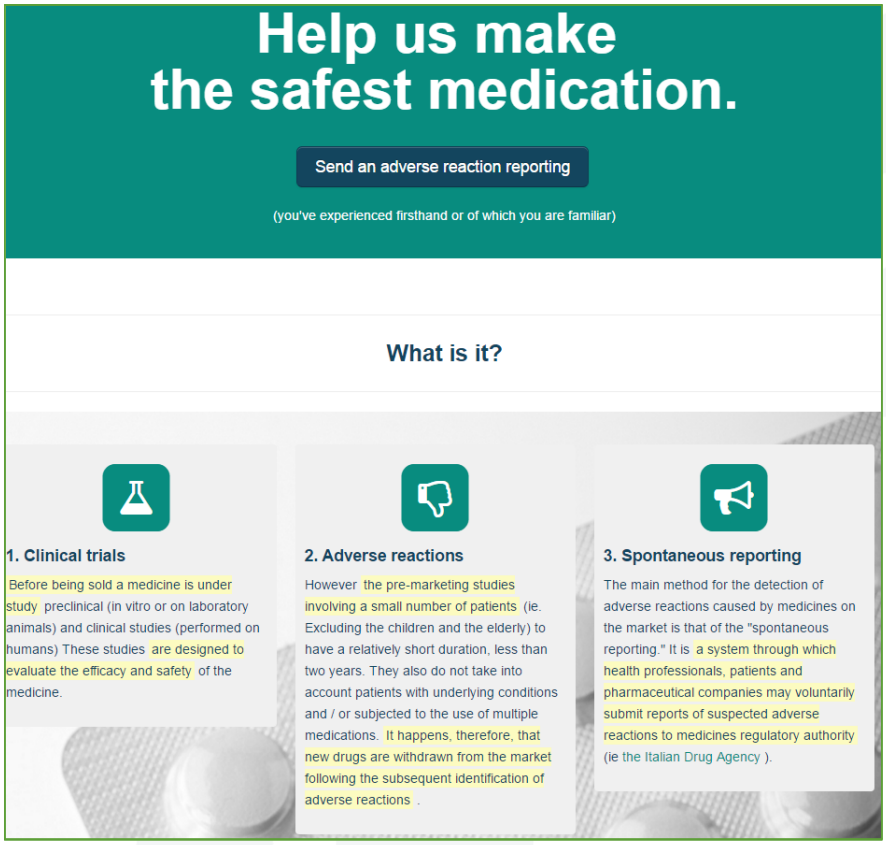


Figure 48. A screenshot of VigiFarmaco – the AIFA application developed by the RPC of the Veneto

A third mini example is the 'MEREAFaPS project' within the Lombardia RPC. This project organised the active monitoring of the suspected ADRs in Emergency Room departments within their region, which increased reporting.

All three examples confirm the important role and impact of the Italian RPCs. In Italy, AIFA indicate that the regions that have RPCs make up 58% of the total Italian population but account for 83% of the total suspected ADR reports. The system has not only increased the number of suspected ADR reports collected but has also improved the data received.

Latvia

Suggestion 15 – recognise and reward reporting

Rewards to HCPs that report the highest number of reported ADRs

In 2014 and in 2015 the 'State Agency of Medicines' of Latvia (SAM) presented an award at the 'Annual Awards in Medicine' that is organised by the Latvian Medical Association.

The awards presented were: 'a special award from the State Agency of Medicines for ethical behaviour and significant contribution in reporting of adverse drug reactions' (2014), and 'a special award from the State Agency of Medicines for responsible and ethical behaviour by reporting adverse drug reactions several times during the year' (2015).

The recipient of the award is chosen by SAM PV experts and the reason why it was decided to present the award at the 'Annual Awards in Medicine' was to motivate other HCPs to report suspected ADRs. Although SAM has not encountered any significant challenges in presenting a reward, it is acknowledged that the number of suspected ADR reports received could be higher. SAM receives approximately 300 suspected ADR reports annually with an increasing trend.

The awards were therefore publicised in three main ways:

- On the SAM website:
  - 'Award presented for reporting of adverse drug reactions' (4 February 2014)[23]
  - 'GP from Riga receives an award for reporting ADRs' (11 February 2015)[24]
- Within the 'SAM informative bulletin for physicians, pharmacists and other HCPs Cito!':
  - 'Award presentation (Cito! 2014/1 (56)', P. 1)[25]
  - 'Award to a general practitioner for reporting ADRs' (Cito! 2015/1 (60), P.7)[26]

[23] https://www.zva.gov.lv//?rel=1775

[24] https://www.zva.gov.lv/?id=201&sa=201&top=201&large=&rel=2155

[25] https://www.zva.gov.lv/doc_upl/cito-2014-01.pdf

[26] https://www.zva.gov.lv/doc_upl/cito-2015-1.pdf

- Via other national and HCPs specific media:
  - 'Award presentation in medicine. Photographs' (2 February 2014, media: www.kasjauns.lv)[27]
  - 'Award to the doctor Georgs Andrejevs for a lifetime contribution in medicine' (2 February 2014, media: www.nra.lv) [28]
  - 'Award to a GP of Riga for reporting ADRs' (9 February 2015, media: www.farmacija-mic.lv)[29]

Suggestion 24: explore and maximise any promotional opportunities for joint collaborations and partnerships; aim to promote through low/no cost outward facing communication channels

Collaboration with the National Health Systems to develop national rules for PV and also with the Centre for Disease Prevention and Control (CDPC) for Adverse events following immunisation (AEFI) data exchange.

A book on PV

The first campaign run by SAM, in April 2005 to November 2005, resulted from a Twinning Project with Germany and the Netherlands. A book was created called: 'Introduction into pharmacovigilance'. It was published by the SAM with support of the EU PHARE program in 2005. The book was provided in the campaign to professional bodies and universities to increase awareness levels about suspected ADR reporting and PV.

The book was the first in Latvian on the safety issues around medicinal products. It recommends the reader to consider use of a medicine only if it is indicated for the health disorders for which it is prescribed for. The book reveals the importance of a physician's observations in facilitating the safer use of medicines by reporting suspected ADRs. The book informs HCPs how to act when a suspected ADR is observed, what to do and the importance of reporting within the PV and regulatory system for medicines. The book is available free of charge from SAM[30] to HCPs, medical or pharmaceutical students, as well as medical establishments.

[27] http://www.kasjauns.lv/lv/zinas/143756/pasniegtas-gada-balvas-medicina-foto

[28] http://nra.lv/latvija/110628-balva-par-muza-ieguldijumu-medicina-pasniegta-arstam-georgam-andrejevam.htm

[29] http://farmacija-mic.lv/gimenes-arsts-no-rigas-sanem-balvu-par-zinosanu-par-zalu-blakusparadibam/

[30] https://www.zva.gov.lv/?id=389&sa=389&top=298 SAM book on PV; accessed 14 April 2016

Figure 49. Latvia's first book on drug safety available for free: 'Introduction to PV'

Campaign case study: Physicians, pharmacists and other HCPs

Latvia's State Agency of Medicines (SAM) conducted its second campaign, from March 2013 to May 2013. It was called 'Reveal the other side of medicines, report adverse reactions!' and included promotional material such as printed posters and stickers for hospitals, educational institutions and the general public. The campaign audience focused on physicians, pharmacists and other HCPs and involved collaboration with Municipal Clinical hospital Gaiļezers.

Figure 50. Example of SAM's campaign material included a sticker (left) and a poster (right)

A press conference was held in which senior figures such as the Minister for Health and heads of professional societies were invited. A key topic was promoting the safe use of medicines to the public to promote suspected ADR reporting.

Figure 51. Photo showing collaborative working with professional bodies and representative of patient organisations in a press conference held by SAM to promote suspected ADR reporting

The campaign also included several press releases and presentations regarding the significance of reporting suspected ADRs and was supported by an article within the SAM's safety bulletin called 'Cito!'

Cito!

2013/2 (53)

Zāļu valsts aģentūra

Pieaug pacienta loma zāļu drošuma uzraudzības procesā

Ir sākta Zāļu valsts aģentūras informatīvā kampaņa

Figure 52. SAM's bulletin for HCPs: 'Cito' contained information about reporting ADRs and the campaign with a photo of the press conference held

Lithuania

Suggestion 24 explore and maximise any promotional opportunities for joint collaborations and partnerships; aim to promote through low/no cost outward facing communication channels

Health Ministry and Contaminated Disease Centre: joint discussion with the public in relation to vaccines safety. Collaboration to participate in meetings organised by others institutions for HCP and pharmacists and the presentation of the annual report on suspected ADRs to promote reporting several times a year.

Malta

Strategy on raising awareness of national ADR reporting system

The 'Medicines Authority' delivers lectures to HCPs which are planned as an ongoing target at least on a yearly basis. The strategy is implemented through various projects related to training of healthcare professionals on ADR reporting.

One project, for example, is the establishment of a role that is responsible for visiting HCPs and giving information to them. This is conducted using specially developed training tools which include when to report a suspected ADR, methods to report, and how ADRs contribute to the PV system and post-authorisation data.

Another project focuses on the involvement of pharmacists in suspected ADR reporting. It focuses on how they can have a more active role in both community and hospital settings in terms of suspected ADRs. Although the document is not publicly available, it contains background and legislation drivers which are followed by key actions implemented to increase ADR reporting from the new legislation and communicating core business publications and projects.

The specific Strategy document includes themes with dedicated timelines associated alongside implementation activities:

- 'Stress testing' the current ADR form for appropriate use and an analysis to identify gaps in order to develop a new online ADR form to increase the quality of reports and facilitate signal detection
  - Use of WHO report to evaluate completeness scores
  - Collating different types of reports from all stakeholders via different forms
  - Using validations
  - Decision tree for ease of completion
  - New ADR form for medication error
- Free postage
  - For all paper ADR and medication error forms
- To promote electronic reporting transmission
- Update guidelines and FAQs
  - So that they are in line with legislative requirements and GVP

- Forums and seminars
  - With a focus on HCPs
  - Poster presentations
- The model of 'Train-the-Trainer' for reporting suspected ADRs
  - Sessions for HCPs within seminar
  - For industry to improve quality of ICSRs
- A business target for the NCA is to have an ADR reporting seminar, at least every 2 years
- Publications
- Printed materials
  - Post-licensing directorate to consider new projects e.g. leaflets and reporting articles to raise awareness levels of patient and HCPs on drug safety and ADR reporting
- Social media
  - To reach out and educate stakeholders about reporting
  - Develop a Facebook page which would include information to promote side effects, including a URL link to ADR reporting.

The document ends appropriately with a small section on monitoring the efforts of promoting ADR reporting to measure the effective of the strategy. This is done by presenting a management report that includes suspected ADR reporting trends to the Post-Licensing Directorate.

Benchmarking – a formal assessment of awareness levels

The 'MA' conducted telephone interviews before and after the launch of their patient information campaign to assess benchmarking of awareness levels. Although not specific for ADR reporting, this was to see whether patients had awareness of the NCA and its role and activities.

Suggestion 15 – set up a national network of ADR reporting champions

A network is being set up within a project which will have an external facing role as a representative to encourage ADR reporting. The aim of the role would be to visit HCPs and provide information using specially developed training tools specific to ADR reporting – for example how to report, the importance of reporting ADRs, contributing to the national PV system and to post-authorisation data.

Measuring success

The Medicines Authority in Malta monitors the number of suspected ADR reports following educational sessions and from stakeholder surveys.

The effectiveness of communication with stakeholders has been measured through using PV queries and its annual evaluation. This evaluation consists of an electronic log book available on an internal server and evaluation of the log book indicates if a Q&A or circulars on certain subjects are issued by the agency. Measurement of the number of queries using the contact form of the Agency's website is also analysed, including any stakeholder feedback.

In addition, a stakeholder survey also evaluated effective communications in 2011. Although this is aimed wider than ADRs, it shows the good practice methodology used that is similar to independent evaluations of patient reporting seen in other countries. The methodology of Malta's use of polls, interview and surveys and results are shown in Annex 6 of the 'How awareness levels are raised for ADR reporting systems through campaigns and how they are measured' document. The results show that 74% of respondents perceived the Medicines Authority as very effective or effective in providing information, and further suggested improvement of dissemination of information through SMS alerts which was taken up by the agency in 2011.

Netherlands

Strategy on raising awareness of national ADR reporting system

The Netherlands Pharmacovigilance Centre 'Lareb' has a strategy is to increase the number of reports, especially among HCPs. Their Strategic Business Plan (SBP) for the coming 5 years, in Dutch, highlights this: http://issuu.com/lareb/docs/lareb-beleidsplan_2015-2019.

There is a focus on:

- Developing a reporting tool to link data from the hospital system to the Lareb reporting form
- Raising awareness in hospitals about the importance of reporting

The main aspects for raising awareness are through:

- Education for undergraduate and graduate students
- Facilitating reporting for HCPs
- Proactive methods for collecting data both from HCPs and consumers.

Suggestion 3 – integrate suspected ADR reporting into clinical IT systems

Professional bodies and GPs in the Netherlands are now implementing an electronic reporting module linked to the GPs medical records.

The Netherlands' PV Centre Lareb integrated the reporting of suspected ADRs in health care systems in two ways:

- Once a physician enters an ADR in the patient record, an alert pops up to encourage the reporting of the ADR. This then opens a partly completed reporting form within the GPs IT system for further completion.
- Automatic sending of reported ADRs that are recorded in registries to Lareb.

An Application Program Interface (API) is a set of routines, protocols, and tools for building software applications. One was set up by Lareb for authorised organisations to transmit ADR reports to. These reports are subsequently imported to the PV database (registry). The API specifies how software components should interact and APIs are used when programming graphical user interface (GUI) components. Lareb's Web API also has the ability to lead an end user to a form where data can be completed. If organisations cannot use the Web API, for example due to infrastructural limitations, data can be uploaded in a CSV format.

There is no dictionary used for the reporting of ADRs by reporters but there is a free text field which the PV centres use to manually code MedDRA terms for reactions. The PV centre uses the Z-index for drugs in the Netherlands, which is a list maintained by the Dutch pharmacist's association and contains all drugs available in the Netherlands.

The initiative commenced in 2014 and the first reports from the registry arrived in December 2015. Both initiatives are still in a pilot phase with a few sites that are sending reports. From mid-March 2016, plans are focused to develop reporting forms in the GP information system. The data set of the ADRs that are automatically sent is currently under review and once the dataset is improved, more registries will be offered to report ADRs automatically.

About 50% of the GPs have access to the GP information system. The number of current registries in the Netherlands is unknown but 4 other registries are using the same platform and will be offered the opportunity of being able to automatically send ADR reports in the same way.

Challenges faced from this part electronic integration:

- From the GP information system – the biggest challenge was integrating the reporting form in the system in a logical, acceptable way without asking too much or too little extra information, while ensuring the privacy of the patient
- From the registry system – sending the best dataset for reporting ADRs and to conduct signal detection. Also to fine-tune the information received from a registry into the spontaneous reporting database.

Each stakeholder pays for its own maintenance costs. The maintenance costs for the system at the site of the Netherlands' PV Centre is paid by the PV centre. The GP information is paid by that system and the registries pay for the connection on their own sites.

Lareb note that the quality of the GP reports (NHG-doc) received in this way is comparable with spontaneous reports from GPs, and can be even better as the sending of extra information is facilitated. The reports of registries contain less information since at first instance a limited set of data is sent. Currently, the dataset is under review in order to improve the data quality.

There has been no extra education for reporting ADRs by these two new methods due to the early stages of both projects.

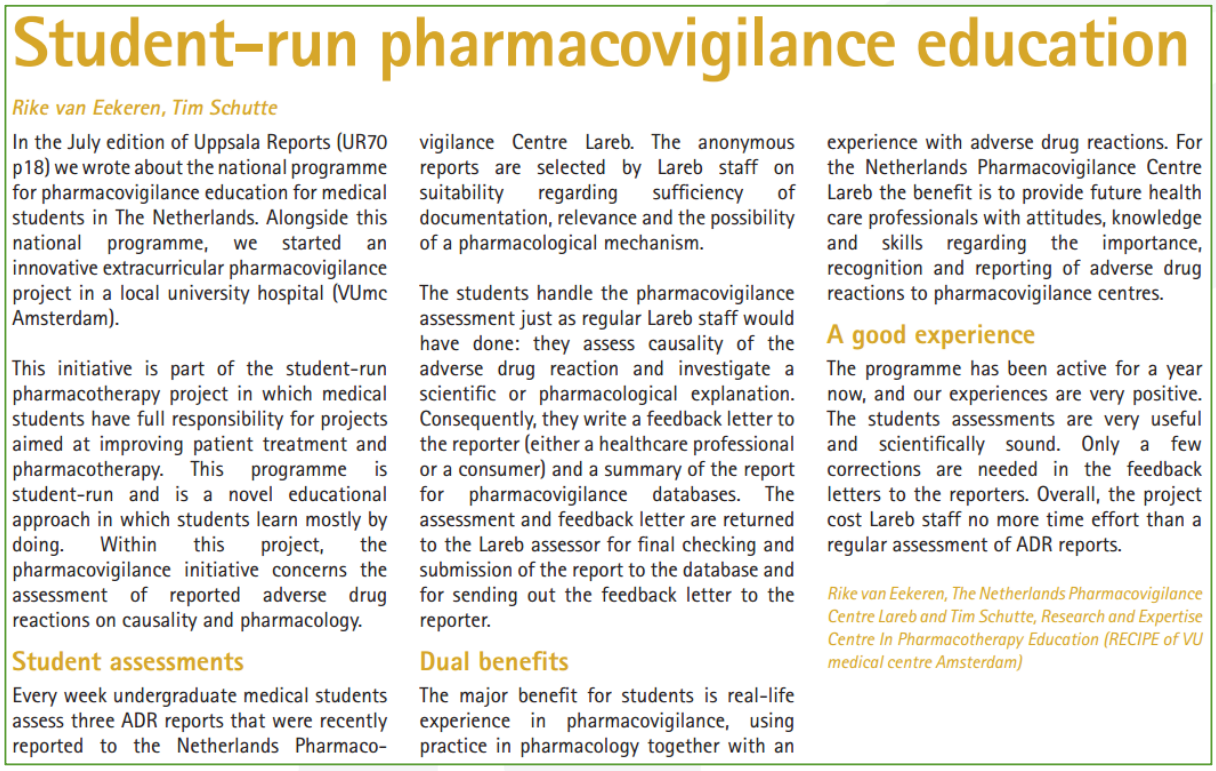
Suggestion 4 – consider developing a mobile application for ADR reporting

The second WEB-RADR app was launched for the Dutch in January 2016 by Lareb. It allows the public, HCPs and caregivers to report suspected ADRs to medicines directly to Lareb, in real-time. Users can also receive news about side effects. The Lareb app is available for worldwide download, from the App Store and Google Play. Lareb have targeted HCP and patient journals specifically to facilitate use and to raise awareness in this respect.

Suggestion 10 – aim to introduce reporting ADR reporting in examinable undergraduate courses

Lareb has worked alongside a national programme to develop an innovative extra-curricular PV project in a local university hospital (VUmc Amsterdam) where medical students assess three suspected ADR reports reported to Lareb weekly. Students learn by doing – providing them with real life PV experience that also uses practice in pharmacology together with gaining early exposure and experience of suspected ADRs.

Reports are selected by Lareb staff for completeness, relevance and the possibility of a pharmacological mechanism associated with the suspected medicine and suspected ADR. The students then assess the causality, and investigate a pharmacological or scientific explanation for each case. The medical students draft a feedback letter to the reporter and provide a draft summary of the case for the national PV database. Subsequently, Lareb staff carry out a final check of what is produced prior to sending out the feedback letter.[31]



Student-run pharmacovigilance education

Rike van Eekeren, Tim Schutte

In the July edition of Uppsala Reports (UR70 p18) we wrote about the national programme for pharmacovigilance education for medical students in The Netherlands. Alongside this national programme, we started an innovative extracurricular pharmacovigilance project in a local university hospital (VUmc Amsterdam).

This initiative is part of the student-run pharmacotherapy project in which medical students have full responsibility for projects aimed at improving patient treatment and pharmacotherapy. This programme is student-run and is a novel educational approach in which students learn mostly by doing. Within this project, the pharmacovigilance initiative concerns the assessment of reported adverse drug reactions on causality and pharmacology.

Student assessments

Every week undergraduate medical students assess three ADR reports that were recently reported to the Netherlands Pharmacovigilance Centre Lareb. The anonymous reports are selected by Lareb staff on suitability regarding sufficiency of documentation, relevance and the possibility of a pharmacological mechanism.

The students handle the pharmacovigilance assessment just as regular Lareb staff would have done: they assess causality of the adverse drug reaction and investigate a scientific or pharmacological explanation. Consequently, they write a feedback letter to the reporter (either a healthcare professional or a consumer) and a summary of the report for pharmacovigilance databases. The assessment and feedback letter are returned to the Lareb assessor for final checking and submission of the report to the database and for sending out the feedback letter to the reporter.

Dual benefits

The major benefit for students is real-life experience in pharmacovigilance, using practice in pharmacology together with an experience with adverse drug reactions. For the Netherlands Pharmacovigilance Centre Lareb the benefit is to provide future health care professionals with attitudes, knowledge and skills regarding the importance, recognition and reporting of adverse drug reactions to pharmacovigilance centres.

A good experience

The programme has been active for a year now, and our experiences are very positive. The students assessments are very useful and scientifically sound. Only a few corrections are needed in the feedback letters to the reporters. Overall, the project cost Lareb staff no more time effort than a regular assessment of ADR reports.

Rike van Eekeren, The Netherlands Pharmacovigilance Centre Lareb and Tim Schutte, Research and Expertise Centre In Pharmacotherapy Education (RECIPE of VU medical centre Amsterdam)

Figure 53. Uppsala Reports article on PV education

[31] Uppsala Reports 71, October 2015 http://www.who-umc.org/graphics/30653.pdf Accessed 20 May 2016

Suggestion 21 – publish ADR trending data to encourage promotion and research

Lareb frequently publishes case reports, review articles and methodological articles on its website[32] that are free to download. These also are published in scientific journals for physicians and pharmacists, both nationally and internationally. The use of this information for public presentations or publications is permitted, provided that Lareb is mentioned as the source.

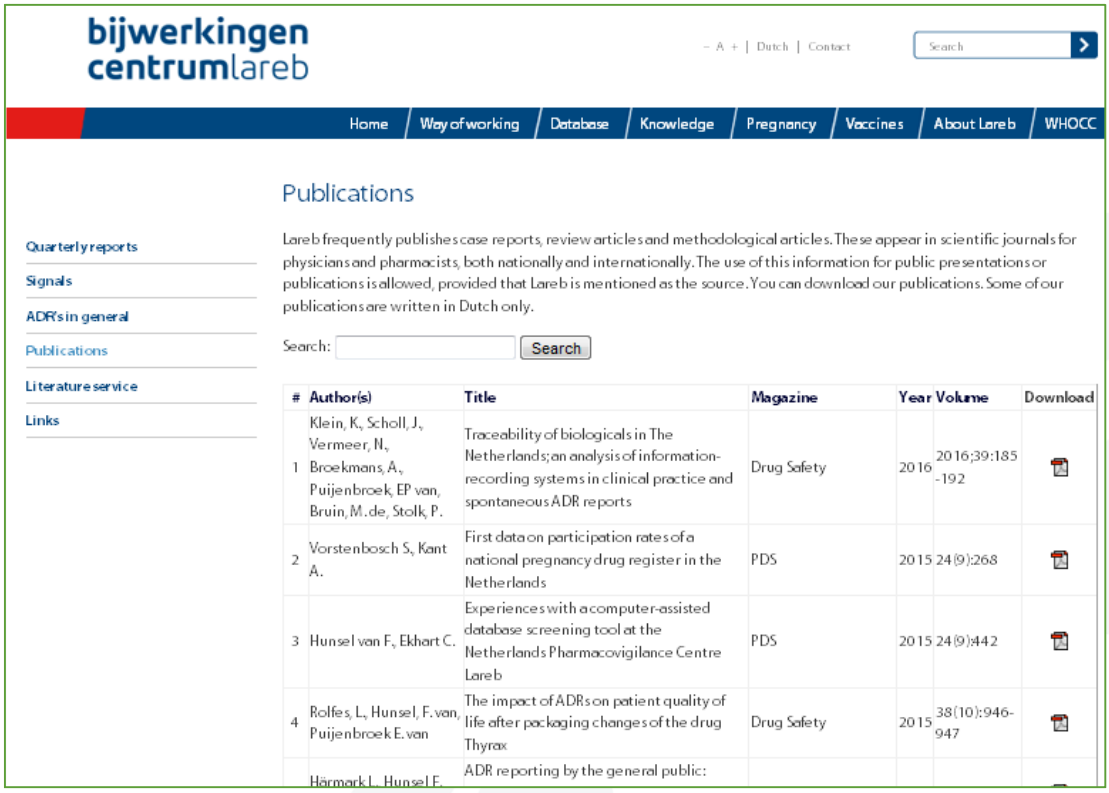


Figure 54. Screenshot of publications posted by Lareb

In addition, Lareb also publishes its signals[33] and quarterly reports[34] on its website alongside links to other worldwide databases, regulators, global PV organisational societies such as International Society of Pharmacovigilance and International society for Pharmacoepidemiology, and PV magazines.

[32] http://www.lareb.nl/Informatie-bijwerkingen/Kwartaalberichten Lareb publications; accessed 5 April 2016

[33] http://www.lareb.nl/Informatie-bijwerkingen/Signalen Lareb Signals. Accessed 5 April 2016

[34] http://www.lareb.nl/getdoc/5b91ea04-4bae-47be-ad8f-9ba7ce413fdf/Kwartaalberichten.aspx Lareb quarterly reports. Accessed 5 April 2016

Suggestion 24: explore and maximise any promotional opportunities for joint collaborations and partnerships; aim to promote through low/no cost outward facing communication channels

Netherlands – Collaboration with patient organisations to increase knowledge about drug use and side effects via the ADHD network

A survey[35] was conducted in June 2015 by the Dutch Association for people with ADHD, dyscalculia and dyslexia through the patients association 'Impuls & Woortblind' in collaboration with Lareb. Participants were ADHD medication patients that were 16 years or older. Results showed that:

- 75% of the adults using medication for ADHD experience side effects
- The most frequently mentioned side effects reported were described in the patient information leaflets
- In general, participants experienced a positive effect on taking the medication to relieve their symptoms
- Experiencing side effects or lack of effect from the medication can be a reason to discontinue use.

The survey was online and sent by email to members of Impuls & Woortblind and to clients in two private practices resulting in 1160 respondents completing the questionnaire. 848 of those were analysed further. On the last page of the survey, respondents were asked to report the side effects experienced to Lareb. In addition to this, all respondents who mentioned a side effect and provided their email address were subsequently contacted for further information and were asked to report their side effects to Lareb. By the end of September 2015, 44 respondents had completed a suspected ADR report.

The study shows that collaborations with patient organisations are an important method of raising the awareness about PV amongst patients. It can also be used to collect information about drug use.

[35] http://www.lareb.nl/getattachment/56af7c5e-e8dd-4bd9-9b52-58cc5532ec39/20160309-ENG-Summary-ADHD-report.pdf accessed 3 June 2016

Campaign case study: Patients

The Netherlands Pharmacovigilance Centre 'Lareb' has conducted three public campaigns. The first was between May 2009 and December 2009, the second between January 2011 and December 2011, and the third was conducted in 2013.

Promotional material focuses on increasing awareness about patients reporting suspected ADRs. Materials are designed with the aim of being striking and recognisable, coupled with a short clear message:

- Awareness of the possibility of being able to report: 'You can report an ADR'
- Awareness of the importance to do so: 'You should report'

The approaches used to increase awareness levels include:

- Posters and leaflets to advertise reporting
- Radio commercials
- Interviews about the importance of reporting and a call to report
- A magazine[36] – explaining what Lareb does and the importance of suspected ADR reporting, including some information on signals found
- Publications
- Stands on fairs
- Partnerships with patient organisations
- Media appearances
- Celebrity endorsement – singing outside a pharmacy with the Lareb posters in the background window
- Video – a general information film about Lareb and what Lareb does.

Lareb have also collaborated with the largest patient organisation in the Netherlands. This resulted in a column called the 'Bitter pill' in which Lareb highlights a certain ADR within a health magazine of the patient organisation. The copy sold 43,000 copies.

[36] http://www.lareb.nl/getmedia/4aa9f3de-3224-4fce-b529-49b535f5210e/Bijgelicht-magazine.pdf Accessed 9 June 2016

Figure 55. An example of patient posters used in Lareb's campaigns

Figure 56. Another more striking example of a poster for patients

In partnership with an umbrella organisation of pharmacies posters and information cards were put up within pharmacies to increase reporting as shown below. For promotional activities to patients, Lareb uses a different website link compared to HCPs.

Figure 57.Two example posters which hold small wallet sized cards which are placed on display in waiting rooms

Lareb endorse maximising all media attention opportunities to contribute to reporting culture and aim to be transparent by communicating with patients and the public. Some media tips from Lareb include:

- Formulate a clear message
- Be short and to the point with a nuance. For example: "a relation is possible, not proven, more research is needed"
  - Why is this important for whom?
  - What to do?
- Be aware of the receiver of the message
  - Show empathy, regardless of the message – for example when speaking about the benefits and risks of medicines
  - Be specific about what you are talking about
  - Give an example of how suspected ADR reporting may affect the audience

Lareb is also a WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting. In April 2015, Lareb organised its first Conference on Patient Reporting in the Dutch National Museum for the History of Science and Medicines in Leiden. The meeting attracted 60 participants from 21 countries discussing a range of subjects relating to patient reporting. Numerous presentations[37] were given.

Measuring success

The Netherlands PV Centre Lareb monitors the changes in the number of reports but also at media coverage before and after ADR campaigns.

[37] http://www.lareb.nl/whocc/Conference-on-Patient-Reporting accessed 14 April 2016

Norway

Suggestion 8 – develop case studies show the importance of reporting

Although NOMA do not have any written case studies, examples are used to show regulatory action. This is done in the form of very short bullet points on slides (e.g. drug event combinations) or graphs which would not make much sense without an oral explanation. The regional centres also create their own ad hoc and tailored examples for their audience – again by using short bullet points on slides.

Suggestion 22 – use social media channels regularly

Upon follow up NOMA indicated that like many NCAs there is no specific plan for using social media for promoting suspected ADR reporting. The use of Twitter and Facebook was an official recommendation from The Ministry of Government Administration and Reform as a channel to reach the public or target groups. Social media is used whenever it is considered suitable to, for example, linking information related to drug safety.

Figure 58. NOMA's Facebook page: https://www.facebook.com/legemiddelverket

Figure 59. NOMA's Twitter page: https://twitter.com/Legemiddelinfo

Regional Monitoring Centres in Norway

Norwegian Medicines Agency (NOMA) has 4 RMCs which are called RELIS's. Each is located with the largest hospital within each 'health region':

- Health Region South-East (RELIS Sør-Øst, based in Oslo)
- Health Region West (RELIS Vest, based in Bergen)
- Health Region Middle-Norway (RELIS Midt-Norge, based in Trondheim)
- Health Region North (RELIS Nord-Norge, based in Tromsø)

The centres are distributed largely in the middle region of each health region to minimise the distance of a centre for HCPs so they are readily accessible.

Figure 60. Map of Norway's RMCs called RELIS locations

Each RELIS is responsible for promoting suspected ADR reporting in their own regions and for educating HCPs about suspected ADRs. This is achieved mainly through local information days and courses. RELISs are also responsible for collaborating with NOMA, HCPs and their bodies. In addition, RELISs are responsible for answering drug related questions from local HCPs and, more recently, from patients, although queries from pregnant and women who are breast feeding were answered for some years.

ADR reporting is mainly conducted via forms and paper based systems, but the centres are reachable via phone and email and use such methods to promote reporting. The name and addresses for the centres are printed on the ADR reporting form.

Awareness is also raised by RELISs through:

- Articles in medical journals
- Information on the RELISs websites
- Their newsletters
- Their Q&A services
- Lectures at a post-graduate level with medics, pharmacists, dentists and nurses
- Lectures with practicing HCPs
- Media articles

- The internet
- Collaborations
- Local drug committees at hospitals.

Recently the RELISs have been involved in pilot projects to educate a large proportion of the primary care physicians in their area. It is expected that this activity will contribute to an increase in the numbers of suspected ADR being reported and also an increase of awareness about the centres.

NOMA plan to launch an ADR campaign with RELISs when their electronic reporting tool goes live. Measurement of the success of the campaign will also be planned.

RELISs have increased awareness levels of suspected ADR reporting with HCPs through previous campaigns which are often targeted. Sometimes they are coordinated nationally and involve NOMA, but not always – as each RELIS should meet the needs within their own regions. The main target stakeholder groups are: physicians (GPs and hospital staff), but also other groups such as pharmacists. Communication channels used in campaign work include: their websites, relevant ADR information on hospital intranets, promotion of e-learning courses, local leaflet distribution, and the publishing of articles in professional and medical journals.

It is mainly NOMA that engages with patient organisations as the reporting system for patients is handled by NOMA and RELISs have not been as involved.

Pharmacological departments at University Hospitals and the 'Norwegian medicines for children network' are amongst the main collaborators working with RELISs to raise awareness about suspected ADRs and to encourage reporting.

E-learning material has been developed by one centre which has subsequently been made available to all other RELISs for HCPs.

NOMA uses a train-the-trainer model to increase awareness of suspected ADR reporting with regular meetings held between a person from each RELIS and NOMA staff.

The centres publish an annual report detailing their respective activities. However, RELISs also report on key performance indicators to NOMA. Some of these can be used to measure the effectiveness of awareness level activities, such as the monitoring over time of numbers associated with:

- Enquiries from doctors and other HCPs
- Suspected ADRs from doctors and other HCPs per 1000 000 inhabitants
- Publications and electronic newsletters
- Recipients of electronic newsletters
- Website hits.

Portugal

Benchmarking – a formal assessment of awareness levels

Portugal (with Netherlands) – a preliminary patient reporting study[38]

A year after launching patient reporting in 2013, the Portuguese National Pharmacovigilance System (SNF) received 3,461 spontaneous ADR reports, of which only 1.4% (n = 50) were from patients. Subsequently, 'Infarmed' sanctioned a descriptive-correlational study to ascertain the attitudes and knowledge of the general public regarding spontaneous ADR reporting and the reasons and opinions that were influencing underreporting.

The study formed part of a Pharmacy Master thesis through collaboration with Lareb (Netherlands). A 6-month survey from June to November 2013 was conducted in adult patients at a community pharmacy in Coimbra, Portugal. Patients who used prescribed medicines or over-the-counter (OTC) drugs were approached. Attitudes and opinions were surveyed by personal interview in a closed answer questionnaire using a Likert scale.

1,084 questionnaires were collected with a response rate of 81.1%. 948 completed questionnaires were selected for analysis. Results included:

- 44.1% had never heard about SNF
- Younger people and those with a higher education were significantly more likely to be aware of SNF
- Only one patient had previously reported a suspected ADR
- Reporting through a HCP was preferred by 62.4%
- The main reason for patients reporting spontaneous suspected ADRs would be the severity of reactions (81.1% agreed or strongly agreed) and worry about their situation (73.4% agreed or strongly agreed).

The study concluded that patients are more likely to report severe reactions if they are worried about the symptoms. In addition it was found that tailored and proactive information on ADR reporting and educational interventions for patients could increase the number of reports in Portugal.

[38] http://www.lareb.nl/Nieuws/2015/Experiences-with-consumer-reporting-in-Portugal; Accessed 1 April 2016

Suggestion 24 explore and maximise any promotional opportunities for joint collaborations and partnerships; aim to promote through low/no cost outward facing communication channels

Interaction with National Health Systems and Professional bodies, specifically to discuss protocols, including raising awareness about the importance of reporting suspected ADRs.

Regional Monitoring Centres in Portugal

The National Authority of Medicines and Health Products in Portugal (Infarmed) coordinates its 4 regional centres which were introduced in 2001 to be closer to HCPs and to carry out PV training sessions for HCPs initially, but now sometimes includes patients. The RMCs are integrated within Medicine and Pharmacy Colleges and a Science Research Centre. Two RMCs form one regional centre as they are located within the same region.

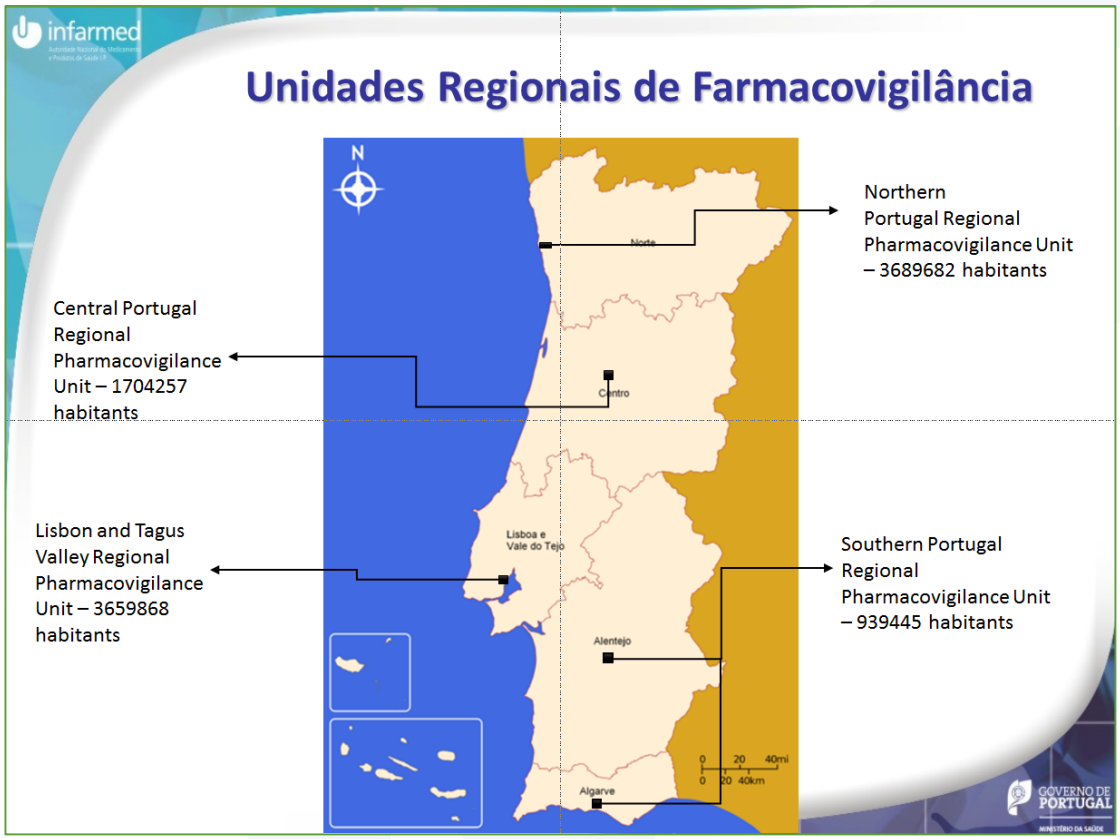


Figure 61. Portuguese RMCs locations and number of inhabitants within the respective regions

All four RMCs are coordinated centrally by Infarmed. Although they are not directly linked to local National Health Systems, they organise training activities within hospitals and healthcare centres to encourage suspected ADR reporting. Each is responsible for their own specific geographical areas as shown in the illustration above and have their own websites, similar to other MS RMCs, for example:

- http://www.ufn.med.up.pt/ – northern RMC
- http://www.ff.ul.pt/ufs/ – southern RMC
- http://www.ufc.aibili.pt/ – central RMC

In addition to encouraging and educating HCPs to report suspected ADRs, RMCs disseminate PV information and perform research activities. Stakeholders include patients and HCPs through public or private health institutions, HCP academic institutions.

RMCs increase awareness with HCPs (and patients through them) via telephone and email correspondence. Until now no interaction with patient organisations has occurred. Infarmed intend to take this forward through nursing homes, municipal services, and the targeting reporting in the elderly in future.

Each RMC uses social media to raise awareness to prompt the reporting of suspected ADRs, such as Facebook:

- https://www.facebook.com/uflvt/
- https://www.facebook.com/Unidade-de-Farmacovigil%C3%A2ncia-do-Norte-1420513208163954/?fref=ts
- https://www.facebook.com/ufsff/?fref=ts

Figure 62. Example of the active RMC Facebook page from the Northern region that is up to date with posts has 895 followers; accessed 13 June 2016. The example on the right is a post shared from a public health journal about an article encouraging hospitals to have protocols and links to report suspected ADRs that the RMC shared to its followers.

Being positioned within healthcare institutions allows further opportunities to raise awareness with HCPs. Collaborations have been made with the all the regional healthcare institutions, with the Faculties of Pharmacy and Nursing schools to raise awareness through training about suspected ADRs. In addition, RMCs help HCPs in drug safety research when requested, have a Journal Club, organise an annual PV course and have local workshops with HCPs. For undergraduates, training and internships are offered within the RMC centre.

HCPs and undergraduates are encouraged and reminded about reporting to the national ADR system via email twice per semester. Further efforts are made via social media such as Facebook and LinkedIn pages, the websites, and local training sessions.

RMCs also publish work in periodic scientific journals[39] and on their websites to publicise the importance of reporting.

[39] Adverse drug reactions in children: a ten-year review of reporting to the Portuguese Pharmacovigilance System. Nogueira Guerra L, Herdeiro MT, Ribeiro-Vaz I, Clérigo MI, Rocha C, Araújo A, Pêgo A, Rebelo Gomes E. Expert Opin Drug Saf. 2015 Dec;14(12):1805-13. doi: 10.1517/14740338.2015.1105214. Epub 2015 Nov 7 http://www.ncbi.nlm.nih.gov/pubmed/26549822; accessed 20 April 2016

One RMC implemented a study within hospitals for the detection of serious ADR at the emergency services, through the medical diagnoses and the medication used for patient treatment. Although this was conducted once, the study resulted in over a hundred suspected ADR reports being received through this method.

Effectiveness is measured by Infarmed through biannual reports from RMCs on activity indicators (i.e. the change in number of suspected ADR reports and correlations between the number of training sessions conducted, measurement of the amount of contact made with potential reporters etc.).

Romania

Strategy on raising awareness of national ADR reporting system

The strategy for 'NAMMD' mentions the concern for raising the awareness levels for ADR reporting without any specific terms and indicators. NAMMD participates in conferences and meetings with HCPs, with dedicated presentations on ADR reporting. NAMMD also publishes scientific articles and professional publications on ADR reporting. NAMMD intends to continue these activities and to extend the activity of raising the awareness levels both for HCPs and for patients. The NAMMD communication strategy (2015-2017) is available on NAMMD website – only in Romanian language at the following link – http://www.anm.ro/anmdm/strategii.html

Suggestion 24 explore and maximise any promotional opportunities for joint collaborations and partnerships. Aim to promote through low/no cost outward facing communication channels

Collaborations with a number of organisations for newsletters and for DHCPs. Namely these were; National Health Insurance House, Ministry of Health, Romanian College of Physicians, Romanian College of Pharmacists.

Slovenia

Regional Monitoring Centres in Slovenia

The Agency for Medicinal Products and Medical Devices of the Republic of Slovenia (JAZMP) indicated it had two RMCs within the SCOPE WP4.3 survey.

The first is the National Centre for Pharmacovigilance (NCPHV) that was established by the Ministry of Health based on national legislation and functions in the University Clinical Centre in Ljubljana. NCPHV contact details are promoted on every SPC rather than JAZMPs.

The second is the National Institute of Public Health (NIJZ), which is in charge of most public health in Slovenia. This organisation receives suspected adverse reaction reports for vaccines only, and similarly to NCPHV it sends suspected ADR reports on a weekly basis, via post, to JAZMP. National vaccination policy is led by this organisation. Instructions for reporting and the ADR forms are promoted to HCPs via their website: http://www.nijz.si/en.

Education about suspected ADR reporting via lectures and promotion is a part of the responsibility for both RMCs. Primarily, promotion is targeted at doctors and pharmacists. NCPHV covers topics on drug safety and suspected ADR reporting through printed materials that are distributed to participants. Both RMCs cover the whole of Slovenia and SOPs are in place for their activities.

Annual reports are published by JAZMP for suspected ADRs reports received and include reports from all sources. NIJZ also publish an annual summary of suspected ADR reports for all vaccines in Slovenia.

Campaign case study: Launch of e-reporting form

NCPHV in cooperation with JAZMP developed a web based portal for ADR reporting in 2015. Activities related to promotion and raising awareness focused on promoting and encouraging online reporting of suspected ADRs with HCPs and patients. Many lectures were given to doctors and pharmacists. JAZMP acknowledge further work still needs to be done to reach patients. The instructions on how to report suspected ADRs were included in the promotion with additional communications messages referring to the JAZMP's web site[40]

NIJZ has led vaccination campaigns and promoted suspected ADR reporting related to vaccinations for many years. The tradition of sending these reports to them is well established amongst Slovenian HCPs.

[40] https://www.jazmp.si/zdravila_za_uporabov_humani_medicini/farmakovigilanca/porocanje_o_nezelenih_ucinkih_zdravil/ - JAZMP website suspected ADR information page, accessed 13 June 216

Spain

Suggestion 3 – integrate suspected ADR reporting into clinical IT systems

Spain has shown best practice in this area. In some Autonomous Communities[41] the information of ICSRs are obtained directly from electronic health records, primary care and the e-prescription system. The information is received by their regional PV centres (RPhCs), but the upload into AEMPS own FEDRA database it is not yet automatic and there is an intention to automate.

AEMPs have provided two examples on the way reports are received and managed in this way.

Spain's first RPhC example

The electronic yellow card was integrated in the electronic healthcare record, primary care and e-prescription in 2010 and no testing process was performed before implementation. The information required for a valid electronic yellow card is similar to the paper yellow card: patient, drug, ADR and reporter.

In the toolbars of these applications there is an icon available for HCPs to access to complete a report for a suspected ADR. Upon clicking the icon, an electronic yellow card appears in a new window.

For primary care and e-prescription reports, the reporter patient and drug fields are automatically populated; however, for the electronic healthcare record in public hospitals only the reporter and patient fields are automatically populated with a manual drug field available to be entered by the reporter. The reporter is able to manually populate the other fields and then press send.

Both systems use 'Nomenclator' dictionary maintained by AEMPs to pull across the drug information. It is the same dictionary used in FEDRA, the Spanish database. Indications and ADRs are free texts fields but the International Classification of Diseases (ICD), ninth revision, is recommended. For medication error reports, a mandatory field is included where a HCP can indicate if a medication error has occurred. If 'yes' is selected, the personal data of the primary source is automatically deleted.

Additionally, the system allows attaching files in different formats.

[41] https://en.wikipedia.org/wiki/Autonomous_communities_of_Spain accessed on 18 February 2016

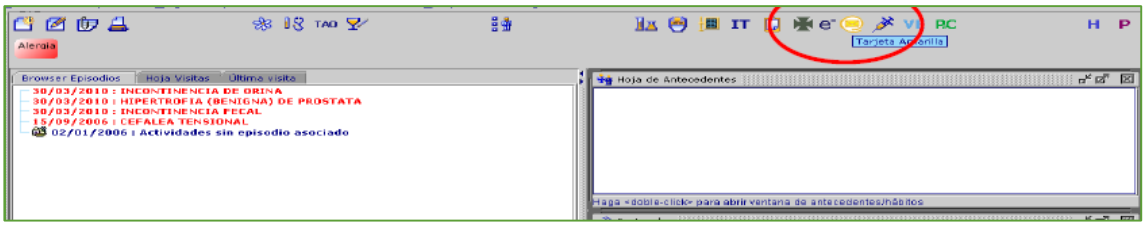


Figure 63. Screenshot of the Spanish electronic healthcare record system within one of its regional centres which HCPs can click onto to access and complete a suspected ADR report

Upon submission, an acknowledgement thank you letter is sent automatically to the reporter. These ICSR are automatically loaded into the local database. The reports are recoded and manually loaded in FEDRA. In the next version of FEDRA it is planned for this information to be automatically integrated and loaded to facilitate the work of RPhCs.

Training activities are carried out by RPhCs to encourage and motivate HCPs to report ADRs and to do it using the integrated electronic yellow card. Training includes how to use the functionality coupled with a guide on how to use the system which has been developed by the RPhC and is available to HCPs.

The integration of ADR reporting in the electronic healthcare record, primary care and e-prescription allows facilitating HCPs to report suspected ADRs and has shown an increase in the quantity of reports and the quality of information received, the latter unquantifiable as yet.

Spain's second RPhC example

In another RPhC region, the electronic yellow card is available on the desktop of computers of medical specialists and included as a link on the RPhCs website. In addition, the ADR reporting system is also integrated in the electronic medical record in primary care and in e-prescription. Information is manually entered by medical specialists and there are dictionaries used for reporting medicines or ADRs. After completion of the electronic form, reports are sent electronically and are included automatically in a local database. Then, technicians enter the reports manually in the national database (FEDRA).

In primary care, when GPs add the International Classification of Primary Care (ICPC) classification of A85 which corresponds to 'Adverse Drug Effect; Correct Dose' within the patient's electronic medical record, the system prompts the GP to complete an ADR report. Should the GP select to do so, a new window appears where information relating to the ICPC and the patient are automatically populated, ready for the GP to complete details about the ADR. For the suspected medicine, the system allows the GP to specify the medication as free text, or to select between the patient´s prescriptions for inclusion into the clinical ADR record or through the Spanish database (Nomenclator).

Upon completion, the report is sent to the RPhC by email where it is then included manually into the local database and also into the Spanish national database (FEDRA).

Collaborate with other organisations to capture reports of all types of harm from medicines

Since 2015, within one of the Spanish RPhCs (regional PV centres) a collaborative partnership agreement was made between the Regional Centre of Navarre and Patient Safety Events Reporting and Learning system (SiNASP) to exchange information about medication errors through the electronic yellow card available on the RPhCs website.

Regional Monitoring Centres in Spain

The Spanish Agency of Medicines and Medical Devices (AEMPS) indicated Spain had 17 regional pharmacovigilance centres (RPhC) for the 17 Autonomous Communities.

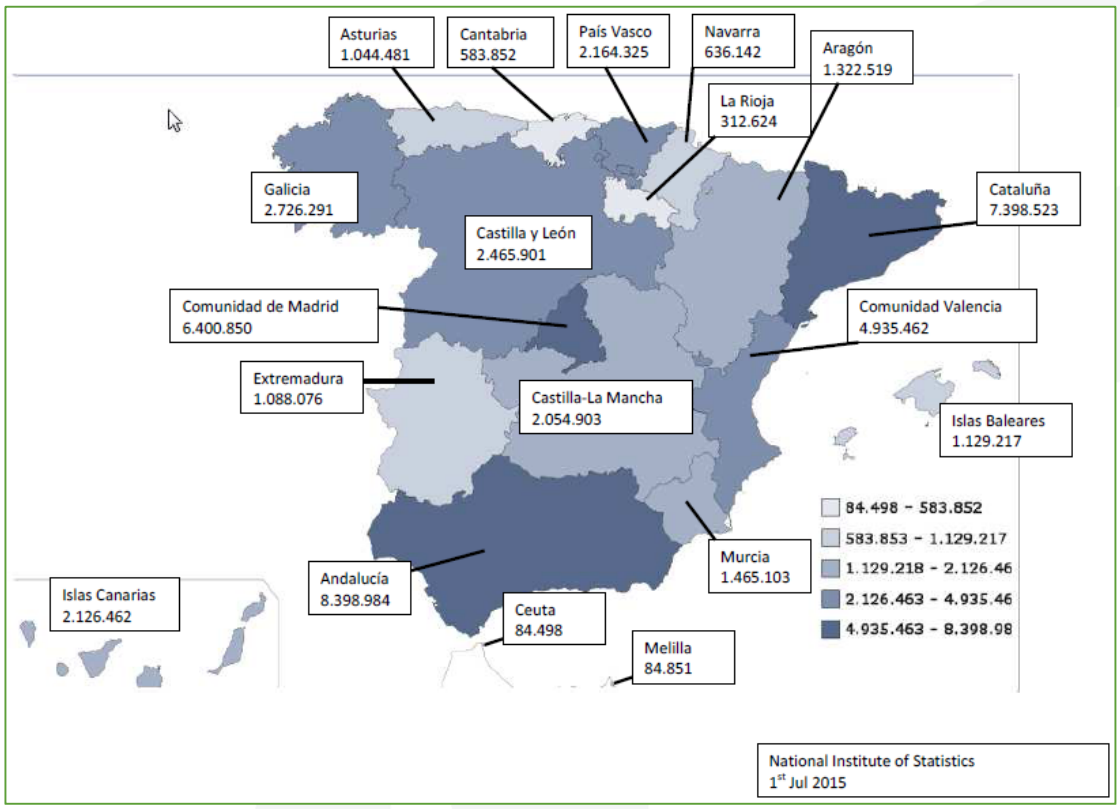


Figure 64. Seventeen Spanish RPhC locations and populations

The 17 RPhCs are situated within: a university (1), hospitals (4) and health departments of the Autonomous Communities (12). Information regarding to where regional centres are and a directory are available on the AEMPS website[42],[43].

[42] http://www.aemps.gob.es/vigilancia/medicamentosUsoHumano/home.htm#sisteEspanol_FV – AEMPS PV page – accessed 13 June 2016

[43] http://www.aemps.gob.es/vigilancia/medicamentosUsoHumano/docs/dir_serfv.pdf; directory of RPhCs – accessed 13 June 2016

Figure 65. Directory location of the 17 RPhCs in Spain from AEMPs website

RhPCs are the contact point for safety queries from HCPs. They also are responsible for stimulating reporting. In particular, they actively encourage HCPs to report suspected ADRs through training and promotional activities. The training is aimed at undergraduate and practicing HCPs such as GPs, community pharmacy, nurses, and specialist physicians. Training activities include online or face-to-face courses aimed at pharmacists, physicians, dentists and nurses. Moreover, ad hoc training sessions are also organised to improve education and training in drug safety at hospitals or health centres.

RhPCs also collaborate with HCP professional bodies and their respective associations to actively promote reporting through them.

Some RPhCs publish bulletins with a variable frequency, which are targeted at patients and HCPs. These are distributed by email or electronic communication channels, sent on paper via post, and published on the website. Some example bulletins are:

- Navarra RPhC's bulletin: http://www.navarra.es/home_es/Temas/Portal+de+la+Salud/Profesionales/Documentacion+y+publicaciones/Publicaciones+tematicas/Medicamento/Boletin+farmacovigilancia/
- Madrid RPhC's bulletin: http://www.madrid.org/cs/Satellite?cid=1142340302454&language=es&pagename=Portal-Salud%2FPage%2FPTSA_pintarContenidoFinal&vest=1142331884078
- Andalucía's bulletin: http://www.juntadeandalucia.es/salud/servicios/farmacovigilancia/pagina.asp?id=62

Communications between the centres and the AEMPS is done via a Coordination Unit and conducted by email and by eRoom, which is a shared workspace on the internet. Important issues are shared and discussed at Technical Committee meetings. Moreover, working groups have been created to address specific issues such as medication error, training activities, good PV practice, harmonization of criteria, and coding. AEMPS are working on new SOPs to harmonise training and procedures between centres and a specific working group was created to implement a Continuous Training Plan.

Case study: Training course for PV

One RPhC has developed a two day training course for undergraduate pharmacists. The course is particularly aimed at students in their final year. It is run twice a year in January and June. Attendance over the years varies: 5 students in 2013, 13 students in 2014, 10 students in 2015 and 6 students in 2016.

Participants are recruited by their tutors during their pre-registration period of training in hospitals or pharmacies. Students fill in a survey to identify their existing PV knowledge and after the course another feedback survey is completed to identify learning. Upon completion, the RPhC issues participants a certificate of attendance.

The course includes a theoretical session on what the PV is, the legislative framework, the types of ADRs, the Spanish PV System, the importance of reporting suspected ADRs and a practical session where students evaluate anonymised cases.

Sweden

Suggestion 7 – have downloadable ADR reporting forms and materials for raising awareness

MPA's website[44] introduces the subject of reporting side effects alongside useful links on the left hand side of the information. These include links to electronic suspected ADR reporting forms for patients and HCPs, downloadable forms, publications, related information for patients on reporting. Amongst the links there is also an additional link to two presentations for e-learning.

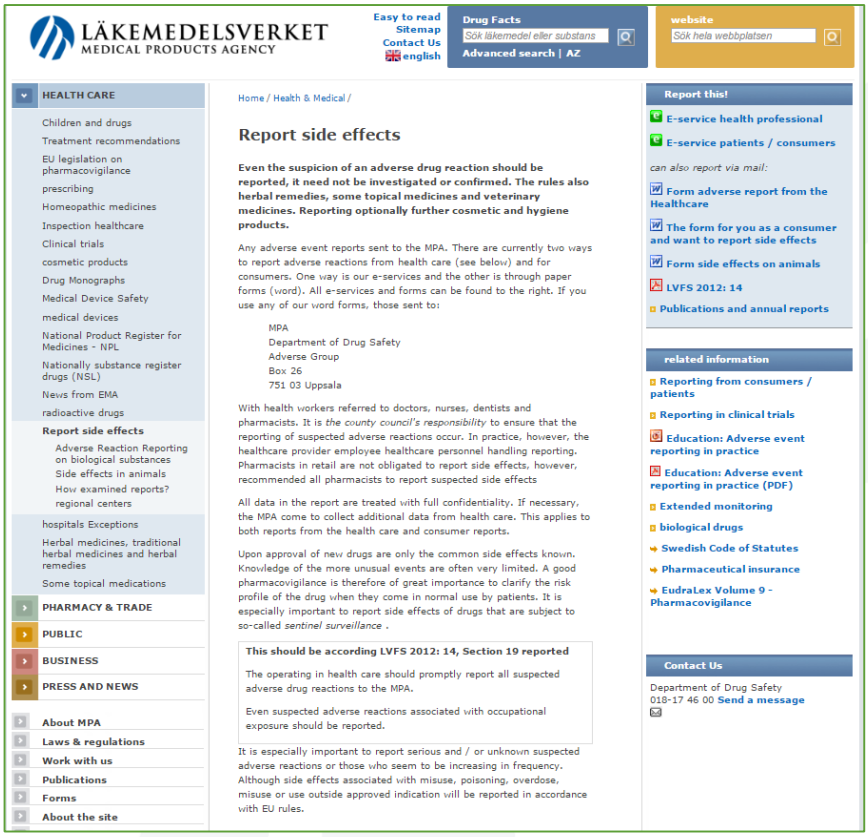


Figure 66. MPA's website with downloadable links on the left hand side

[44] https://lakemedelsverket.se/malgrupp/Halso---sjukvard/Rapportera-biverkningar/ - Accessed 26 May 2016

Suggestion 9 – develop an e-learning module on ADR reporting for HCPs or use the SCOPE package

The MPA have developed e-learning packages for medical students and for nurse prescribers. This is signposted on their website and is downloadable in the form of an educational PowerPoint presentation[45].

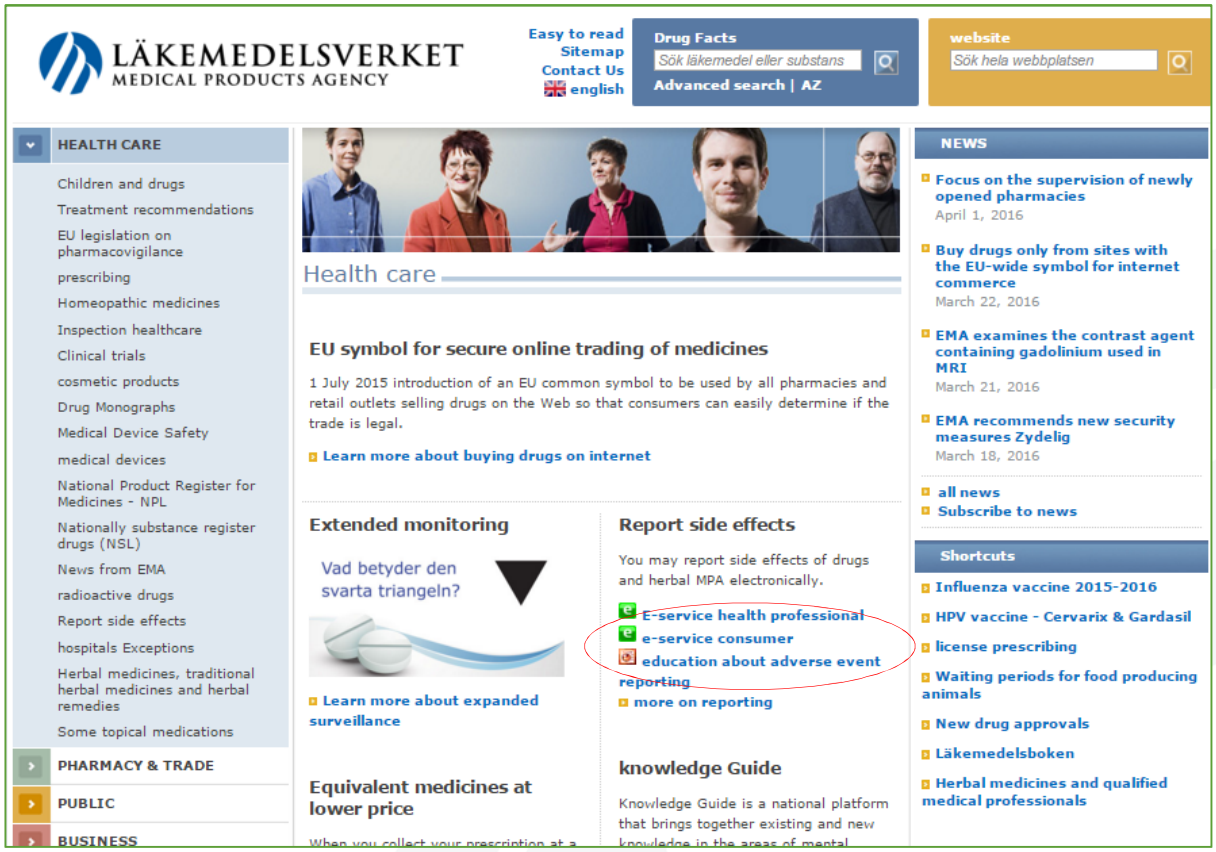


Figure 67. Highlighted in red is the good practice example on the MPA website of the educational PowerPoint presentation about adverse event reporting which can be downloaded for use. The page also includes a section on reporting side effects and corresponding URLs to the electronic reporting forms for HCPs and patients.

Measuring success

The MPA use the number of reports, polls and analysis of the digital views to measure success, including views of its bimonthly online journal and on their website.

[45] https://lakemedelsverket.se/upload/nyheter/2015/biverkningsrapportering-i-praktiken-utbildning.pptx PowerPoint educational presentation from MPA website. Accessed 1 April 2016

United Kingdom

Strategy on raising awareness of national ADR reporting system

The 'MHRA' presents a documented mature strategy called the Yellow Card Strategy. It has evolved with periodic review and updated versions to strengthen direct suspected ADR reporting over the years. It has adapted to the change in PV legislation and some of the major activities from the strategy are also incorporated within the corporate MHRA business plans as objectives.

Following an independent review of the Yellow Card Scheme[46], the MHRA developed its Yellow Card Strategy after a period of detailed analysis of reporting trends across different groups to identify various areas to focus on. The key objective of the Yellow Card Strategy presented which was adopted has remained the same: '**to strengthen the reporting of suspected ADRs by increasing both the number and quality of reports**'.

The initial strategy in November 2006, looked at an in depth analysis of trends in reporting specific to each of the direct reporting groups of the Yellow Card Scheme over 5 years. The report highlighted a number of key issues of concern, specifically:

- A 50% reduction in reporting by GPs during this time period
- Relatively low levels of reporting by community pharmacists
- Disappointing uptake of reporting by electronic mechanisms
- An increasing trend of reports via the pharmaceutical industry rather than being provided directly to the NCA on Yellow Cards.

Together with the decline in reporting by patients and nurses during 2006, all the above issues were regarded as priorities to be addressed by a specific strategy to strengthen the Yellow Card Scheme. The resulting strategy was developed in consultation with a new Expert Advisory Group specifically set up to review and provide advice on the newly formulated strategy.

The table below shows an example of the type of analysis conducted and presented in the first Yellow Card Strategy paper in November 2006 presented to the expert advisory group which established efforts were needed to reverse the decline in GP reporting. This resulted in objectives to facilitate reporting for GPs and a campaign to increase reporting.

[46] http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con2015008.pdf ; Accessed on 15 January 2016

Table 2. Extract showing the an example of suspected ADR trending data by GPs between 2001 and 2005

	2001	2002	2003	2004	2005
Total number of reports (% of all reports)	10378 (48%)	6669 (38%)	5946 (31%)	5985 (31%)	4878 (23%)
% serious reactions	48.1%	52.1%	54.0%	58.9%	59.1%
% fatal reactions	1.5%	1.8%	2.6%	2.7%	3.2%
% black triangle drugs	58.2%	41.9%	33.6%	31.5%	36.4%
% herbal products	0.3%	0.4%	0.4%	0.4%	0.4%
% vaccines	4.9%	7.7%	8.8%	6.1%	10.3%
% children	3.5%	5.4%	7.0%	5.2%	6.9%
% elderly	23.6%	28.5%	29.1%	33.1%	31.4%
% electronic reports	6.0%	5.4%	8.4%	22.8%	13.6%

The strategy recommended four key specific areas to incorporate a number of strands of work so that it could be adapted to the needs of particular reporter groups. These are summarised and commonly referred to as the 4 pillars or elements that make up the UK's Yellow Card strategy:

- **Education** – raising understanding about the purpose, value and importance of Yellow Card reporting, embedding the Yellow Card Scheme and pharmacovigilance into health professional education programmes, to make reporting of suspected ADRs a more visible aspect of the responsibilities of healthcare professionals.
- **Promotion** – develop and maintain promotion and communication strategies and campaigns for the scheme
- **Facilitation** – making reporting easy and accessible to meet the needs of reporters e.g. electronic reporting
- **Motivation** – making reporters more likely to report through approaches to incentivise reporting through acknowledgment and feedback

The key objective of the strategy was to strengthen the reporting of suspected ADRs both then and into the future. This was envisaged through sustainable improvements in reporting to the Yellow Card Scheme by both HCPs and patients, in line with reporting guidelines and through collaborations with their related organisations.

The general aim of strengthening reporting by all groups was also refined with more specific objectives focussing on particular areas where improvements were sought, namely:

- To halt and then reverse the decline in reporting by GPs
- To strengthen reporting by community pharmacists
- To halt and then reverse the recent decline in nurse reporting
- To further develop patient reporting and awareness
- To increase electronic reporting

In order to make progress on these objectives, efforts were made so that reporters receive appropriate education about the Scheme; to ensure potential reporters have an appropriate baseline level of understanding of the Scheme, as well as to promote the Scheme, to ensure that reporters remain alert to potential ADRs and the need to report them.

However, the work was envisaged to be underpinned by efforts to increase accessibility of reporting, in particular through electronic Yellow Card reporting. This thereby supported the aim of strengthening the Scheme in its then current state for the short to medium term, as well as moving away from the traditional paper-based reporting system in favour of electronic capture and collection of reports for the medium to long term period.

The Yellow Card strategy subsequently informed the HMA strategy which was then adopted in principle as levers to improve reporting rates, as outlined in the strategy guidance document.

Progress on these strategy objectives is reviewed formally at least annually through formal and informal progress update reports or position papers. This involves conducting ADR trend analyses to establish whether reporters are continuing to follow the guidelines on reporting and to monitor changes in the number of suspected ADR reports received by the MHRA from various subsets of direct reporters. It also considers the environment of reporting and stakeholders involved to evaluate where to focus future activity. The aim of this is to evaluate objectives, for any findings to help review and inform the shape of future strategy, and review associated resources to improve reporting.

Initially the strategy mainly focussed on a patient reporting campaign launched through community pharmacy and GPs, alongside attending national conferences. However, over time, the Yellow Card Strategy has progressed and changed to refocus its objectives and activities. This evolution has a greater emphasis on facilitation and electronic reporting, especially within the GP sector. Motivation activities are concentrated on greater collaborative work with HCP and patient organisations, and setting up national networks to encourage HCPs locally through feedback. This involves education and joint working with other national organisations. Another aspect includes sustainable approaches through the establishment of quality indicators for reporting suspected ADRs for HCPs – the aim of this being a measure of good patient safety practice. Educational aspects have shifted towards e-learning and showing the value and importance of reporting through case studies, clinical scenarios and incident reviews. The promotional elements have also shifted from the traditional form and poster distributions to reporters and where they can access them readily to more use social media and low or no cost forms of raising awareness. This is mainly due to government marketing restrictions and expenditure. Forms are now distributed through partner organisations such as pharmacy bodies, regional centres and upon request.

Further information on the areas where good practice is demonstrated can be found under the relevant sections as case studies within this WP4.3 SCOPE guidance document.

Although none of the Yellow Card strategy papers are formally published, the MHRA has shared the latest two documents of its updated Yellow Card strategy (both can be found in the annexes of the strategy guidance document):

- Annex 3 – Yellow Card Strategy
- Annex 4 – Yellow Card campaign phase 1 Master Content Final

Analysing ADR trends and reporter groups

Clustered column chart graphs in Microsoft Excel are a useful way of displaying such information. An example is shown in the graph below adapted from the UK's Human Medicines Regulations 2012 Advisory Bodies annual report 2014[47].

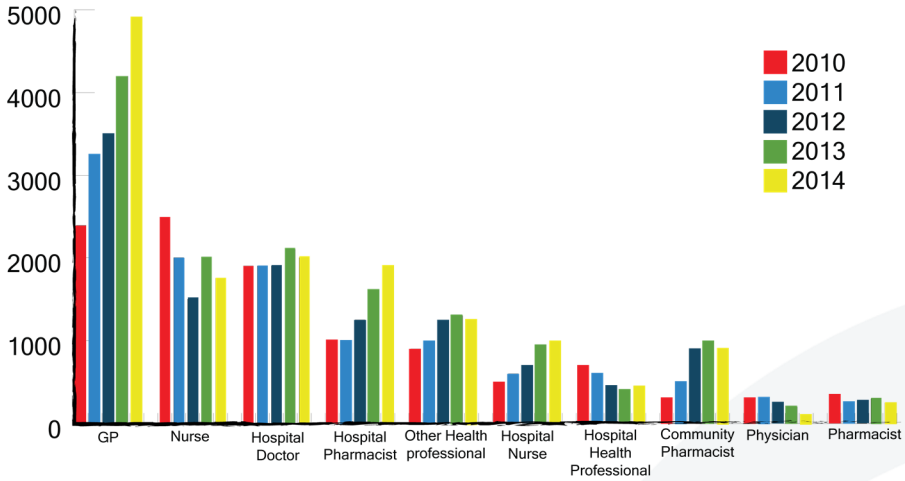


Figure 68. Number of direct UK spontaneous suspected ADR reports received by the Yellow Card Scheme between 2010 and 2014 broken down by reporter qualification

*Other health professionals include: dentists, optometrists, coroners, healthcare assistants, paramedics, chiropodists, medical students and other non-specified health professionals

[47] https://www.gov.uk/government/publications/human-medicines-regulations-2012-advisory-bodies-annual-report-2014, reporting of suspected adverse drug reactions, Pg 34, Figure 2: accessed on 28 January 2016.

Identifying your stakeholders and knowing your audience

A detailed stakeholder analysis can help shape both messages and responses. There are many methods for doing this. An example from the UK is a stakeholder matrix model which looks at current behaviours and attitudes moving to future and desired behaviour and attitudes. The example is shown below for patients. It can be tailored for each stakeholder and can help inform strategy implementation or communication tasks. In this example, one can start to produce messages that are specific to patients by answering the four questions within each quadrant. For example, it helps to formulate specific messages such as: to only report online, the Agency monitors the safety of medicines, the reporting of their side effects matter and it can help to contribute to patient safety.

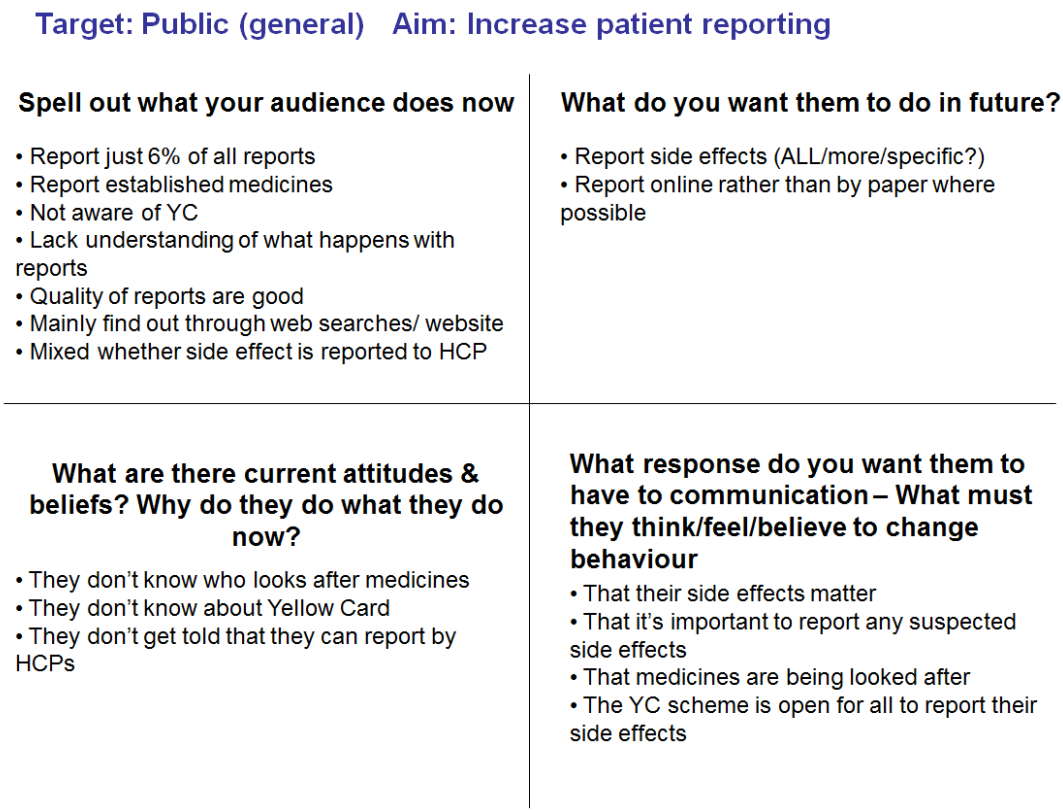


Figure 69. UK example of a basic stakeholder analysis matrix for patients from campaign in 2012. In 2015, patients account for 16% of suspected ADR reporting.

Benchmarking – a formal assessment of awareness levels

Conducted for the entire MHRA, four large omnibus surveys were commissioned by three different independent professional research companies. The large polls were carried out with a range of NCA stakeholders between 2006 and 2010 and these are outlined below. Each are referenced at an archived URL link[48] and are examples of good practice in measuring baseline awareness levels for patient and HCPs. The four polls are outlined below.

1. In 2006, the perceptions, communication and regulation of the risks and benefits of medicines and medical devices was conducted by Ipsos MORI. It showed the perceptions of the general public and of HCPs.

2. Research conducted by two organisations: Opinion Leader (for off-line engagement) and Delib (for on-line engagement) to confirm the desirability of providing regulatory information about medicines online to HCPs and patients. It was also used as an opportunity to explore and gain an understanding of:
   - Where patients and HCPs expect to find information
   - How they might want to search the data
   - The functionality required by the Agency system
   - The impact of making this information available.

   A survey in 2009 followed on from the 2006 Ipsos MORI baseline survey commissioned by the MHRA to discern and quantify the perceptions of the general public about the risks and benefits associated with medicines, and of how well they are regulated in the UK. The 2009 survey was intended as the first measurement to indicate the direction of travel in public opinion in these areas. Core objectives of the survey were to explore:
   - Perceptions of risks, benefits and safety associated with medicines
   - Experiences of medicines
   - Knowledge of and attitudes towards regulation
   - Attitudes towards the communication of information about medicines

3. Another omnibus survey was undertaken by Ipsos MORI in 2008, set out to discover:
   - What pharmacists believe they currently get from MHRA by way of communications and what they think of then
   - What information they want from MHRA
   - How they want this information, taking account of all available channels and sources of communication
   - How often, if at all, they want these various forms of communication.

[48] http://webarchive.nationalarchives.gov.uk/20150121113625/http:/www.mhra.gov.uk/Publications/Corporate/Research/index.htm ; accessed on 29 January 2016

Some of the results from the surveys above that have helped shaped ADR related awareness raising work included:

Pharmacists are the most likely to spontaneously cite MHRA as the organisation that regulates medicines (52%), followed by one in five GPs (21%) and fewer physicians and surgeons (11% and 8% respectively). For GPs, MHRA is the joint second most commonly mentioned organisation after Committee of Safety of Medicines (CSM)/Commission on Human Medicines (CHM). Subsequent messages, where possible, in campaigns now include that the MHRA runs the Yellow Card Scheme and what the MHRA does, including that the Scheme is run on behalf of the CHM.

Pharmacists would be most likely to turn to the MHRA if they wished to report an ADR (22%), compared to fewer GPs (7%) and hospital physicians (5%). No nurse mentioned MHRA in this regard. Nurses differ more generally in their choice of organisations to report adverse drug reactions to. Bearing this result in mind, it was another driver to develop an e-learning module and also attend conferences aimed at encouraging nurses to report and to identify with the MHRA.

The Yellow Card Scheme is a service provided by MHRA and so it was considered important to look at proportions of HCPs that mention both Yellow Card and or MHRA in the same context. Among GPs, 85% cite the MHRA and/or Yellow Card and this proportion reduces to 84% among pharmacists, 59% among hospital physicians and 26% among nurses. This has helped reiterate messages in promotional articles through their respective professional bodies.

Pharmacists and GPs are most likely to have heard of MHRA, (after prompting) which goes some way to explain why they are most likely to mention MHRA as a regulator, and as the organisation to which they would report an adverse incident with a drug (92% and 62% respectively of Pharmacists and GPs have heard of MHRA after prompting). In contrast, only around 4 in 10 of each of hospital physicians, nurses and surgeons have heard of the MHRA. These results gave an impetus to the drivers on collaborative work with NHS organisations to form networks in future and for ensuing communications activity such as the specific tailored campaigns that were devised for GPs and pharmacists. Over 8 in 10 GPs and pharmacists say they would notify the MHRA or use its Yellow Card Scheme to report an adverse reaction to a medicine but only 6 in 10 hospital physicians and a quarter of nurses would do that. E-learning modules for HCPs developed by the MHRA through collaboration with other organisations have tried to also strengthen and clarify such messages to raise awareness. MHRA were also able to organise stands at various conferences to raise the Agency's profile using these results as part drivers.

Through a general public Ipsos MORI Omnibus poll, 915 people were interviewed using a questionnaire focusing on medicines. Interviews were carried out face-to-face, in respondents' homes, with the aid of Computer Assisted Personal Interviewing (CAPI) terminals (laptops). Fieldwork was conducted between 16 and 21 March 2006. When asked who or which organisation they think regulates medicines to make sure they work and are safe enough to use, around half (49%) say they don't know. In a later poll, 2009, the large majority say they would report an unexpected side-effect of a medicine to their doctor or GP, aside from that, few particular individuals or organisations are mentioned by any significant number of people. The proportion who would report it to the MHRA remained the same as it was in 2006 at 1% as does those who would fill in a Yellow Card (less than 1%). For this reason, messages to patients now always introduce the MHRA and what the Yellow Card does. It is also the reason for campaigns to promote patient reporting being targeted via GPs and pharmacists, and why the Yellow Card is signposted and explained on trusted webpages referred to by patients.

In 2011, the independent review which formally evaluated patient reporting of ADRs outlines questions that can be adapted for use to gain further insight for patient benchmarking, their experiences and tailoring messages for future campaigns.[49] For example, from patients interviewed, almost one-half learned about the Yellow Card Scheme from a pharmacy (n = 667; 49.0%) – this result reinforced the strategy of reaching patients via tailored campaigns with community pharmacists.

Parents were surveyed by a third party organisation called YouGov before and after the paediatric campaign in November 2013 and May 2014. Results showed that between 14% and 17% parents have heard about the Yellow Card Scheme. The omnibus survey results helped to inform the effective measurement of the communication campaign. It also made it possible to target specific reporter groups with considered and tailored messages for respective key audiences and enable the measurement of any change in behaviours. It has also led to an impetus to strengthen undergraduate and post graduate reporting. It is one of the factors behind developing e-learning modules for HCPs which also count for CPD credits.

[49] http://aura.abdn.ac.uk/bitstream/2164/2957/1/mon1520_YCS.pdf - see Appendix of the Health Technology Assessment report 16 to 22 - accessed on 29 January 2016

Sharing best practice: A template of questions to ask and methodology

Who, or which organisation, if any, do you think regulates medicines to make sure they work and are safe enough to use?

Example answers can be broken into different categories such as: healthcare professional regulators, healthcare professional bodies, NHS, pharmaceutical companies, the government, quango/department/agency, NCA, Don't know, other.

Who or which organisation, if any, would you personally contact if you wished to report an unexpected side effect with a medicine (or ADR if aimed at HCPs)?

Example answers can be broken down into different options such as: doctor/GP, hospital, the NHS, list national professional organisations and organisations which regulate HCPs, pharmaceutical company, friend/relative/work colleague, nurse, pharmacists, NCA, none – I would not know who to contact, none – I would not report it, don't know.

If a patient reports an ADRs to you, to whom or to which organisation would you report it, if anyone?

A doctor, nurse, pharmacist, National ADR reporting system, NCA, local authority / trusts, patients doctor, professional regulators, escalate with a superior, the manufacturer/pharmaceutical/drug company, surgery/hospital/place where patient received treatment, the patient's doctor

How much, if anything, would you say you know about the way medicines are regulated?

How much confidence, if any, do you have in the way medicines are regulated?

Example answers can be broken into different categories such as: a great deal, a fair amount, not very much, nothing at all, don't know.

Which, if any, of the following things would help you to report ADRs?

Example answers can be broken down into different options such as: online reporting, clearer guidelines on what to report, easier/faster access to reporting, forms, feedback on reports, telephone reporting, paper supplies of reporting forms, nothing, other, don't know / can't recall

Suggestion 1 – a freepost service for paper forms

One example is the MHRA's paper forms which all have a freepost address on the back. The HCP forms are designed so they can be folded and sealed and the patient form has a detachable pre-paid envelope that the form can be inserted into. Both types have the address pre-printed on the front side of the envelope.

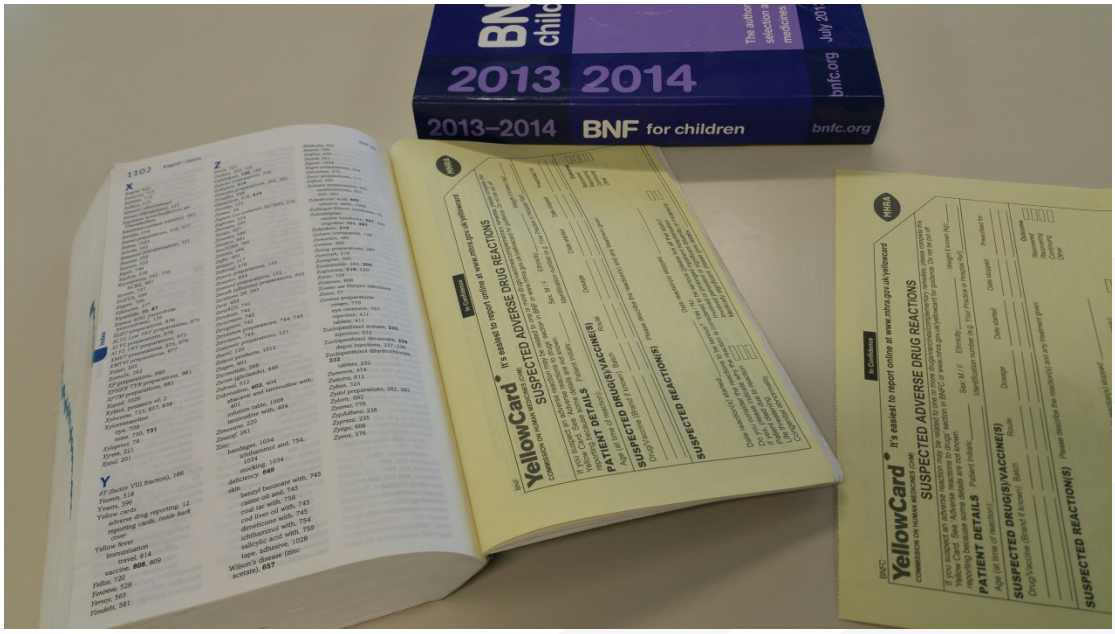


Figure 1. An example of a detachable free post Yellow Card reporting form, with free postage to the MHRA, is at the back of each British National Formulary. It is also within the BNF for children and Nurses Prescribers' Formulary (NPF)

Suggestion 2 – keep improving the functionality of your e-form

Initially user tested through a specific patient user group, since launching the online Yellow Card reporting site for collecting suspected ADR reports the MHRA has strengthened and enhanced it as a result of various interactions with stakeholders and internal recommendations by the PV team. The aim is to develop a seamless reporting experience for the reporter. The Yellow Card reporting site for suspected ADRs has the added functionality of smart dropdowns from existing dictionaries for suspected drugs and MedDRA Lower Level Terms for ADRs which are auto populated as the user types – it also includes the option to add free text for both fields. The site also includes smart fields to request additional information depending upon previous answers.

Some improvements were based on considered feedback and interaction with patient organisations to enable reporting of different scenarios such as in pregnancy[50], and to capture changes in legislation requirements (medication errors and biological traceability of batch numbers and corresponding help information). This improvement work has occurred through planned and scheduled periodic review for IT enhancements. There is also a feedback box for reporters to contact the MHRA on such matters and general PV queries. There have also been changes as a result of recommendations from the independent review to harmonise reporting discrepancies between HCPs and patient forms[51]

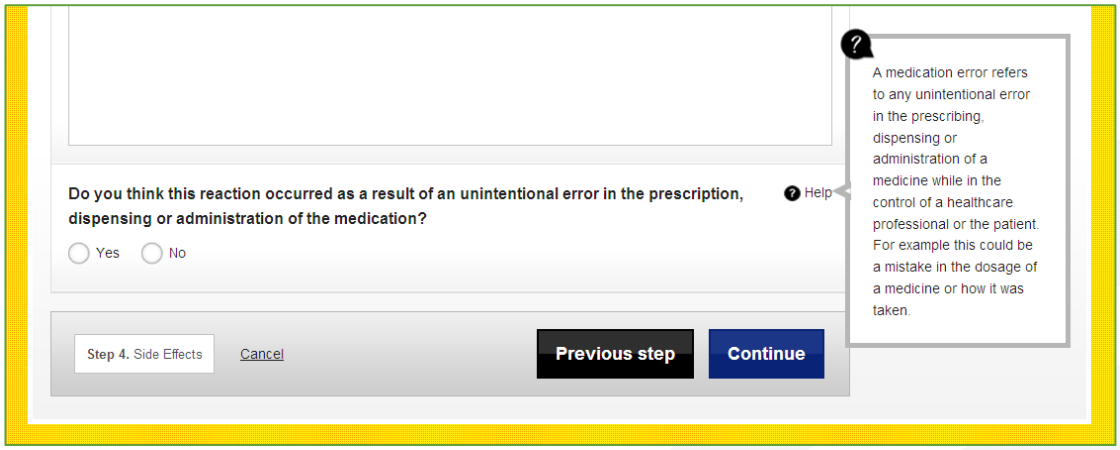


Figure 71. Screenshot of Yellow Card reporting site asking for medication errors and an example of help boxes for what is being asked

Figure 72. Screenshot of Yellow Card reporting site asking for batch numbers which was also supported by a Drug Safety article[52] to increase the quality of reports

Initially, the MHRA had to make contact with some large organisations (e.g. large multiple pharmacy chains) to ensure reporters were able to access the Yellow Card reporting site from their organisational web browsers and systems.

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[50] https://www.gov.uk/drug-safety-update/yellow-card-update-to-form accessed 9 March 2016

[51] http://aura.abdn.ac.uk/bitstream/2164/2957/1/mon1520_YCS.pdf accessed 9 March 2016

[52] https://www.gov.uk/drug-safety-update/reporting-suspected-adverse-drug-reactions-to-vaccines-and-biological-medicines accessed 9 March 2016

In November 2015, the reporting site evolved to simplify the MHRA's different reporting systems for medicine and device incident report systems by facilitating a single point of reporting under the brand of the Yellow Card Scheme after user feedback[53]. In addition to the traditional reporting of suspected ADRs, medical device incidents, defective medicines and suspected counterfeit products are now reportable through the Yellow Card Scheme's online reporting site.[54] The site evolved again in May 2016 to also capture reports of problems suspected to be associated with e-cigarettes[55].

Suggestion 3 – integrate suspected ADR reporting into clinical IT systems

The UK has also shown best practice in this area. As part of Yellow Card strategy several projects are currently underway to facilitate electronic Yellow Card reporting through integration into clinical IT systems used by HCPs. Electronic reporting via both the Yellow Card website and clinical systems continue to be increasing in popularity amongst HCPs. This has been showcased at ISOP and the MHRA's Yellow Card 50th anniversary scientific conference in March 2015.[56]

GPs are considered to be the cornerstone of Yellow Card reporting, and have historically been the single largest reporter group. In 2009 it was noted that although overall Yellow Card reporting was continuing to increase each year, a decreasing trend in the number of reports received from GPs was observed. Surveys investigating reasons for HCP failing to report include a lack of time, difficulty in accessing a reporting form or access to the Yellow Card website[57].

Electronic reporting has been used by the MHRA as a means to facilitate reporting. This reduces the amount of resource needed for manual entry of ADR data, whilst also making data available for signal detection more quickly as the data can be loaded automatically into the MHRA's pharmacovigilance database.

Reporting directly from clinical systems has a number of benefits. It improves access to Yellow Card reporting and reduces the effort required to complete the form through automatic population of information from the patient record. Reporters can be prompted to complete a Yellow Card within the system when specific tasks are completed, such as a medication being withdrawn.

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[53] https://www.gov.uk/drug-safety-update/yellow-card-extended-to-include-devices-counterfeits-and-defective-medicines accessed 9 March 2016

[54] www.mhra.gsi.gov.uk/yellowcard accessed 9 March 2016

[55] https://www.gov.uk/guidance/e-cigarettes-regulations-for-consumer-products - accessed 24 May 2016

[56] Establishing electronic adverse drug reaction reporting in UK primary care clinical IT systems. ISoP Abstract & Poster 2012 Barrow P, Foy M, Jadeja M; Yellow Card 50th Poster 2015 same authors plus Owen R

[57] Hazell L, Shakir SAW. (2006) Under-Reporting of Adverse Drug Reactions A Systematic Review. Drug Safety 29(5): 385-39

One particular example in this respect to reverse a declining trend from GPs was the introduction of an electronic Yellow Card reporting facility which was integrated into a primary care system, SystmOne. This system is used by GPs and nurses in approximately 20% of the primary care practices in England. By the end of 2015, this has led to an extra 12,374 Yellow Card reports submitted by GPs from this clinical IT system alone, since implementation in November 2010.

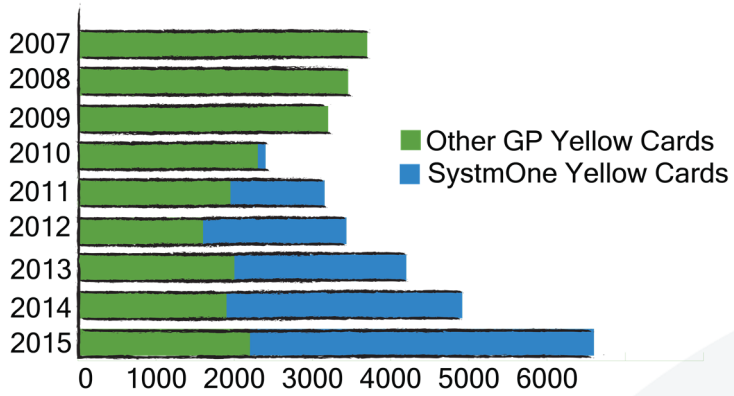

Figure 73. Direct GP Yellow Card reports of suspected ADRs received by the MHRA between 2007 and 2015

Subsequently, in 2012, an information standard for electronic Yellow Card reporting (ISB 1582[58]) was developed for the English National Health Service (NHS) based around the ICH E2B(R2) standard[59]. It defined the electronic Yellow Card message, standard requirements and a number of triggers for a user to prompt completion of an electronic Yellow Card. Primary care systems are the main target for the standard, however IT systems across healthcare are also able to implement the standard, such as pharmacy electronic prescription service (EPS) systems, patient medical record (PMR) systems, and secondary care local risk management systems (LRMS).

The implementation of the standard into primary care IT systems began through a partnership with the Health & Social Care Information Centre (HSCIC). This resulted in the standard being incorporated into the core requirements for the GP Systems of Choice (GPSoC) programme. This meant that all GP systems in England must include the capability of reporting an electronic Yellow Card to the MHRA directly from their respective systems. Testing of these systems with providers commenced in August 2014. SystmOne adopted the new standard in April 2015. Although GPSoC only applies directly to England, the clinical systems that are also used in devolved administrations (Scotland, Wales and Northern Ireland) will have the ability to use the same functionality. As part the testing process, a step-by-step user guide has also been developed with the system providers to support GPs and their healthcare team in reporting.

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[58]‘ ISB 1582 Electronic Yellow Card Reporting’ standard. Accessed on 8 March 2015 (although archived) at http://www.isb.nhs.uk/documents/isb-1582

[59] ICH M2 EWG Electronic Transmission of Individual Case Safety Reports Message Specification. http://estri.ich.org/e2br22/index.htm Accessed 8 March 2016

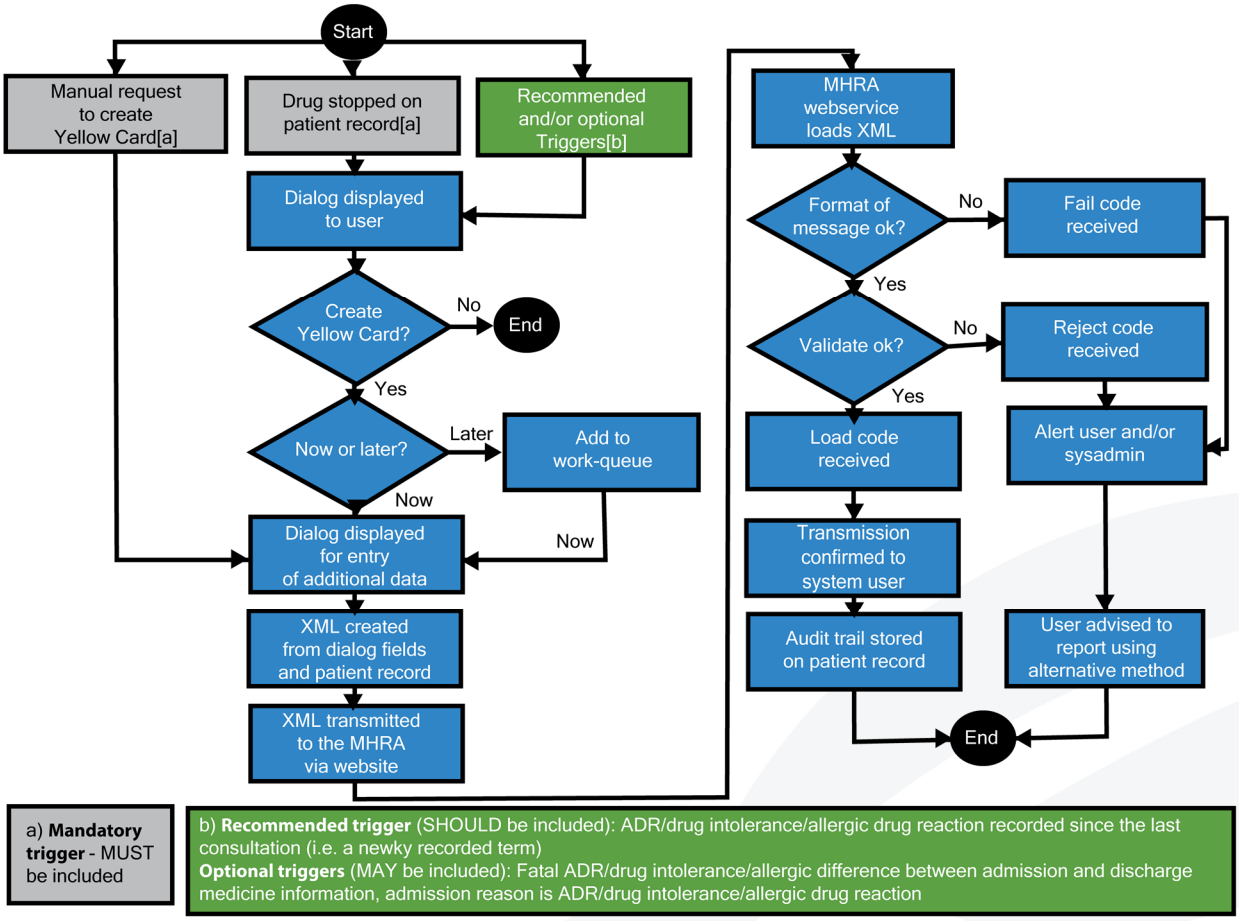


Figure 74. The electronic Yellow Card reporting workflow from ISB 1582 Standard

As MedDRA terms are not used in NHS clinical systems, the ISB 1582 electronic Yellow Card reporting standard specifies that medical terms used to code suspected ADRs in an electronic Yellow Card can and should be coded using SNOMED CT[60] concept terms, although MedDRA is also acceptable to the MHRA. So that no information is lost in mapping a synonym to a SNOMED CT concept, the originally coded term name (from the terminology used in the clinical system) is also collected in the message sent to the MHRA in XML format.

[60] What is SNOMED CT? http://systems.hscic.gov.uk/data/uktc/snomed Accessed 8 March 2016

The MHRA have built up mapping between SNOMED CT concept terms and MedDRA Preferred Terms (PTs) from Yellow Cards received from clinical systems. An internal process converts SNOMED CT concepts to MedDRA PTs before the Yellow Card is processed automatically through to the MHRA PV database without intervention. Yellow Cards received where the SNOMED CT codes have not been mapped fall into a web service staging area where manual mapping is performed by a team of PV signal assessors. When a suitable term is selected for an unmapped term by an assessor, it is stored as a mapping for any future Yellow Cards. This enables future reports with the same term to remain in the workflow and be automatically loaded into the MHRA's PV database. There are plans for a quality audit process to be introduced in future to ensure mapping of terms between SNOMED CT and MedDRA are still current and appropriate.

Other GP systems are being tested and will be rolled out over 2016-17. Implementation in 100% of GP systems in England is estimated to result in an increase of approximately 10,000 Yellow Cards per year, an increase of about 60% on total Yellow Cards currently received annually from GPs.

Medicines Information Pharmacists – MiDatabank software

In a similar approach to the one used with SystmOne, in collaboration with Southampton University Hospitals NHS Trust and UK Medicines Information (UKMi) service, the MHRA have integrated automated production of Yellow Card reports using their MiDatabank software with medicines information pharmacists usually based within NHS hospitals in the UK.

To help continue the installation of MiDatabank software including Yellow Card, reporting has been supported by a number of activities. A letter was sent from the CEO of the MHRA to NHS Chief Executives encouraging prioritisation of the installation of this software within NHS Trusts in 2012. In addition, various workshops and posters on ADR reporting have been presented at UKMi annual conferences between 2012 and 2015. A league table of reporting statistics is regularly provided to all UKMi centres to encourage reporting and installation. A survey is being developed to further understand the barriers trusts face in installing this software and to increase reporting via this integrated method.

The majority of hospital pharmacist reporting is now electronic – in 2015, 31% (889 reports) were reported directly from the MiDatabank system used within 118 different Medicines Information Centres, whilst 56% (1590 reports) were reported through the MHRA's electronic Yellow Card website with only 12% (336 reports) received via the paper form. Reports through both electronic methods have increased by approximately 40% compared to 2014. It is encouraging to note that the number of Yellow Cards received from hospital pharmacists have almost tripled between 2011 and 2015.

Other clinical systems – a third system for direct ADR reporting from a secondary care setting was also established towards the end of 2012 as a result of collaboration between MHRA, Cerner and Newcastle upon Tyne NHS Foundation Trust. Cerner provides triggers to report to the Yellow Card Scheme when a suspected ADR leads to stopping treatment.

Work is ongoing to roll out this system across the UK. All future e-Prescribing deployments of the Cerner software will have the latest version with Yellow Card reporting functionality built into it. However, there is a planned upgrade schedule from now into 2017 for nine clients based in major hospitals across England who are using the older software. This is anticipated to further increase suspected ADR reporting

Other secondary care systems are also in the process of developing Yellow Card reporting functionality directly within their risk management IT systems too.

Suggestion 4 – consider developing a mobile application for ADR reporting

The UK's Yellow Card Scheme app was launched by Minister for Life Sciences[61], [62] in July 2015 and is available free for download the app from the iTunes App Store and Google Play for IOS or Android devices. The app can be can be used by patients, carers and HCPs. Key features of the app are that it enables users to:

- Have a convenient alternative to using paper forms or using the website
- Use the app for free on iOS and Android systems
- Easily report side effects directly to the Yellow Card Scheme
- Create a 'watch list' of medications to receive official news and alerts on
- View numbers of Yellow Cards received by MHRA for medicines of interest
- See an immediate response that shows Yellow Card has been accepted
- Submit updates to Yellow Cards already submitted
- View previous Yellow Cards submitted through the app.

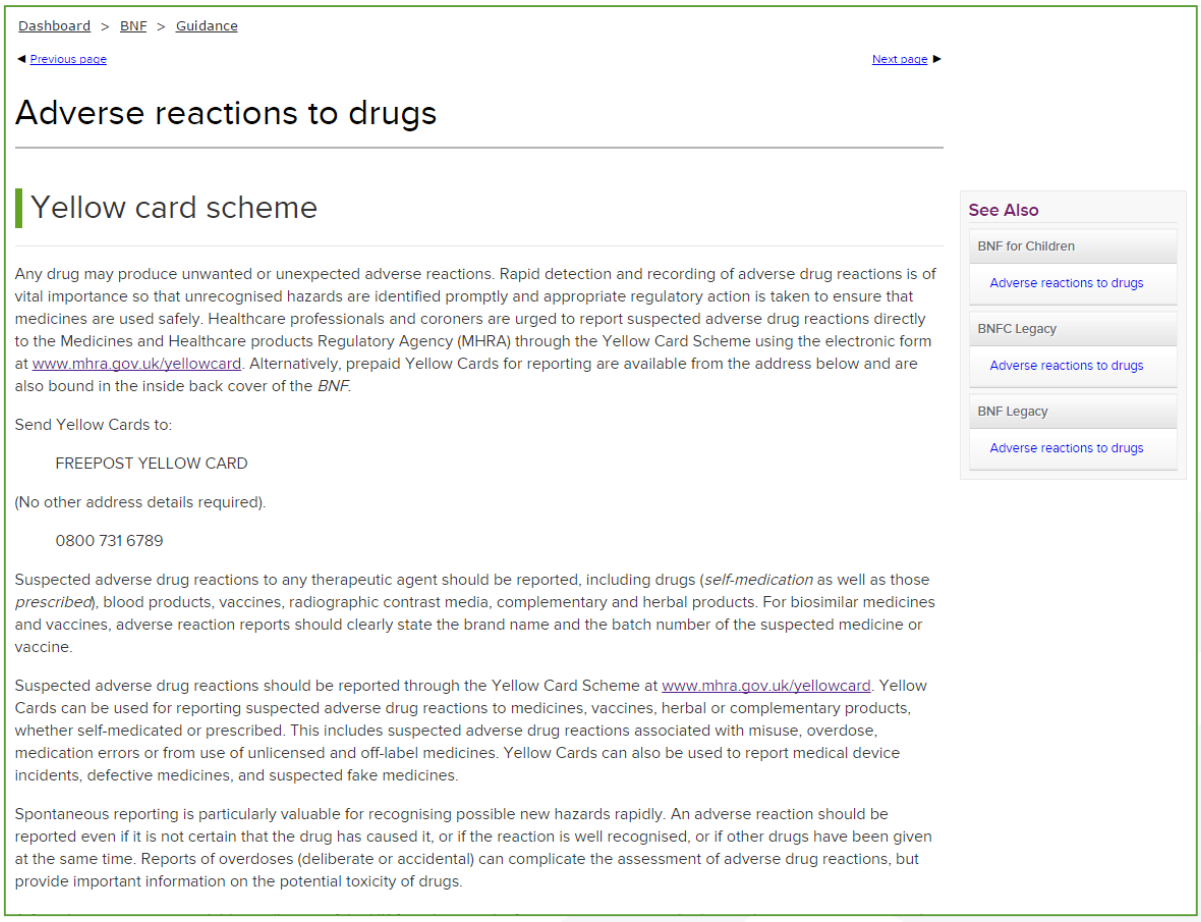
[61] https://www.gov.uk/government/news/digital-evolution-for-ground-breaking-yellow-card-scheme accessed 9 March 2016

[62] Yellow Card app - Ministerial launch: https://www.youtube.com/watch?v=OoSdiXINj1c accessed 9 March 2016

Suggestion 6 – ensure paper forms are widely accessible with relevant information

The MHRA has worked with various organisations to facilitate reporting forms into HCP publication resources alongside supporting information on: the importance of reporting suspected ADRs, reporting guidance, information about additional monitoring, special populations, preventing ADRs, regional centres and links to report online. Most importantly a few copies of detachable paper forms are included at the back of the formularies in yellow paper. These are freepost to the MHRA. The main publications that contain similar paper forms and information about suspected ADR reporting include:

- National formularies such as the:
  - British National Formulary (BNF)
  - British National Formulary for Children (BNFC)
  - Nurse Prescribers' Formulary (NPF)
- Monthly Index of Medicinal Specialities (MIMS) – a prescribing and clinical reference for GPs published every quarter and sent out to all GPs in the UK
- Proprietary Association of Great Britain OTC directory – a UK trade association for manufacturers of over-the-counter medicines and food supplements that is updated annually and mailed to GPs and other HCPs groups across the UK.



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Adverse reactions to drugs

Yellow card scheme

Any drug may produce unwanted or unexpected adverse reactions. Rapid detection and recording of adverse drug reactions is of vital importance so that unrecognised hazards are identified promptly and appropriate regulatory action is taken to ensure that medicines are used safely. Healthcare professionals and coroners are urged to report suspected adverse drug reactions directly to the Medicines and Healthcare products Regulatory Agency (MHRA) through the Yellow Card Scheme using the electronic form at www.mhra.gov.uk/yellowcard. Alternatively, prepaid Yellow Cards for reporting are available from the address below and are also bound in the inside back cover of the *BNF*.

Send Yellow Cards to:

FREEPOST YELLOW CARD

(No other address details required).

0800 731 6789

Suspected adverse drug reactions to any therapeutic agent should be reported, including drugs (*self-medication* as well as those *prescribed*), blood products, vaccines, radiographic contrast media, complementary and herbal products. For biosimilar medicines and vaccines, adverse reaction reports should clearly state the brand name and the batch number of the suspected medicine or vaccine.

Suspected adverse drug reactions should be reported through the Yellow Card Scheme at www.mhra.gov.uk/yellowcard. Yellow Cards can be used for reporting suspected adverse drug reactions to medicines, vaccines, herbal or complementary products, whether self-medicated or prescribed. This includes suspected adverse drug reactions associated with misuse, overdose, medication errors or from use of unlicensed and off-label medicines. Yellow Cards can also be used to report medical device incidents, defective medicines, and suspected fake medicines.

Spontaneous reporting is particularly valuable for recognising possible new hazards rapidly. An adverse reaction should be reported even if it is not certain that the drug has caused it, or if the reaction is well recognised, or if other drugs have been given at the same time. Reports of overdoses (deliberate or accidental) can complicate the assessment of adverse drug reactions, but provide important information on the potential toxicity of drugs.

See Also

BNF for Children
Adverse reactions to drugs

BNFC Legacy
Adverse reactions to drugs

BNF Legacy
Adverse reactions to drugs

Figure 75. Example online information within the BNF guidance that contains supporting URL links for reporting[63].

Suggestion 7 – have downloadable ADR reporting forms and materials for raising awareness

The MHRA's reporting site contains links to posters on the Yellow Card Scheme, printable reporting forms for HCPs and patients, information and guidance on reporting to the Yellow Card Scheme and also information about the Scheme in other languages:

- https://yellowcard.mhra.gov.uk/downloadable-information/
- Downloadable videos that have been used to raise awareness levels are included on the MHRAs YouTube channel: https://www.youtube.com/playlist?list=PLSF-BoykD5J2ZNVO1VdyxVkdgAXlONXokO

[63] https://www.medicinescomplete.com/mc/bnf/current/PHP97237-adverse-reactions-to-drugs.htm BNF: Guidance – Adverse reactions to drugs. Accessed 9 March 2016

Suggestion 9 – develop case studies to show the importance of reporting

MHRA has created a document[64] published on their reporting site as well as their general website. Case studies are used in campaigns and also have been linked digitally through partnership organisations to promote ADR reporting and show the value of reporting.

The document outlines the value of the Yellow Card Scheme through demonstrating the numerous important safety issues that reporting has helped to identify – many of which were not recognised as being related to a particular medicine until information was received via Yellow Cards. The document shows a table of safety issues:

Table 3. Examples of how MHRA presents cases where Yellow Cards have helped identify or contributed to the assessment of safety issues

Year	Medicine	Adverse Reaction	Resulting action or advice
October 2014	Interferon beta (Rebif, Avonex, Betaferon, Extavia)	Thrombotic microangiopathy (TMA) and suspicion of increased risk with new formation of Rebif	Collaborative assessment with NIBSC. Need for better risk minimisation identified. Class warnings implemented for all products. Warnings to be vigilant for early signs or symptoms issued and added to the product information including diagnostic tests descriptions, treatment options and advice on the action to take. Further requirements were made for the pharmaceutical company to do further study on the possible increased risk of TMA with new formulation Rebif.
September 2014	Pregabalin	Abuse, misuse and dependence	Strengthened product information warnings regarding abuse, misuse and dependence

The table is followed by example case studies which were developed based upon regulatory action taken and have been used to educate reporters in campaign work:

- Yasmin and hair loss (alopecia)
- Amlodipine and grapefruit interaction

[64] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/396811/Contribution_of_Yellow_Cards_to_identifying_safety_issues.pdf accessed 11 March 2016

- Warfarin and Cranberry juice interaction
- Phenytoin and Purple Glove Syndrome (for pharmacists)
- Ranitidine and breast disorders (doctors)
- Varenicline (Champix▼) and somnabulism (sleep walking)
- Corn plasters and skin ulceration (patients/physicians)

Below is a full example aimed at patients. The case study is followed by a summary of key 'take away' messages for the reader:

Case study: Yasmin and hair loss (alopecia) – aimed at patients

After three months of being prescribed Yasmin for oral contraception, a female in her twenties suffered substantial hair loss (alopecia). She suspected this might be due to the medicine she was taking so she checked the Patient Information Leaflet (PIL) inside the packaging of her medicine, as advised to by her pharmacist when she collected her medicine – there was no mention of hair loss under the possible side effects section. She decided to go into her local community pharmacy.

Her pharmacist advised her make an appointment with her GP but at the same time also had an important discussion with her about side effects and medicines. The pharmacist asked her if she was taking any other medicines at the time – this enabled the possibility of a potential interaction between Yasmin and any other medicines to be ruled out. The pharmacist also asked her if she any of her family members had hair loss, which they did; however, she also mentioned that she had never had any history of hair loss herself.

Even though the pharmacist was not certain that Yasmin was responsible for causing hair loss, they encouraged her to complete a Yellow Card – as only a suspicion that a side effect is occurring because of a medicine is needed to complete a Yellow Card. So she went online and completed a report (www.mhra.gov.uk/yellowcard).

Through routine assessment by MHRA experts, her Yellow Card report triggered a more thorough review of this issue. This identified a further 14 similar reports for patients ranging from 18 to 37 years old – 7 of which were received directly from patients. At the time of the review, most cases of hair loss were recovered or recovering. The review resulted in the Patient Information Leaflet (PIL) being updated to include hair loss (alopecia) under 'uncommon side effects': out of every 1,000 women who use Yasmin between 1 and 10 may be affected.

Key 'take- away' messages for patients

- Patient reporting via the Yellow Card Scheme adds value to medicines safety.
- Pharmacists and GPs have a key role to play in promoting patient safety about side effects.
- Check the PIL supplied with your medicine which lists all recognised side effects and interactions.
- Anyone is able to report suspected side effects: www.mhra.gov.uk/yellowcard
- If you are concerned about a side effect, ask your doctor or pharmacist for advice

Suggestion 9 – develop an e-learning module on ADR reporting for HCPs or use the SCOPE package

The UK has created a number of free learning modules which all count to CPD points for HCPs. Each are described in high level below.

- **E-learning modules for pharmacists** – The MHRA in collaboration with Centre for Postgraduate Pharmacy Education (CPPE) has developed a series of three e-learning programmes with the Wales Centre for Pharmacy Professional Education. The programme has been endorsed by the Drug Safety Research Unit.

  The three e-learning modules aim to help pharmacists understand how to identify, report and prevent ADRs:

  – Adverse drug reactions and medicines safety
  – Reporting adverse drug reactions
  – Patients and adverse drug reactions

- **E-learning module for nurses** – The MHRA in close collaboration with The Nursing Times have developed an interactive e-learning module for nurses. The module is free once a nurse registers with the Nursing Times Learning site and upon completion counts for 2 hours continuing professional development (CPD) credits.

- **For all healthcare professionals and doctors** – based on the first learning unit created by the MHRA, a BMJ Learning module on pharmacovigilance[65] was developed. Due to the cost of maintenance, this the module was archived. The module is still accessible and counts for 1 CPD credit. It is also accredited by a variety of other organisations and countries.
- **Regional courses** – MHRA regional centres have also developed their own regional ADR modules to increase reporting and awareness through education, all count for CPD credits. The e-learning modules are for the NHS, undergraduates, and there is a safer prescribing course for foundation year doctors that contains information on ADR reporting.
- **Medicines modules** – to supplement learning, MHRA has produced a series of free e-learning modules for HCPs based around clinically-relevant aspects of medicines regulation as well as topics on the risks of commonly-prescribed specific classes of medicines[66]. They are written for HCPs responsible for prescribing, supplying or administering medicines. They can be used by: trainees, established clinicians to refresh or update their knowledge, or for clinicians moving from one specialty to another. Questions within the modules test users' understanding of the materials. Feedback on the questions are also included. All of these education modules have been accredited for continuing professional development (CPD) points by relevant Royal Colleges:
  - Antipsychotics – accredited for 3.5 CPD credits
  - Benzodiazepines – 2.5 CPD credits
  - Corticosteroids – 2 CPD credits
  - Opioids– 2 CPD credits
  - Oral anticoagulants– 1.5 CPD credits
  - Selective serotonin reuptake inhibitors (SSRIs) – 3 CDP credits

  Work is continuing to get these materials introduced into undergraduate training courses for health professionals.

[65] http://learning.bmj.com/learning/module-intro/pharmacovigilance-adverse-drug-reactions.html?moduleId=10042344 BMJ Pharmacovigilance – identifying and reporting adverse drug reactions- Archived – accessed 14 March 2016

[66] MHRA E-learning modules: medicines: https://www.gov.uk/government/publications/e-learning-modules-medicines-and-medical-devices/e-learning-modules-medicines-and-medical-devices#contents. Accessed on 10 March 2016

Suggestion 10 – aim to introduce reporting ADR reporting in examinable undergraduate courses

The MHRA has worked with regulators of HCPs to add relevant information about ADR reporting into HCPs guides and codes of conduct. Examples are provided below, including the specific wording used.

Doctors

The following are competencies included within the UK Foundation Programme Curriculum[67] for doctors produced by the Academy of Medical Royal Colleges (from the Medical Foundation Programme 2012, with August 2015 updates[68]):

Relationship and communication with patients
Section 2.4 – Complaints:

- *Understands and addresses common reactions of patients, family and clinical staff when a treatment has been unsuccessful or when there has been a clinical error*

Good clinical care
Section 7.6 – Safe prescribing:

- *Takes an accurate drug history, including self-medication, use of herbal products and enquiry about allergic and other adverse reactions*
- *Notifies regulatory agencies of reportable adverse drug reactions to medicines and blood products*
- *Administers blood products safely and recognises transfusion reactions*
- *Anticipates, prevents and manages adverse drug and transfusion reactions, and understands how and when to report suspected adverse reactions to the Medicines and Healthcare product Regulatory Agency (MHRA)*

The above also maps under domain 2 – Safety and Quality of Mapping the Foundation Programme Curriculum 2012 to GMC good medical practice standards: Contribute to and comply with systems to protect patients[69]:

[67] http://www.foundationprogramme.nhs.uk/pages/trainers accessed 14 March 2016

[68] http://www.foundationprogramme.nhs.uk/download.asp?file=FP_Curriculum_2012_Updated_for_Aug_2015_-_FINAL.PDF accessed 14 March 2016

[69] http://www.gmc-uk.org/guidance/good_medical_practice/systems_protect.asp. GMC guidance: domain 2: safety and quality. Accessed 14 March 2016

Contribute to and comply with systems to protect patients

22. You must take part in systems of quality assurance and quality improvement to promote patient safety. This includes:

a. *taking part in regular reviews and audits of your own work and that of your team, responding constructively to the outcomes, taking steps to address any problems and carrying out further training where necessary*
b. *regularly reflecting on your standards of practice and the care you provide*
c. *reviewing patient feedback where it is available.*

23. To help keep patients safe you must:

a. *contribute to confidential inquiries*
b. *contribute to adverse event recognition*
c. *report adverse incidents involving medical devices that put or have the potential to put the safety of a patient, or another person, at risk*
d. *report suspected adverse drug reactions*

This is also mirrored within GMC Good medical practice in relation to guidance on prescribing and managing medicines and devices[70]:

Prescribing guidance: Reporting adverse drug reactions, medical device incidents and other patient safety incidents

46. Early, routine reporting of adverse reactions, incidents and near misses involving medicines and devices can allow performance and systems issues to be investigated, problems rectified and lessons learned. You must make reports in accordance with your employer or contracting body's local clinical governance procedures.

47. You must inform the MHRA about:

a. *serious suspected adverse reactions to all medicines and all reactions to products marked with a Black Triangle in the BNF and elsewhere using the Yellow Card Scheme.*
b. *adverse incidents involving medical devices, including those caused by human error that put, or have the potential to put, the safety of patients, healthcare professionals or others at risk.[71] These incidents should also be reported to the medical device liaison officer within your organisation.*

48. You should provide patients with information about how they can report suspected side effects directly to the MHRA.

[70] http://www.gmc-uk.org/guidance/ethical_guidance/14323.asp accessed 14 March 2016

[71] http://www.gmc-uk.org/guidance/ethical_guidance/14323.asp#20

Figure 76. Screenshot from GMC website showing prescribing guidance in support of suspected ADR reporting for doctors.

Pharmacists

Pre-registration training[72] for pharmacists calls for an understanding of reporting arrangements and within the General Pharmaceutical Council Pre-registration manual[73] trainees must show that they can under the section:

Managing the dispensing process:

C1.3 Assess the prescription for safety and clinical appropriateness. This will include:

- *possible side effects*
- *risk of adverse drug reactions*

Provide additional clinical and pharmaceutical services:

C2.7 Recognise possible adverse drug reactions, evaluate risks and take action accordingly**

this may include advising and informing the patient or their representative, discussions with colleagues and reporting in line with local and national protocols.

[72] http://www.pharmacyregulation.org/preregmanual accessed 14 March 2016

[73] http://www.pharmacyregulation.org/sites/default/files/prm_pdf/pre-registration_manual_version_5.1_march_2016.pdf GPhC pre-registration manual for pharmacists. V5.1 Accessed 14 March 2016

The pre-registration examination can also include questions on reporting suspected ADRs. One such example scenario was when to report a Yellow Card for a patient presenting with a suspected ADR. Feedback from the assessment showed that 86% of candidates selected the correct response. There is some variation depending on the question asked but this is representative of the response seen.

The Royal Pharmaceutical Society's Professional Standards for Public Health Practice for Pharmacy[74], specifically within Standard 5.0 on Health Protection, shows examples in practice that are applicable to all pharmacists and pharmacy teams working in England and Wales. It states:

In community pharmacy:

- *Encouraging and supporting the appropriate reporting of adverse drug reactions through the Medicines and Healthcare products Regulatory Agency (MHRA) Yellow Card Scheme*

In hospital pharmacy:

- *Encouraging and supporting the appropriate reporting of adverse drug reactions through the MHRA Yellow Card Scheme*

Nurses

The Nursing and Midwifery Council (NMC) has within the Standards for medicine management[75] a Standard to report suspected ADRs:

Standard 25: Reporting adverse reactions

As a registrant, if a patient experiences an adverse drug reaction to a medication, you must take any action to remedy harm caused by the reaction. You must record this in the patient's notes, notify the prescriber (if you did not prescribe the drug) and notify via the Yellow Card Scheme immediately.

Standard 25 is further supported with guidance on reporting and where to find a Yellow Card report.

[74] http://www.rpharms.com/support-pdfs/professional-standards-for-public-health.pdf RPS, Professional Standards for Public Health Practice for Pharmacy. Accessed 14 March 2016

[75] NMC - Standards for medicines management: https://www.nmc.org.uk/globalassets/sitedocuments/standards/nmc-standards-for-medicines-management.pdf accessed 14 March 2016, pages 10 and 38.

Suggestion 13 – using ADR reporting as a quality indicator for HCPs

Pharmacy indicator

The New Medicine Service (NMS)[76], launched in October 2011 was the fourth Advanced Service to be added to the NHS community pharmacy contract in England. It aims to provide early support to patients with long-term conditions to maximise benefits of newly prescribed medication and improve patient adherence, initially focussed on particular patient groups and conditions.

One of the criteria for successful implementation of the NMS that was envisaged by the Pharmaceutical Services Negotiating Committee (PSNC) and NHS Employers was:

> *to include an increase in the reporting of Yellow Cards; thereby supporting improved pharmacovigilance, the monitoring of drug safety and detection of new safety signals by the MHRA.*

Suspected ADR reports from community pharmacists increased from 518 reports in 2011 to 928 reports in 2014 (44% increase over 3 years) since Yellow Card reporting was introduced as a quality indicator for successful implantation of the NMS for community pharmacy. This was also supported by previous communication campaigns targeted at community pharmacists. Further information about the impact of the NMS can be found in the published article by the MHRA [77] which was also used to raise awareness at the time. This was supported by a news item on MHRA website which was picked up via professional pharmacy trade media[78].

The NHS New Medicine Service Intervention Worksheet[79] was a template for pharmacists during interviews with patients enlisted on the NMS service. It specified agreed patient actions and actions taken by the pharmacists. One of these actions is whether a Yellow Card report was submitted to the MHRA to report a suspected ADR.

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[76] NMS - http://psnc.org.uk/services-commissioning/advanced-services/nms/ accessed 21 March 2016

[77] M. Jadeja and McCreedy, The Pharmaceutical Journal, Vol. 289, p159 | URI: 11104737; http://www.pharmaceutical-journal.com/news-and-analysis/news/positive-effect-of-new-medicine-service-on-community-yellow-card-reporting/11104737.article accessed 21 March 2016

[78] http://www.thepharmacist.co.uk/c34-pharmacy-practice-old/more-yellow-card-reports-from-pharmacists9007/

[79] NMS intervention worksheet: http://psnc.org.uk/wp-content/uploads/2013/07/NMS-Intervention-worksheet-July-2013.pdf Accessed 21 March 2016

In the patient interview – within the Patient interview topic guide (NMS patients), one of the topics focused upon PV which should be discussed with those patients enlisted to take part in the NMS:

- Are you more aware of side effects from your medicine / compare with previously prescribed medicines?
- What would you do if you thought you were suffering from a side-effect? Explore patients Yellow Card report awareness

Within the evaluation report[80] to support continuation of the pharmacy service, under the NMS implementation and perceived benefits, pharmacists were asked specifically about PV:

- Can you tell me about any examples where you have acted on an adverse event as a result of an NMS?
- Have you ever filled in a Yellow Card report as a result?

Several pharmacists reported filling out a Yellow Card form because of a side effect that was severe. Patients agreed to have these completed. A typical response was: *'Yes, I've done two [Yellow Card reports], both angioedema with Ramipril.'*

GPs and Health Boards – one the MHRA's Yellow Card Regional Centres – Yellow Card Centre (YCC) Wales whose role is to educate and promote the Yellow Card Scheme successfully worked with All Welsh Medicines Strategy Group to add Yellow Card reporting into the National Prescribing Indicators[81] for GPs. A target was also issued to each health board. Both are measured via the number of Yellow Card reports submitted from GPs by Health Board.

Table 4. Example from the All Wales Medicines Strategy Group, National Prescribing Indicators 2015–2016

Indicator	Unit of measure	Target for 2015-2016
Yellow Cards	Number of yellow cards submitted per practice and per health board	Target for GP practice – GPs to submit one yellow card per 2,000 practice population. Target for each health board – submit yellow cards in excess of one per 2,000 health board population.

A full case study in this document on this initiative Case study: YCC Wales set-up local 'Yellow Card Champions' - a prescribing indicator in Wales' showcases how Regional Centres have increased awareness levels.

[80] NMS evaluation report. Understanding and appraising the NMS in the NHS in England. Nottingham School of Pharmacy. (029/0124) http://www.nottingham.ac.uk/~pazmjb/nms/downloads/appendices/index.html Accessed: 21 March 2016

[81] http://www.awmsg.org/docs/awmsg/medman/National%20Prescribing%20Indicators%202015-2016.pdf Welsh National Prescribing Indicators 2015-16, accessed 21 March 2016

Suggestion 14 – set up a national network of ADR reporting champions

The Yellow Card hospital pharmacist Champion Scheme was launched in March 2013 by the MHRA's Welsh regional centre. Each Health Board in Wales nominated a minimum of one hospital pharmacist or hospital pharmacy technician to be a 'Yellow Card Champion'. The aim of the role is to promote the Yellow Card Scheme through education and training on PV. The outcome of such a role was envisaged to improve reporting rates amongst hospital based reporters, particularly hospital pharmacists. The success of this champion's scheme showed in an increase of 81% (649 reports) between 2013 and 14 when compared to the previous year and most importantly a reversal in the decreasing ADR reporting trend in the Welsh region.

More on this initiative can be found within this guidance document section D – Managing a Regional Centre.

The UK has also set up a national network of 'Medication Safety Officers'. More on this initiative can be found under the Collaborations section.

Suggestion 15 – recognise and reward reporting

Sir Derrick Dunlop Award

To mark the 50th anniversary of the Yellow Card Scheme a series of events showcased the achievements of the Scheme in protecting public health and looked to the future to develop a new road map with input from stakeholders. Themes under discussion include science and technology, better inclusion of ADR reporting in education programs and academic curricula, and more effective engagement with patients and HCPs. A landmark scientific conference took place in Edinburgh in March 2015. The purpose of the conference was to focus minds on exploring scientific and technological advances that are taking place to ensure the Yellow Card Scheme continues in its role to protect public health.

For the first time in the UK, an award was issued to recognise and reward reporters for their contribution to medicine and patient safety in relation to the reporting of suspected ADRs. The award was named the 'Sir Derrick Dunlop Award', in honour of the founder who pioneered the Yellow Card Scheme. The one time physician to the Queen, in his role as Chairman of the Committee on Safety of Drugs, wrote to every member of the UK medical profession in 1964, in the wake of the Thalidomide disaster to ask that doctors report any untoward condition in a patient which might be the result of drug treatment.

The award was presented for the first report of a major new drug association. Following a five minute video shortlist of nominations[82] from MHRA PV staff, the winner was nominated by Mitul Jadeja, and was decided by a panel chaired by an independent academic expert. The prize consisted of a certificate and a medal which were presented by Sir Dunlop's daughter. It was jointly presented to Dr David Hunt and Dr Oliver Flossmann, who recognised and reported thrombotic microangiopathy (TMA) associated with interferon beta treatment. The conditions were seen to develop over anything from several weeks to several years after starting treatment with the drug. As a result of the Yellow Cards, MHRA advised HCPs and patients to be vigilant for the conditions and how they should be managed if they occur. A paper was published[83] subsequently detailing the association.

Suggestion 16 – create a brand

The UK's national ADR reporting Scheme is branded as the Yellow Card Scheme. Historically, this name has no particular significance except that there was a large supply of yellow paper which was used for the form for the call to report suspected ADRs, sent with Sir Derrick Dunlop's letter in 1964. However, the name stuck and over the years the brand has grown to have a strong recognition with HCPs (see benchmarking case study and polls). Despite changes in the Agency name, the name of the Scheme has not changed.

The brand enables easier promotion, especially where word count and clear messages are needed. For example, it is easier to say report to the Yellow Card Scheme compared to report to the national spontaneous suspected adverse drug reactions reporting system – a detailed message can include further information.

The logo has the name of the Scheme alongside a graphic and a strapline which explains what the scheme does in 3 simple words. The graphic has changed over the years in line with changes in the MHRA logo to depict the association with the MHRA. The font has also changed to make it look more modern and also keep it in line with the MHRA logo font. The two examples below show the connection between the MHRA logo and the Yellow Card Scheme logo through the radial dots which are on both logos. There are specific branding guidelines as to how the logo should be used and where it should be placed depending on format and use.

[82] https://www.youtube.com/watch?v=l61eEg6o-0Q Sir Derrick Dunlop Award nominations; accessed 24 March 2016

[83] http://www.nejm.org/doi/full/10.1056/NEJMc1316118 Thrombotic Microangiopathy Associated with Interferon Beta, N Engl J Med 2014; 370:1270-1271March 27, 2014DOI: 10.1056/NEJMc1316118 Accessed 24 March 2016

Figure 77. The Yellow Card Scheme logo

Figure 78. The MHRA logo

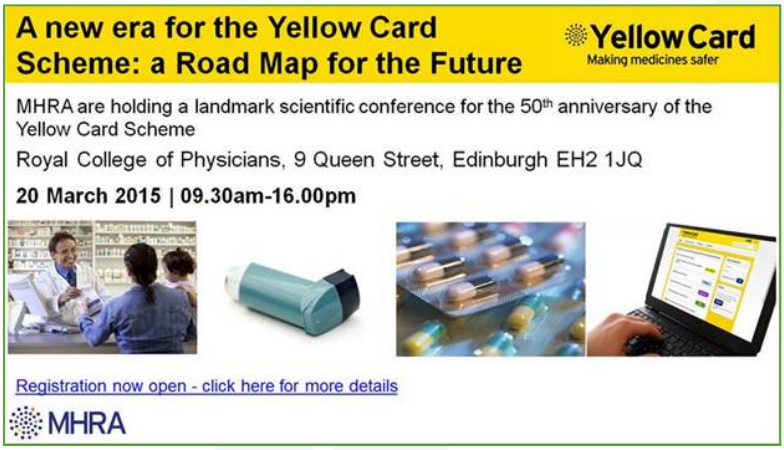
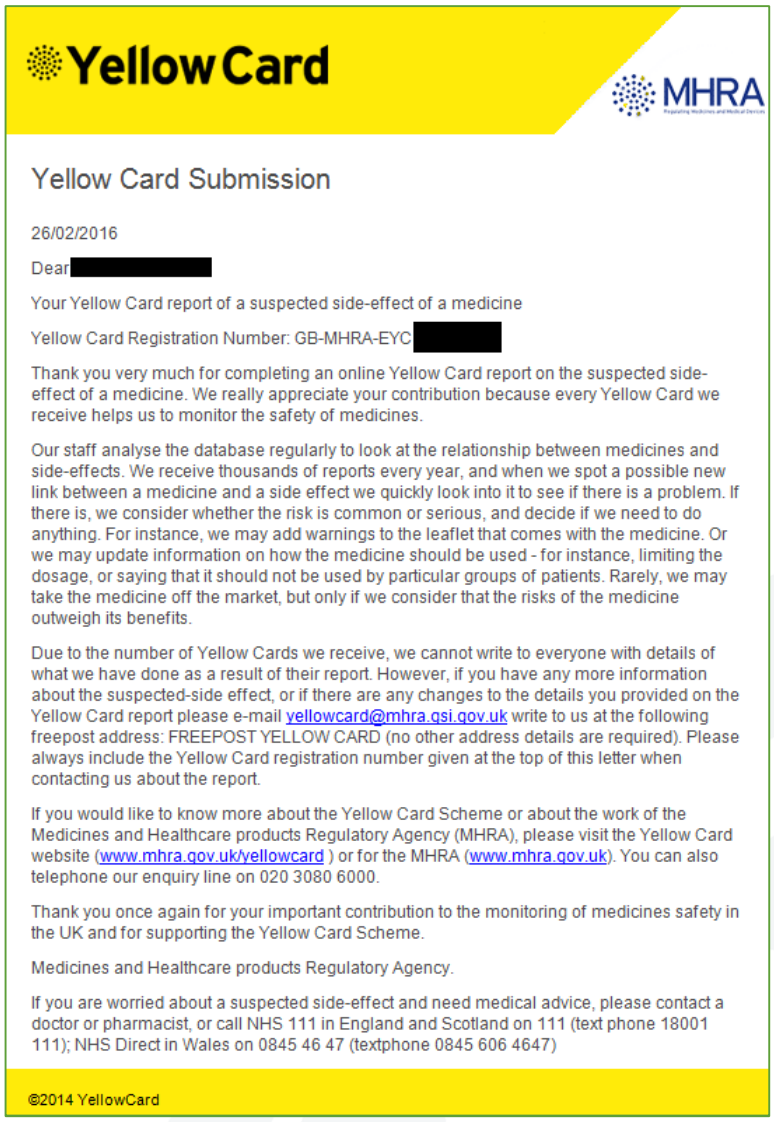


Figure 79. An invitation to a scientific conference



Yellow Card

MHRA

Yellow Card Submission

26/02/2016

Dear [redacted]

Your Yellow Card report of a suspected side-effect of a medicine

Yellow Card Registration Number: GB-MHRA-EYC [redacted]

Thank you very much for completing an online Yellow Card report on the suspected side-effect of a medicine. We really appreciate your contribution because every Yellow Card we receive helps us to monitor the safety of medicines.

Our staff analyse the database regularly to look at the relationship between medicines and side-effects. We receive thousands of reports every year, and when we spot a possible new link between a medicine and a side effect we quickly look into it to see if there is a problem. If there is, we consider whether the risk is common or serious, and decide if we need to do anything. For instance, we may add warnings to the leaflet that comes with the medicine. Or we may update information on how the medicine should be used - for instance, limiting the dosage, or saying that it should not be used by particular groups of patients. Rarely, we may take the medicine off the market, but only if we consider that the risks of the medicine outweigh its benefits.

Due to the number of Yellow Cards we receive, we cannot write to everyone with details of what we have done as a result of their report. However, if you have any more information about the suspected-side effect, or if there are any changes to the details you provided on the Yellow Card report please e-mail yellowcard@mhra.gsi.gov.uk write to us at the following freepost address: FREEPOST YELLOW CARD (no other address details are required). Please always include the Yellow Card registration number given at the top of this letter when contacting us about the report.

If you would like to know more about the Yellow Card Scheme or about the work of the Medicines and Healthcare products Regulatory Agency (MHRA), please visit the Yellow Card website (www.mhra.gov.uk/yellowcard) or for the MHRA (www.mhra.gov.uk). You can also telephone our enquiry line on 020 3080 6000.

Thank you once again for your important contribution to the monitoring of medicines safety in the UK and for supporting the Yellow Card Scheme.

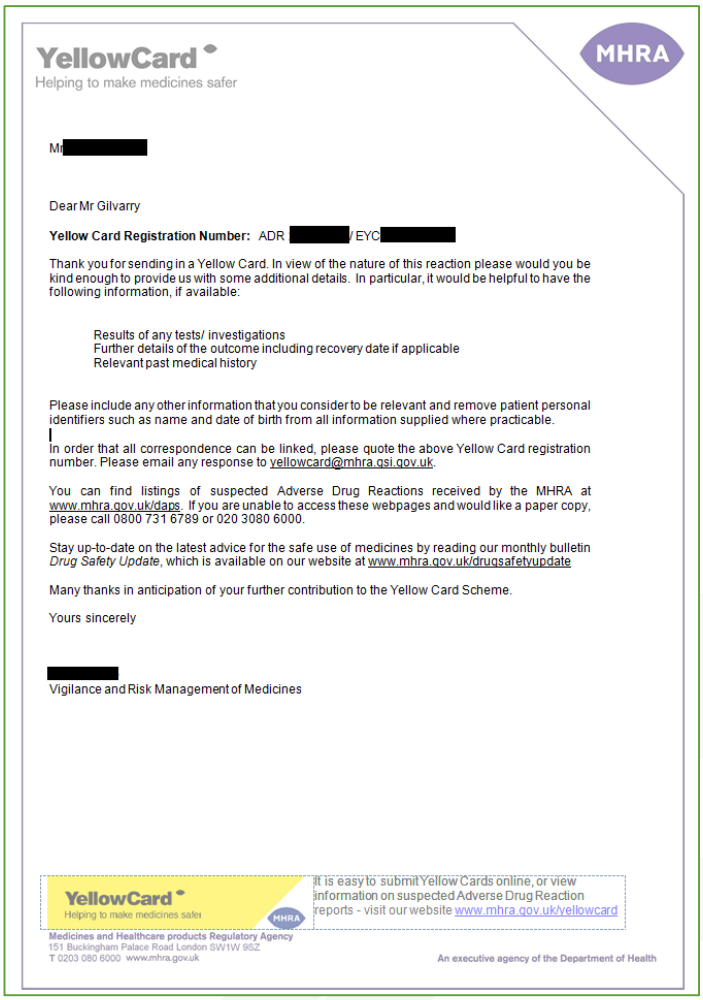
Medicines and Healthcare products Regulatory Agency.

If you are worried about a suspected side-effect and need medical advice, please contact a doctor or pharmacist, or call NHS 111 in England and Scotland on 111 (text phone 18001 111); NHS Direct in Wales on 0845 46 47 (textphone 0845 606 4647)

©2014 YellowCard

Figure 80. An acknowledgement letter to a report post submission of an online Yellow Card report

SCOPE documents on patient reporting contains further information on feedback to reporters. Inserting lines into a query and any correspondence can help with raising brand awareness, support reporting, is good customer service and allows the NCA to thank and show the importance of the contribution to the person reporting. For example: 'Thank you for reporting a Yellow Card, your contribution to the Yellow Card Scheme is greatly appreciated. Each Yellow Card report we receive contributes to medicines safety monitoring.'



YellowCard
Helping to make medicines safer

MHRA

Mr [redacted]

Dear Mr Gilvarry

Yellow Card Registration Number: ADR [redacted] / EYC [redacted]

Thank you for sending in a Yellow Card. In view of the nature of this reaction please would you be kind enough to provide us with some additional details. In particular, it would be helpful to have the following information, if available:

Results of any tests/ investigations
Further details of the outcome including recovery date if applicable
Relevant past medical history

Please include any other information that you consider to be relevant and remove patient personal identifiers such as name and date of birth from all information supplied where practicable.

In order that all correspondence can be linked, please quote the above Yellow Card registration number. Please email any response to yellowcard@mhra.gsi.gov.uk.

You can find listings of suspected Adverse Drug Reactions received by the MHRA at www.mhra.gov.uk/daps. If you are unable to access these webpages and would like a paper copy, please call 0800 731 6789 or 020 3080 6000.

Stay up-to-date on the latest advice for the safe use of medicines by reading our monthly bulletin *Drug Safety Update*, which is available on our website at www.mhra.gov.uk/drugsafetyupdate

Many thanks in anticipation of your further contribution to the Yellow Card Scheme.

Yours sincerely

[redacted]
Vigilance and Risk Management of Medicines

YellowCard
Helping to make medicines safer

It is easy to submit Yellow Cards online, or view information on suspected Adverse Drug Reaction reports - visit our website www.mhra.gov.uk/yellowcard

Medicines and Healthcare products Regulatory Agency
151 Buckingham Palace Road London SW1W 9SZ
T 0203 080 6000 www.mhra.gov.uk

An executive agency of the Department of Health

Figure 81. A follow up letter for a HCP for requesting further information that thanks the reporter, signposts where to access listings of suspected ADRs and explains how to keep up to date with the latest safety information

Figure 82. A general PowerPoint presentation using both logos

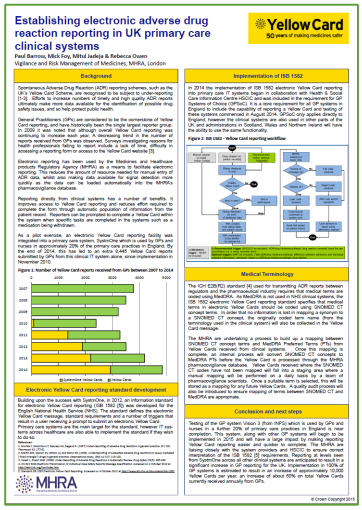


Figure 83. A poster for a congress

Suggestion 17 – include a set of key messages to patients and parents

An independent review by Avery et al in the UK showed that many patients reported for altruistic reasons accompanied by a sense that they did not want someone else to suffer side effects like they had. Some recognised the importance of contributing to a database of reports so that adverse effects could be identified. A considerable number indicated the need for patients to be aware of possible ADRs, through the PIL or advice from HCPs, to help them make informed choices about whether or not to use medicines. A few had reported hoping that they would be linked with similar sufferers. From focus groups, telephone interviewees felt that patient reports would be different and more complete than HCP reports, suggesting patient reports would show a better understanding of the effect of the ADR on a patient's life and that a HCP report might just consist of a list of symptoms. Participants argued that direct patient reporting would avoid information being reported through a professional lens, and this was backed up by comments in response to the questionnaire conducted in the study. The information supports Basch's thesis[84] that patient self-reports of ADRs provide valuable information and capture the subjective elements of patient experiences.

Based on these studies, NCAs may wish to consider using the following set of key messages for developing basic patient messages for promotion purposes.

Key messages for patients

- Your report is important to help make medicines safer
- Only a suspicion is needed to report
- How to report
- Always read the Patient Information Leaflet supplied with your medicine for more information on side effects
- Speak to your HCP for further advice

Regulatory action taken as a result of suspected ADR reporting can help to show the value of reporting. If there is space for this, it is good practice to include such information (refer to suggestion 9). Especially, if the safety issue was not recognised as being related to a particular medicine until information was received from spontaneous ADR reporting.

[84] Basch E. The missing voice of patients in drug-safety reporting. N Engl J Med. 2010;362:865–9.

For parents, a UK study completed by ADRIC[85] (Adverse Drug Reactions in Children) group, funded by the National Institute for Health Research (NIHR), looked at Yellow Card reporting. The study found that parents who had reported suspected side effects experienced by their children were generally happy to report via the Scheme and valued the opportunity to report their concerns. The ADRIC study suggested that the following messages are important. NCAs may also wish to consider these when developing promotional messages aimed at parents.

Key messages for parents

- Reports from parents like you are very useful. Parents know their child better than anyone and can tell us about things that healthcare professionals can't.
- We want parents to send reports even if they only have slight concerns about a medicine – you don't need to be certain that a medicine has actually caused a side effect to send a report.
- Reports are confidential. We won't share the information on your report with your child's doctor if you don't want us to.

Paediatric reporting should be encouraged where possible by mentioning why it is important to report ADRs in children.

[85] ADRIC study - http://www.adric.org.uk/ accessed 29 March 2016

Suggestion 19 – form partnerships with relevant organisations and bodies

The MHRA has worked with various organisations to facilitate reporting through URL links, adding its logo to the ADR reporting website, information about ADR reporting, and including paper forms in respective publications. The main ones are listed below.

- British National Formulary (BNF)
- British National Formulary for Children (BNFC)
- Nurses Prescribers' Formulary (NPF)
- Monthly Index of Medicinal Specialities (MIMS)
- Electronic Medicines Compendium run by ABPI
- Proprietary Association of Great Britain OTC directory – UK trade association for manufacturers of over-the-counter medicines and food supplements.
- 5 regional centre websites:
  - YCC Wales
  - YCC Scotland
  - YCC Northern and Yorkshire
  - YCC West Midlands
  - YCC North West

  – both HCPs and patients
- Paediatric Care Online UK
- (PCO UK) – paediatricians
- MedsIQ – paediatricians and med errors
- UK Medicines Information – pharmacists
- MiDatabank, CoAcS – pharmacists
- Centre for Postgraduate Pharmacy (CPPE) – pharmacists
- Nursing times – nurses
- Professional Bodies, such as Royal Colleges, and their Regulators –all HCPs
- Association of British Pharmaceutical Industry (ABPI)
- British Generic Manufacturers Association (BGMA)
- Through Patient advice and liaison services (PALS) services – patients
- Devolved Administration sites
- NHS Choices – source of info for patients
- UK-CAB network for community HIV treatment advocates – HCPs and patients
- Wikipedia – for patients
- BootsMD – for patients
- Patient.co.uk – for patients
- Medicines for Children – for patients and parents
- PACEY – blog for child-minders

Some examples of the outputs from partnerships to promote suspected ADR reporting by contacting such organisations are highlighted below.

Figure 84. An example of a the Yellow Card logo reporting link on the Boots WebMD website[86] under the medicines & treatments section of its website aimed at patients

Figure 85. Information about the reporting of side effects is also present for each product and substance, in this example beclometasone[87] with a URL link to Yellow Card reporting site. To the right, of this there is also a separate logo with hyperlink present as a promotional reminder to increase general awareness about the Scheme and encourage the reporting of suspected side effects

[86] http://drugs.webmd.boots.com/drugs/ accessed 10 March 2016

[87] http://drugs.webmd.boots.com/drugs/drug-47-BECLOMETASONE.aspx?drugid=47&drugname=BECLOMETASONE&source=2&isTicTac=false

NHS Choices was launched in 2007 and is the official website of the National Health Service in England. It has nearly 50 million visitors per month and is the UK's biggest health website, accounting for a quarter of all health-related web traffic.

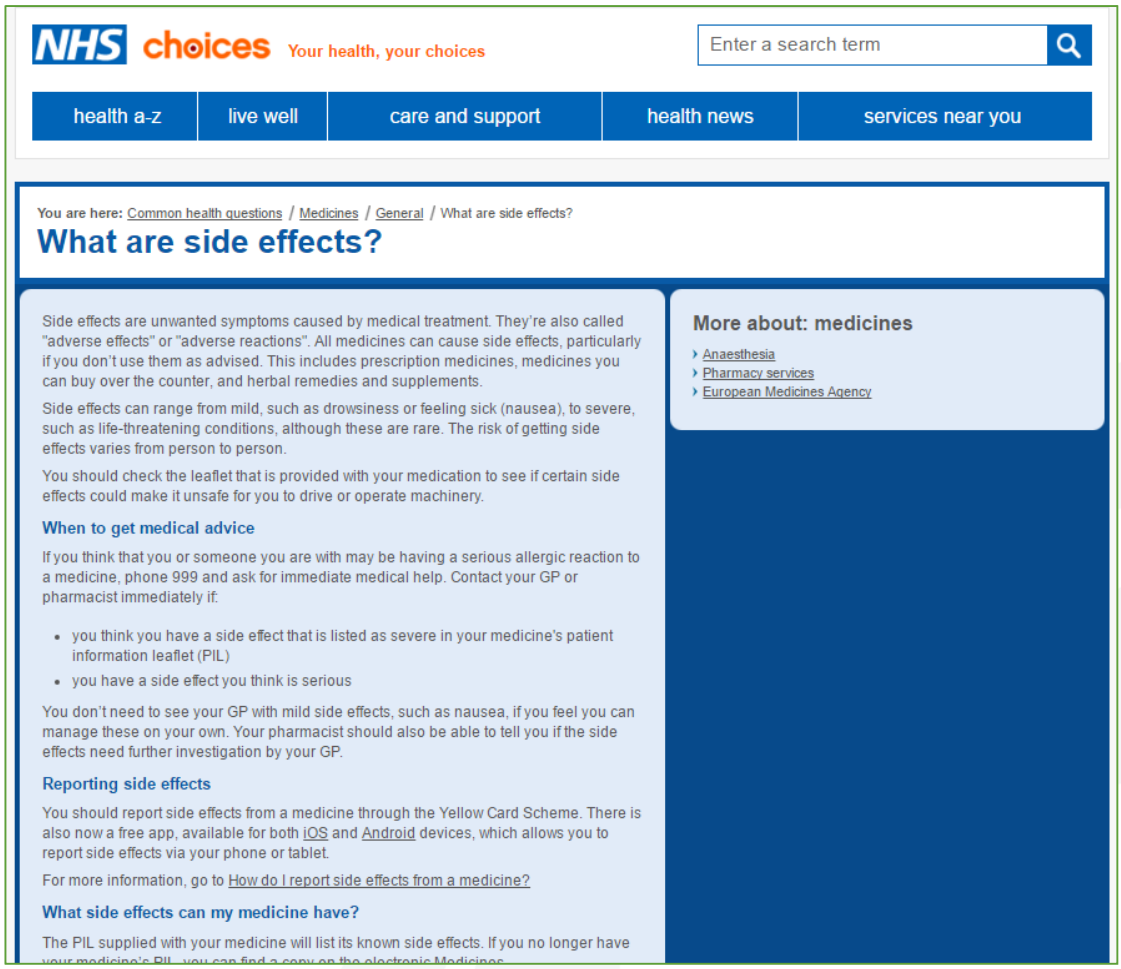


Figure 86. Information about side effects and reporting on NHS Choices – a trusted source of information for patients[88]

The same webpage also includes a number of information links to the mobile app, SPCs and PILs and the following pages:

- How do I report side effects from a medicine?
- What should I do or not do with my medicines?
- Medicines information
- Yellow Card Scheme: report side effects online

[88] http://www.nhs.uk/chq/Pages/997.aspx?CategoryID=73&SubCategoryID=108 accessed 10 March 2016

Suggestion 22 – use social media channels regularly

MHRA has an editorial schedule to ensure messages are posted on social media. For example, during a campaign to increase suspected ADR reporting, different pre-written messages were passed to Communications team from PV colleagues which were posted three times a week across the different Twitter channels and the Facebook page throughout the campaign. For the first time a social media forum was used to interact with doctors to increase suspected ADR reporting and for education through case studies and clinical scenarios. Although reach is improving, the public is generally an untapped audience segment. It is recognised that greater focus is needed on public-facing messages. In a recent campaign, a video for parents was developed to encourage reporting in children, which was also shared using social media channels.

The MHRA has recently started to use Storify: https://storify.com/ as a means of communicating and are monitoring its reach. MHRA has worked with NHS England, NHS Choices and other public facing partners such as Healthwatch England to help strengthen the reach of these messages to the right audiences. There are future plans to work with its five regional centres to promote regular reporting using social media.

- MHRA's Twitter channel: https://twitter.com/MHRAgovuk
- There is a specific channel for medicines: https://twitter.com/MHRAmedicines
- YouTube: https://www.youtube.com/user/MHRAgovuk
- There is a separate channel for the Yellow Card Scheme: Facebook: https://www.facebook.com/mhragovuk

Some examples of suspected ADR promotion on social media channels are highlighted below:

Figure 87. Announcing launch of an app by Member of Parliament

Figure 88. Use of digital material to promote reporting

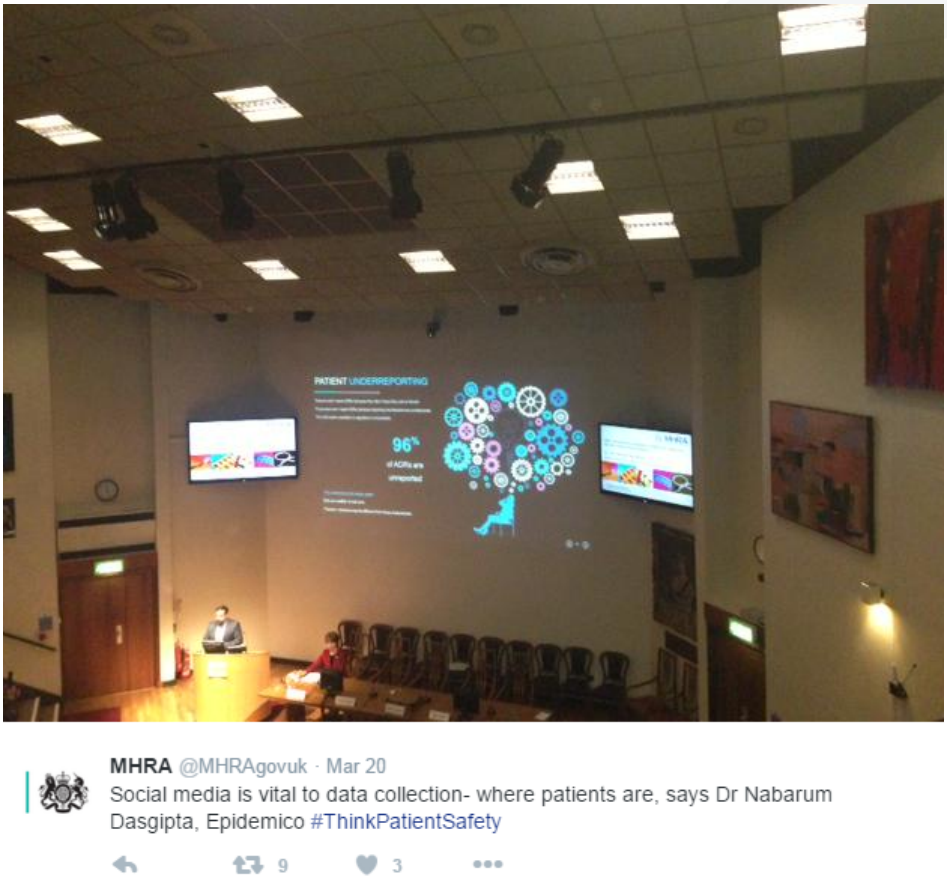


Figure 89. Picture taken on a mobile phone uploaded to official Twitter account to show what is happening at a conference – in this instance the importance of social media in PV

Figure 90. Live updates to Twitter from a conference

The use of online forum for doctors

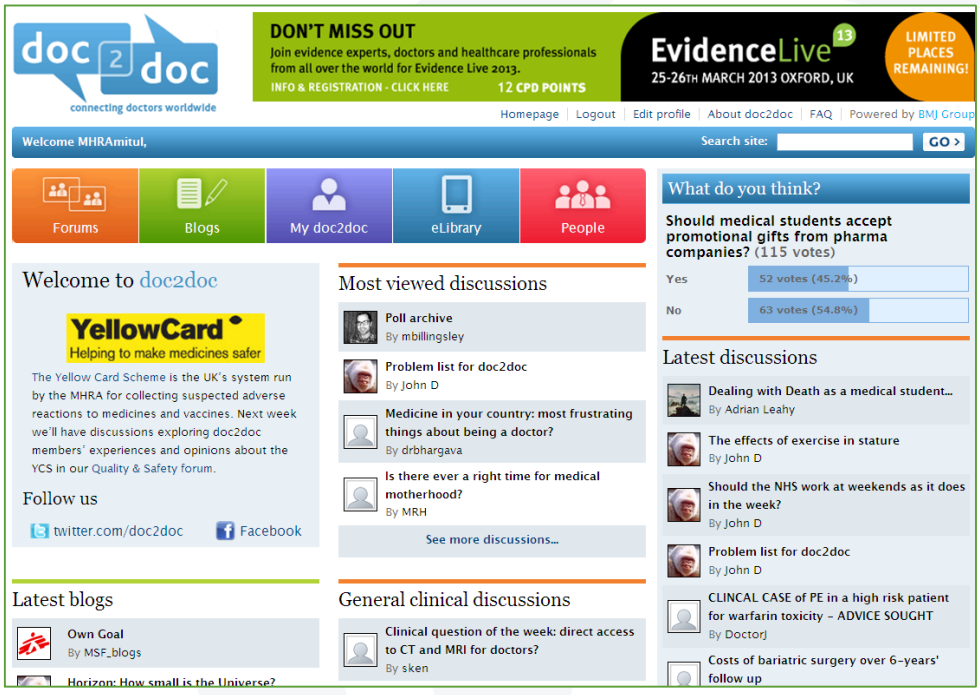


Figure 91. Use of social media forums for doctors

In 2013, interactive case studies were used as part of the campaign to encourage doctors to report more and increase awareness of the Yellow Card Scheme. This was taken forward through collaboration with BMJ doc2doc organisation[89]. Polls and voting were methods used to measure reactions of medics on the collaborating organisations website. Extra information was additionally posted to spark discussion around the specific topic of ADRs.

An email was drafted and sent to the Royal College of GPs, NICE, and the regional centres to promote use of the forum. A pre-determined PV team responded within 24 hours to any questions posted on the discussion forum by doc2doc members during the two-week duration of this initiative. Senior management cleared necessary 'new lines' to take.

This first pilot initiative of its kind reached 1,817 doctors that clicked onto the two forums created to view or take part in the discussion and provide specific feedback on reporting experiences. It has been the most successful way of reaching doctors and interacting with them as part of the Yellow Card campaign via social media. Voting results: 75% of people would complete a Yellow Card for the answers in response to case study 1. 90% of people would complete a Yellow Card although 45% would wait for medical notes to do so in response to case study 2.

[89] http://doc2doc.bmj.com/forums/open-clinical_quality-safety#plckforumsearchtext=yellow%20card&plckforumid=Cat%3AOpenClinicalForum%3Aadbd9112-94fd-4229-b38f-9e254bc9ff41&plckforumpage=ForumDiscussion&plckpostid=&plckdiscussionid=Cat%3AOpenClinicalForum%3Aadbd9112-94fd-4229-b38f-9e254bc9ff41Discussion%3A9a7d17a8-f70b-403d-8fa9-a3a1668d545c&plckforumpostshowfirstunread=&plckforumpostonpage=1&plckfindpostkey= - BMJ doc2doc forum example. Accessed 10 June 2016

Figure 92. Example of social media forum used to raise awareness specifically with doctors

Use of social media examples and digital banners

Using the hashtag #thinkpatientsafety MHRA has used the platform Storify: https://storify.com/MHRAgovuk/thinkpatientsafety

It allows one to build a social media story that can be controlled by the user to pull in tweets, posts, images and video.

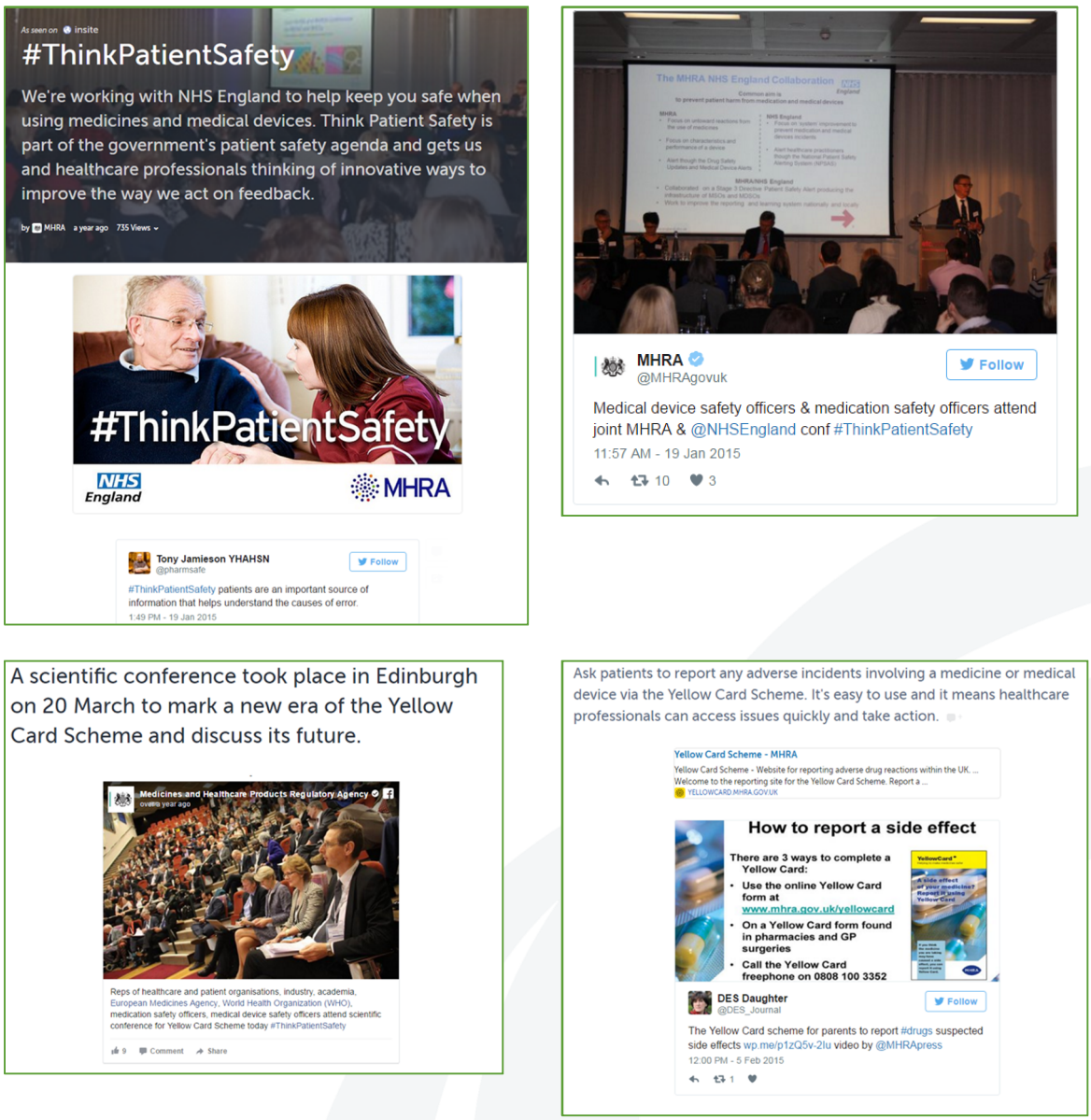


Figure 93. Example of four uses from the #patientsafety Storify page by MHRA to promote Yellow Card Scheme and collaborative working in the NHS to embed reporting into the health system and increase awareness about suspected ADRs.

Figure 94. Example digital banner developed for use within the paediatrics campaign

Suggestion 23 – insert statements to encourage reporting in relevant Agency communications

One such example is: in January 2016, letters were sent to HCPs regarding erlotinib (Tarceva)[90] and fingolimod (Gilenya ▼)[91]. Both contain a call for reporting.

Collaborate with other organisations to capture reports of all types of harm from medicines

The MHRA is seeking to receive reports related to the expanding areas relating to the medication errors, misuse, abuse and overdose from other data collection systems which are separate to its Yellow Card Scheme.

[90] https://assets.digital.cabinet-office.gov.uk/media/56c239d2e5274a036600001d/Tarceva_DHPC_sent_14_Jan_2016.pdf accessed 8 April 2016

[91] https://assets.digital.cabinet-office.gov.uk/media/56c239a9e5274a036900002b/Gilenya_DHPC_sent_22_Jan_2016.pdf accessed 11 April 2016

The NHS Improvement & national Medication Safety Network

In March 2014, a significant piece of partnership work was undertaken by the MHRA in conjunction with the patient safety team at NHS England, which function has now moved to NHS Improvement. Jointly, two patient safety alerts[92] were issued to help healthcare providers increase incident reporting for medication errors and medical devices explaining this work and to emphasise the importance of reporting. The alerts also instructed providers to take specific steps such as board level director (medical or nursing supported by the chief pharmacist) oversight, the establishment of safety officers to improve local reporting and increase data quality; and the establishment of national networks to maximise learning and provide guidance on minimising harm relating to these two incident types.

As of March 2016, 382 Medication Safety Officers (MSOs) and 304 Medical Device Safety Officers (MDSOs) have been established within the two networks in England. These officers are mainly based in hospitals in England. In addition to increasing reporting and data quality, they act as safety contacts to allow better communication between local and national levels. The two networks act as a forum for discussing potential and recognised safety issues, identifying trends and actions to improve the safe use of medicines and medical devices, much of which takes place via monthly webinars. A new online forum for MSOs and MDSOs was also developed to share information and promote discussion on important safety topics. The network has also seen the creation of smaller networks, discussion groups and online information forums in specific regions, clinical specialities and some healthcare settings. Devolved Administrations and independent healthcare organisations are also guest participants of the networks to increase transparency and encourage greater coherent vigilance activities across the UK.

Supporting the networks was the second joint event held in February 2016 by MHRA and NHS England 200 safety officers attending. The network has shown to be an important new route for healthcare professionals to raise potential safety signals which have resulted in regulatory action for both medicines and medical device incidents and an increase in reporting and quality. The MHRA also published a paper on this topic.[93]

[92] https://www.england.nhs.uk/2014/03/med-devices/ Patient Safety Alert issued in March 2014. Accessed 11 April 2016.

[93] Cousins, Gerrett, Richards and Jadeja M. Initiatives to Identify and Mitigate Medication Errors in England. 2015, Drug Safety, 10.1007/s40264-015-0270-3. http://link.springer.com/article/10.1007/s40264-015-0270-3 Accessed 11 April 2016.

The National Reporting and Learning System (NRLS) is the English NHS system for reporting incidents within the NHS. These may include ADRs and have historically included incidents of medication error. MHRA and NHS England have been working together to improve data exchange so that both parties get the data they need to investigate issues within their respective remits. NRLS is to be redeveloped in the coming years and the MHRA will be a key partner to help ensure the format and quality of reports for suspected ADRs meet the needs of the MHRA. This will include working with suppliers of local risk management systems where many cases of interest are initially recorded before transfer into NRLS so they can be sent directly to the MHRA. Since the Scheme covers the whole of the UK and whilst many of the collaborative links mentioned above are for the English health system, parallel discussions continue to be held with the other governments to ensure the benefits of such collaborations can be mirrored across the UK.

Campaign case study: Patients

In 2009 the MHRA developed a nationwide marketing strategy for patient reporting. This included production of an information video[94] for patients shown in GP surgeries and on a TV channel which broadcasted the video throughout 462 GP waiting rooms. The video was played three times each hour, including on a number of electronic poster displays in GP surgeries. The same video was updated and used in subsequent campaigns. For example, it was shown in waiting areas of pharmacies that were part of a large multiple community pharmacy chain. The patient video is available on YouTube and is also embedded into patient facing websites, such as the NHS website for the public.

Both campaigns included an organised poster campaign, and distribution of patient ADR information leaflets to pharmacies and GP surgeries (first campaign only) and a visible presence at HCP and patient conference exhibitions. Some of the campaign material is available to download on the Yellow Card reporting website[95], including translation of information about the Scheme in 10 commonly spoken languages for increased accessibility for patients.

A number of poster presentations were developed for conferences and a special stand was designed for conferences – usually attended where many stakeholders are present to ensure efficient use of expenditure and value. Resent national conferences attended to increase awareness of the Yellow Card Scheme included Patient Safety Congress and Patient First.

[94] https://www.youtube.com/watch?v=M3UDktfbWnE Yellow Card video

[95] https://yellowcard.mhra.gov.uk/downloadable-information/ - downloadable section for awareness raising materials on Yellow Card reporting site.

Figure 95. Example of the stand used in the first campaign at conferences – exhibition space included the stand, a TV to show messages via PowerPoint and the patient video on a loop, leaflets and other printed material are also used as collateral when raising awareness

In 2013, a new communications strategy was devised to raise awareness of the Scheme and increase reporting. The need for sustained communications, showing both the value and importance of suspected ADR reporting through case studies, including the clarity of reporting guidelines were taken forward through this campaign. The strategy aimed to target HCPs as the trusted source to reach patients. The strategy adopted a low/no cost approach maximising the opportunities of digital materials, the use of social media and developing partnerships with other organisations.

Information about the reporting of side effects were placed through the partnerships in well recognised and trusted online sources so they are more accessible to patients. They included www.patient.co.uk, NHS Choices, BootsWebMD, Medicines for Children aimed at parents and young people, the annual 'Ask your Pharmacist Week' campaign web pages, and on the website of each of the Yellow Card regional centres. Much of this work is taken forward by one PV member of staff whose role is primarily Yellow Card Strategy based. Information is regularly reviewed for accuracy of content through liaison with the respective organisations. All organisations have links for reporting and information about side effects specifically for patients. Contact has also been made with patient facing organisations that have online product information on their websites. Through partnership, information about Yellow Card Scheme reporting, including URL links, was added to relevant product information pages in the same style as the content which is now mandatory within paper PILs

Blogs were also used for campaign work to raise awareness about reporting, side effects and where to report them. For example, a blog was written for an umbrella patient organisation called the Association of Medical Research Charities (AoMRC) which encompasses over 130 patient organisations, another was written for carers through an organisation of child-minders. The MHRA has also found that blogs written by other media doctors helps promote awareness levels, one example is the patient.co.uk below[96].

Figure 96. Blog by media doctor promoting awareness about side effects and the importance of reporting

In a second communications phase aimed at paediatrics there was also collaboration with the Royal College of Paediatrics and Child Health's Youth Advisory Panel to raise awareness of reporting and campaign messages. The MHRA also has worked with INFACT patient charity to produce a guide on reporting suspected ADRs in pregnancy.[97] Other work continues to further develop links with patient support organisations and health related charities through posters, campaign collateral, forms and presentations. A number of partnerships were also created from recent Yellow Card campaign to distribute to its member's patient reporting forms and information. The MHRA has also worked with a patient HIV organisation and they now discuss side effects and also help patients complete an ADR report if needed.

[96] http://patient.info/blogs/sarah-says/2013/07/medication-side-effects---protecting-yourself-and-others Dr Sarah Jarvis blog, accessed 15 April 2016

[97] https://www.gov.uk/drug-safety-update/yellow-card-update-to-form

The five regional centres also seek to collaborate with numerous patient organisations and specific disease areas to promote local patient reporting through campaigns, exhibiting and mini-projects of work. Within devolved administration government areas they also coordinate with Expert Patient Programme, supplying leaflets, forms and packs when required.

50th Anniversary

As part of the main 50th anniversary event of the Yellow Card Scheme all MHRA patient stakeholders were invited to attend. Some of these included a number of key identified representatives of therapeutic areas, specifically to engage with and increase awareness of ADR reporting. Over the last 5 years, patient reporting has increased by 228% (3,807) totalling 5,471 in 2015

The MHRA also targets communications to priority groups as necessary. One such case study is described below.

Valproate and of risk of abnormal pregnancy outcomes

In January 2015 a Drug Safety Update (DSU) article by the MHRA advised healthcare professionals that children exposed to valproate in utero are at high risk of developmental disorders and congenital malformations. The EU agreed Risk Minimisation Materials were distributed with the letter and links to both contained in the DSU article. In the subsequent 12 months the MHRA colleagues from pharmacovigilance and also communications divisions worked collaboratively with the MAH concerned and through major consultation with patient groups and professionals produced a final communications toolkit which was released on 8 February 2016. The toolkit consisted of a: patient card, patient guide, checklist and booklet for HCPs and the packaging labelling which the MAH are now rolling out globally.

The MHRA developed these new communication materials for utilisation by organisations and healthcare professionals to discuss risks and benefits with patients. With the MAH the development of the materials involved continuous partnership with stakeholder group meetings, phone calls and written communications. The process also involved meetings with Royal Colleges, voluntary organisations, the Minister and senior members of the MHRA team to explore ways for professional bodies to support the messages. Several members of the Royal Colleges and voluntary groups from across various disciplines also attended stakeholder meetings with patients.

These new communication materials were published in the MHRA's February 2016 Drug Safety Update: https://www.gov.uk/drug-safety-update/valproate-and-of-risk-of-abnormal-pregnancy-outcomes-new-communication-materials

The following groups specifically support the release of the toolkit on their respective websites. These include Epilepsy Action, Epilepsy Research UK, Epilepsy Society, Young Epilepsy, Bipolar UK, FPA – the sexual health charity, Organisation for Anti Convulsant Syndrome (OACS), INFACT, Migraine Action, FACS-Aware, Royal College of Midwives, and the Royal College of Pharmacists.

Campaign case studies

A communications campaign strategy was developed after going through approval stages by PV colleagues alongside Communications colleagues. An example is provided in Annex 3 (MHRA's Yellow Card strategy) of Raising and Measuring Awareness Levels for ADR Reporting Systems through Campaigns and Regional Monitoring Centres.

The plan was for a series of phased activity, subject to evaluation and review. The approach was to use low and no cost communications where possible, maximising the use of partnerships, PR and digital communications, with the recognition that these tools will need to be supplemented by some paid for communications in the form of materials to promote Yellow Card Scheme.

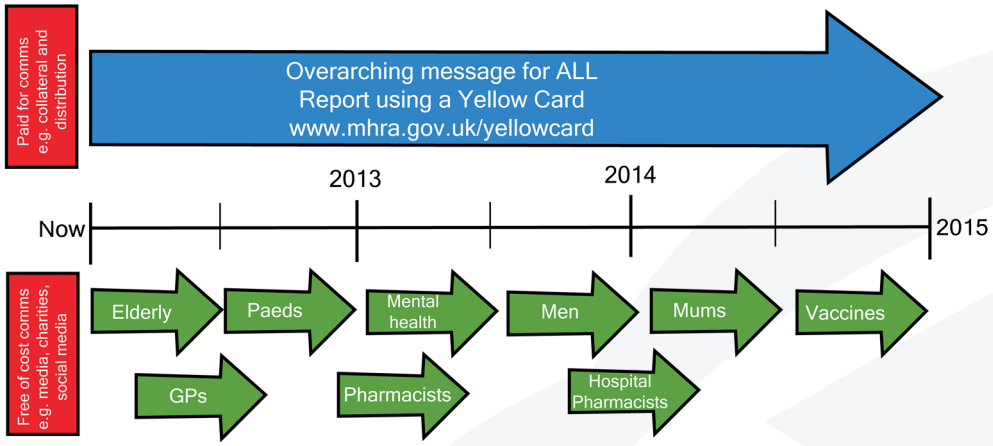


Figure 97. Example illustration of the approach to the Yellow Card communications campaign

A project group was set up and roles were established. This was followed by weekly meetings throughout to evaluate progress, set further direction, prepare reports to management, ensure the steer of project was on track. This enabled the project to be fluid and adaptable to interactions and engagement (including lack of responses) with stakeholders.

The communications plan took the following approach:

- Phase 1 – Public awareness campaign, focussing on pharmacies and GP surgeries
- Phase 2 – Public, GPs and Pharmacists follow up
- Phase 3 – Targeting other groups – paediatrics

For each phase a high level tactical plan was developed for clear communications. Further to this key messages were outlined for use in the campaign as master content for phase 1 – see 'Raising and Measuring Awareness Levels for ADR Reporting Systems through Campaigns and Regional Monitoring Systems', Annex 4 – Yellow Card campaign phase 1 Master Content Final.

This helped as a quick reference guide when producing materials for stakeholders. A digital plan was also created for a new Facebook page and twitter – outlining what to post on a timely basis to keep up campaign momentum. It is realised this was a mixed success. The project team documented successes, risks, learning outcomes, measurable activity to input into the post evaluation phase which was documented in a mini-report.

Phases 1 and 2 – GP, community pharmacists and patients

- A public awareness campaign, focussing on pharmacies and GP surgeries was launched in February 2013. Highlights of the campaign included:
- Support by GPs and pharmacy bodies such as the: National Pharmacy Association, the Royal Pharmaceutical Society, the Company Chemists Association, the Association of Independent Pharmacies and the Royal College of General Practitioners
- The five regional Yellow Card Centres also helped promote the scheme
- General press and media coverage
- National distribution of HCP and patient Yellow Card forms to pharmacies
- The development of case studies showing the value and importance of reporting
- Training materials for pharmacists
- The use of social media to raise awareness with the public,
- Interactive online case studies for doctors
- The production of an updated video about Yellow Card reporting which was displayed for patients in 339 pharmacies across the UK through collaboration with a pharmacy multiple chain.

Phase 3 – Paediatrics campaign highlights

Highlights of the campaign included:

- Benchmarking before and after the campaign to measure success
- Stakeholder workshop to facilitate situation analysis and tailor messages for the campaign
- Polls utilised to develop media attention to the campaign regionally and nationally
- General communications to parents and carers (articles, social media, press activity)
- The NHS patient facing website paediatric content was updated
- Partnership with the UK's biggest pharmacy chain for various items of promotional work – articles, adverts, online information

- A new video developed to promote ADR reporting in children
- Promotion via social media
- Yellow Card information was added into the Personal Child Health Record (the red book) – given to parents of new-borns
- Partnership with the Royal College of Paediatrics and Child Health (RCPCH)
- New paediatric reporting guidance produced for reporting suspected ADRs for HCPs
- A Drug Safety Update article on the new reporting guidelines alongside a RCPCH bulletin to their registered members – mainly paediatricians
- Press release issued which was picked up by media on regional reporting
- 2,500 forms distributed via partnership with National Pharmacy Association to independent pharmacies
- Guidelines and awareness was raise through Medication Safety Network and MHRA's 5 Yellow Card Centres.

Phase 3 – Parents and carers

Some specific output examples included:

- Omnibus survey to gauge awareness levels amongst parents – Nov 2013
- Advert in mumsnet e-newsletter – Dec 2013
- Coverage in parenting magazines including Prima Baby and Pregnancy Magazine, and My Family Magazine – Jan 2014
- Coverage in The Times
- News article on Family Lives website (familylives.org.uk) – Jan to Feb 2014
- Social media activity:
  - Twitter –MHRA and NHS Choices
  - Facebook – Posts on 7 parent/carer focused pages (resulting in Gentle Parenting website posting Yellow Card article – over 8,000 subscribers) – over 60,000 parents/carers reached
  - Tweeting by Public Health England, NHS Choices, and other relevant groups
- News flash item in the UK's biggest pharmacy multiple magazine for patients (Apr-Jul edition)

- Various forms of media coverage (March 2014) – some examples are:
  - http://www.standard.co.uk/panewsfeeds/call-to-report-drug-sideeffects-9164279.html
  - http://www.itv.com/news/update/2014-03-03/one-in-five-fail-to-tell-gp-about-childs-reaction-to-medicine/
  - http://www.nursingtimes.net/nursing-practice/clinical-zones/childrens-nursing/call-to-report-drug-side-effects/5068511.article?blocktitle=News&contentID=4385
- Yellow Card graphic in children's health sections on pharmacy chains website
- NHS Choices – Content update under Children and Medicines page – http://www.nhs.uk/conditions/pregnancy-and-baby/pages/childrens-medicines.aspx
- Media coverage for HCPs:
  - http://www.chemistanddruggist.co.uk/news-content/-/article_display_list/17471068/pharmacy-failing-to-win-parental-confidence-in-medicine-advice
  - http://www.pjonline.com/news/parents_in_london_less_likely_than_those_in_wales_to_tell_a_pharmacist_about_medicine_side_effe
- Yellow card video developed and posted on YouTube – April 2014
  - https://www.youtube.com/watch?v=ZEHAG3D2NJg A social media campaign to promote this Yellow Card video received 24 retweets meaning an audience reach of around 349,000 people

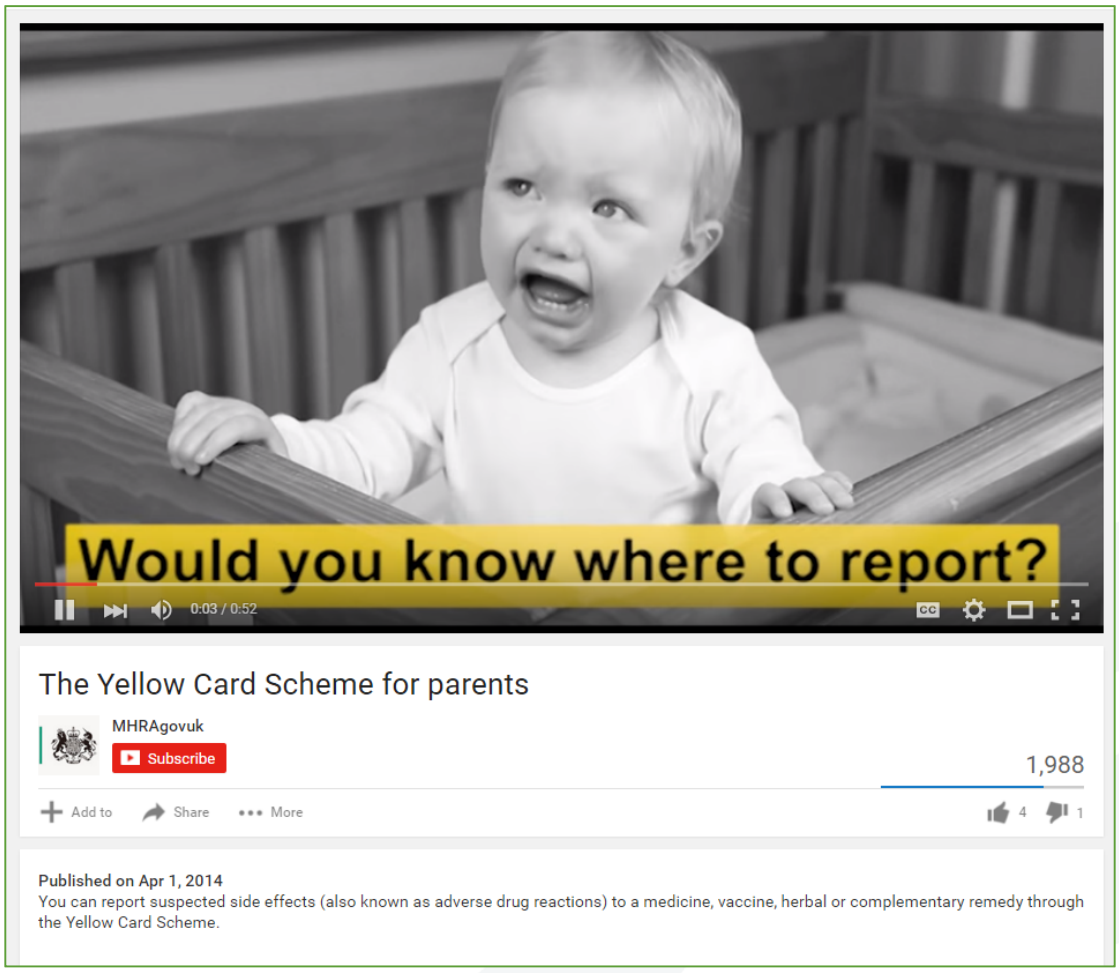


Figure 98. Video aimed at parents and carers developed specifically for the campaign

- In collaboration with ADRIC study colleagues and the RCPCH, a leaflet was developed for the Medicines for Children website on 'side effects from children's medicines' aimed at parents: http://www.medicinesforchildren.org.uk/search-for-a-leaflet/side-effects-from-childrens-medicines/

Phase 3 – Paediatricians and allied healthcare professionals

Some specific output examples included collaborative partnerships to strengthen and embed reporting of suspected ADRs with Royal Colleges and professional bodies. A particularly emphasis to strengthen reporting in children and young people from parents and paediatric healthcare professionals continued in 2015/16 as follow up work. This was enabled via a continued joint partnership with the Royal College of Paediatrics and Child Health (RCPCH) and three separate strands of project work. Through the MedsIQ initiative, the Paediatric Care Online UK (PCO UK) project, and the Personal Child Health Record (the 'red book').

All three now contain sustainable information and champion reporting to the Yellow Card Scheme. PCO UK contains information about the Scheme under each and every product and MedsIQ information about reporting including Drug Safety Update as a tool for safe prescribing. The Red book, given to all parents when a child is born, now contains a page for parents highlighting the Yellow Card Scheme and the importance of reporting suspected side effects.

Further partnerships were established with 'Medicines for Children' a programme run by RCPCH, Neonatal and Paediatric Pharmacists (NPPG) and WellChild to provide information on children's medicines that can be trusted by any parent. Supported by the ADRIC (Adverse Drug Reactions in Children) study and the impetus of the new pharmacovigilance legislation, the MHRA has worked together to add new information about side effects and links to Yellow Card reporting is now integrated into each medicines information leaflet on the Medicines for Children website. This is further reinforced by a readily accessible stand-alone information leaflet for parents about side effects.

Other outputs included:

- Stakeholder workshop – Sep 2013 to help shape the campaign and partner with participants
- Royal College of Paediatrics and Child Health collaboration. Quote from president and article agreed – this was used to do a press release and formulate articles for wider publishing and launch of the campaign.
- New BNF, BNFC guidelines for reporting suspected ADRs in children following a stakeholder workshop and liaison with experts and the RCPCH
- Various professional articles
- Article on Yellow Card in Professional Association for Childcare and Early years (PACEY)
- Survey for pharmacists on reporting suspected ADRs via the biggest pharmacy multiple
- Various promotion about reporting suspected ADRs via pharmacy multiples
- National Pharmacy Association collaboration and communication to their members (May/June edition), including 2,500 HCP and patient forms distribution.

Measuring success

MHRA have shown good practice in this area.

For the MHRA campaign work, a project group was set up with defined roles for individual members. This was followed by weekly meetings throughout to evaluate progress, set further direction, prepare reports to management and ensure that the steer of the campaign is on track to achieve its objectives. It also enabled the project to be fluid and adaptable to interactions and engagement with stakeholders, including any lack of engagement and a discussion on how issues can be approached.

The MHRA's social media pilot using BMJ doc2doc analysed the reach through digital analytics provided by BMJ doc2doc. It showed the reach of 1,817 doctors clicking onto the two forums that were created so that doctors can view or take part in the ADR discussion and provide specific feedback on their individual reporting experiences. It has been the most successful way of reaching doctors and interacting with doctors as part of the Yellow Card campaign conducted via social media. This element of work also used voting results on the doc2doc website forum. The polls for the case studies indicated that 75% of people would complete a Yellow Card for the first case study. They also showed that 90% of doctors would complete a Yellow Card in response to the second ADR case study, although 45% would wait for medical notes to do so. This lead to a response about not to delay reporting a suspected ADR based on waiting for all the information as subsequent follow up can always be made, if necessary.

MHRA practice for campaigns always involves a post campaign evaluation. Two examples are in the annexes of 'How awareness levels are raised for ADR reporting systems through campaigns and how they are measured' document under: annex 8: Yellow Card Phase I evaluation report, and annex 9: Phase II evaluation report.

Regional Monitoring Centres in the UK

The Medicines and Healthcare products Regulatory Agency (MHRA) has 5 RMCs referred to as Yellow Card Centres (YCCs) operating across the UK and covering the main geographical locations and cities on the mainland. MHRA offices are located in London covering the rest of the UK including Northern Ireland areas.

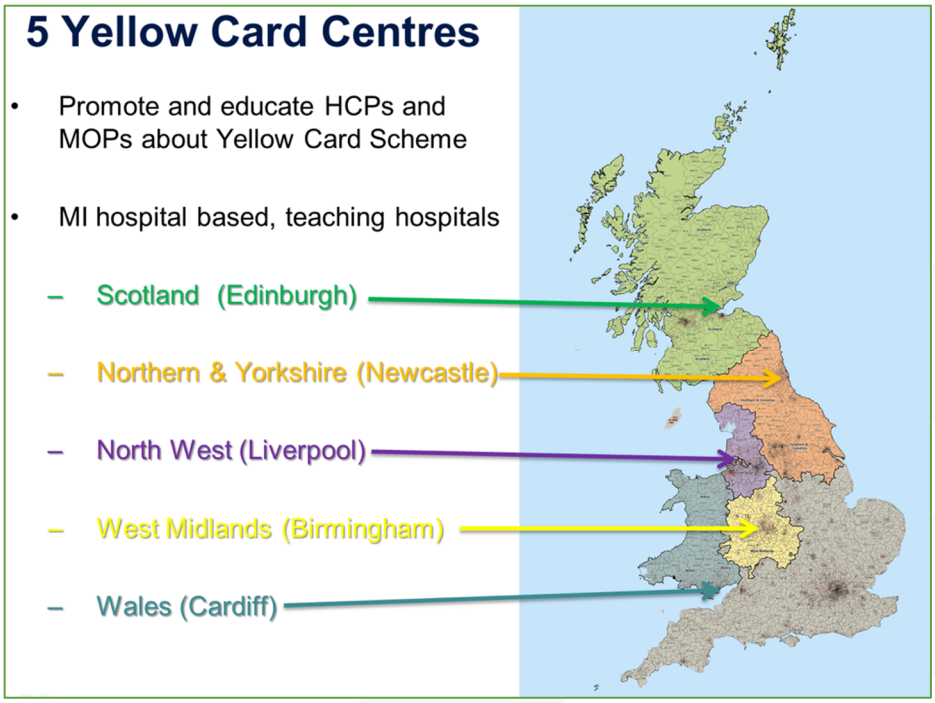


Figure 99. MHRA's five YCCs and their locations

The five YCCs perform an important role in supporting the Yellow Card Scheme through delivering local training, education, communication, feedback, including strategic and promotional activities. Such activities help the MHRA strengthen surveillance locally and nationally to stimulate an increase in suspected ADR reporting and general awareness of the Yellow Card Scheme. Their stakeholders include devolved administrations (for the Welsh and Scottish YCCs), HCPs and their representative organisations – both at primary and secondary care level. Educational elements also include training of post graduates and undergraduates. Over recent years YCCs have also interacted with patients, their organisations and charities to raise awareness and increase suspected ADR reporting.

Overall SMART objectives are set out and agreed for all YCCs which align with the MHRA's Yellow Card Strategy to increase reporting and quality of suspected ADRs. They are mainly in teaching hospitals and provide a valuable resource for providing advice and direction for educational activities so that ADR reporting is on the agenda of student HCPs and those HCPs that are practicing. To this effect, YCCs have developed their own e-learning modules available on their website which are used further to motivate and educate regional reporters. One YCC has worked with a national provider to input into a national e-learning module consisting of 3 units on PV and suspected ADRs.

The MHRA provides quarterly trending data for YCCs to analyse, including reporter qualifications, age, sex, suspected ADR numbers, geographical locations, types of medicines and suspected ADRs. This enables YCCs to focus their strategy and efforts on areas where a drive or campaign is needed locally.

YCCs often run their own campaigns to distribute materials they develop, approved by the MHRA, so there is flexibility for creativity and tailoring to the appetite of local reporters. YCCs also organise and attend workshops, lectures, meetings, write publications, conduct studies that add value to PV and ADR reporting, and organise event days for local HCPs to encourage suspected ADR reporting and educate them. All YCCs attend and are invited to speak at local conferences and congresses to represent the Yellow Card Scheme and encourage reporting for HCPs and patients related topics. YCCs often share their campaign collateral with each other.

Over recent years, YCCs interact more with patients as they seek to collaborate with patient organisations and specific disease areas to promote reporting through campaigns and mini-projects as per their objectives. Within devolved administration government areas they also coordinate with Expert Patient Programme, supplying leaflets, forms and packs when required.

The contact details for YCCs are promoted within the British National Formulary (BNF) and where possible in Agency communications relating to Yellow Card Scheme.

Generic templates for presentations were also issued to YCCs to enable stakeholders to acknowledge and relate that YCCs are commissioned by the MHRA in a formal capacity. This also aids with the gravitas of messages about suspected ADRs and affiliation to a national approach. A new way of working and collaboration now takes place through quarterly telephone conferences with all 5 YCCs and the MHRA to facilitate greater lines of communication, more harmonisation, sharing of good practice and ideas to promote suspected ADR work so more of an efficient focus can be put into campaign efforts. It also allows a multi-pronged feedback system between the MHRA, YCCs and HCPs within the healthcare system. YCCs submit annual reports to the MHRA to reflect on progress and report on their promotional work and future activities.

Some example case studies from particular initiatives to raise awareness levels and educate local reporters by YCCs are described below.

Case study: Liverpool Health Partners Yellow Card Working Group

In the UK there is a national drive to improve patient safety, reporting of adverse drug reactions (ADRs) to the Yellow Card Scheme is seen as an important marker of patient safety and the quality of patient care. In May 2014 a new initiative was introduced within the North West of England, this was a collaboration between the Liverpool Health Partners (LHP) and one of the regional Yellow Card Centres North West. LHP is a combination of twelve hospitals and healthcare organisations, scientific, academic and innovation institutions in Liverpool and Merseyside. A working group, named 'YCWG' was set up and comprises doctors, pharmacists and researchers who meet quarterly to share good practice and provide a networking forum to explore ideas and initiatives and lend support. Five meetings have been held up to the end of 2015.

The objectives of the YCWG are to:

- Improve patient safety
- Improve quality of care of patients
- Improve education and training in drug safety for HCPs
- Develop Liverpool as a centre of excellence for improving drug safety by use of innovative approaches.

Initiatives identified and shared within the group so far include:

- A designated 'Champion' within organisations to increase ADR reporting. Several sites identified a motivated individual and saw a substantial rise in reporting – reporting from LHP organisations increased from 298 reports in 2013/14 to 488 in 2014/15 – a 64% increase. This experience has stimulated all member Trusts to identify a Champion. Support from LHP Chief Executives has reinforced the importance of this approach.
- The opportunity for LHP Champions to network and share ideas leading to raised awareness, improved engagement and increased ADR reporting has stimulated the development of a North West-wide network of YC Champions.
- The inclusion of ADR reporting in a proposed PGcert module for foundation medics is under discussion as part of the educational focus of the LHP.
- A short audit on current practice in ADR reporting in an Acute Medical Admissions unit was conducted in one Trust. Prior to the audit ADR reporting via the YCS was extremely low – reporting was not considered unless the reaction was serious and unusual. Over the eight week audit period 12 suspected ADRs were identified and reported. The findings showed that improved awareness alongside a designated reporting pathway results increased YC submissions.

Case study: e-Learning modules on ADR reporting in Scotland

During the summer of 2014, YCC Scotland, in collaboration with NHS Education for Scotland (NES) launched 6 interactive eLearning modules. NES host the modules on their website and are also accessible via NHS Scotland LearnPro platform to Scottish HCPs and the YCC Scotland website: www.yccscotland.scot.nhs.uk/training/Pages/Educational.aspx

Each interactive module takes 20-30 minutes to complete and they cover:

- Module 1 – Basic principles of ADRs
- Module 2 – Categorisation
- Module 3 – Drug allergy classification
- Module 4 – Diagnosis, interpretation and management of ADRs
- Module 5 – Avoiding ADRs
- Module 6 – Pharmacovigilance

The modules, initially identified as core learning for all pre-registration pharmacists, were recommended for all foundation year doctors in Scotland. In addition, they have been promoted in the health board press, during various teaching sessions and are being incorporated into 'blended learning' at a number of Scottish universities for those undertaking non-medical prescribing. Between June 2014 and March a total of 549 modules were completed. Over 9 months a total of 1,231 modules were completed (137 per month). This is a significant increase on the previous period which averaged 76 per month. This reflects, amongst other factors, the increase in blended learning which has become more popular recently.

YCC Scotland has liaised closely with Community Pharmacy Scotland and in the autumn of 2015 it was identified that ADR reporting was a key element of patient safety for community pharmacists. Subsequently it was agreed that each community pharmacy in Scotland could claim a small fee in return for all pharmacy staff successfully completing the 6 modules before the end of March 2016 via the NES platform. At the same time NES increased their promotion of the modules. In the 9 months of financial year 2015/16 the number of tests, in the form of an MCQs, completed on the NES portal, which incorporates community pharmacy input, is approximately 207 (averaging 23/month) – a noticeable increase on the 16 per month during the previous 6 months since the first test was completed. NES also have data on the number of unique visits to the ADR section of the NES website indicating that, over 2015 there have been 4,695 unique visits to the section on their website covering the ADR modules i.e. an average of 391 different people visiting the modules per month.

The above data suggest that the e-Learning modules are recognised as useful resources in promoting patient safety through suspected ADR reporting, and are steadily growing in popularity, showing such awareness activities are working.

Case study: Community pharmacy poster campaigns in Scotland

By providing posters and support materials for the Scottish Community Pharmacy Public Health Scheme on three different occasions, involving all 1,200 community pharmacy in Scotland, pharmacies received a small remuneration for displaying posters and other relevant materials over a 6 week period for each public health subject. YCC Scotland designed and printed posters for display in February/March 2008, January/February 2011, and April/May 2015.

The 2008 campaign coincided with the UK-wide launch of patient Yellow Card reporting and similar posters were produced by the MHRA and also distributed to pharmacies across the rest of the UK on a less formal basis. The MHRA were also promoting patient reporting via other media across the UK at the time of the launch. Data on reporting rates for patients (parents, patients and carers) for Scotland were compared with those of YCC Northern & Yorkshire, the closest comparator region in England.

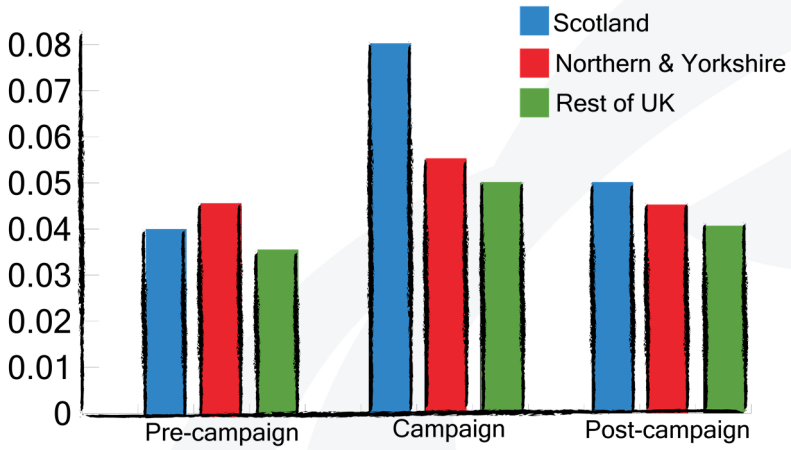


Figure 100. Patient Yellow Card reports submitted per week, per 10,000 population during Scottish campaign

The data suggest that the more formalised system of promoting patient Yellow Card reporting where pharmacists were actively encouraged and paid to display the posters was more effective.

However, when a second similar campaign was run in January/February 2011 analysis of reporting data did not find any significant difference in reporting between Scotland and Northern & Yorkshire on that occasion. This second campaign focussed on reporting of suspected ADRs associated with herbal medicines to coincide with the European Traditional Herbal Medicinal Products Directive which was being enforced that year. However, it was subsequently felt that this might have been too specialised a subject and this, combined with the poor weather at the time when the posters were being displayed, may have had a negative impact on the response to the campaign.

Figure 101. A third campaign was run from April to May 2015 using a more generic poster developed again by YCC Scotland

Distribution of this poster via the Scottish Community Pharmacy Public Health Scheme was combined with promotion of the 6 E-Learning modules on ADRs to all community pharmacists in Scotland via the Community Pharmacy Scotland website. Early results suggest that this campaign may have had an impact on patient and carer reporting. Compared with patient/parent/carer reporting for the same time period the previous year, reporting by this group had increased by 46% however, there had been an upward trend in patient reporting over the past few years so it is not possible to identify if the poster campaign had had any significant effect until a full statistical analysis can be done using data over several years.

Case study: YCC Wales set-up local 'Yellow Card Champions'[98]

The number of Yellow Cards reported in Wales to the MHRA fell by 26% in 2011-2012 and represented the lowest number of Yellow Cards submitted annually for the past 10 years.

In an attempt to improve reporting rates amongst hospital based reporters in Wales, YCC Wales submitted a proposal to the All Wales Chief Pharmacist Committee (AWCPC) recommending the introduction of a Yellow Card Hospital Champion Scheme.

The role specification for the Hospital Champion Scheme was agreed by the AWCPC in November 2012 to:

- Act as an information resource, provide guidance and to deal with local queries on PV and Yellow Card reporting
- Proactively assist other colleagues in the completion of Yellow Cards as a result of suspected ADRs
- Provide education and training sessions on PV and Yellow Card reporting to hospital staff
- Increase local publicity of the Yellow Card Scheme
- Keep up to date with legislative changes at the MHRA and EMA and communicate these and other drug safety issues to the relevant parties
- Attend a training session at YCC Wales
- Provide YCC Wales details of all training sessions undertaken.

Chief Pharmacists from all Health Boards in Wales nominated a pharmacist or pharmacy technician. Some Health Boards nominated one representative whereas others nominated 1 champion per hospital. In total, 14 champions were recruited. Public Health Wales nominated a pharmacist to act as a Public Health Yellow Card Champion. The Champions were invited to a PV and Yellow Card Scheme training day. Education, training and resources were developed and provided. YCC Wales also regularly communicated any latest PV news and data. 2 teleconferences were held to share ideas and review the progress being made. Reporting data was analysed and compared to the previous annual figures by reporter type and overall Health Board figures.

[98]Yellow Card Hospital Champions Scheme poster –the benefits of Champions and their positive impact on reporting culture in relation to PV, Alana Adams, Alison Thomas, Emma Carey, Fiona Woods, Philip Routledge, Robert Bracchi

A total of 1,177 reports of suspected ADRs originated from the YCC Wales region in 2013/2014. This represents an increase of 81% when compared to 2012/13 (649).

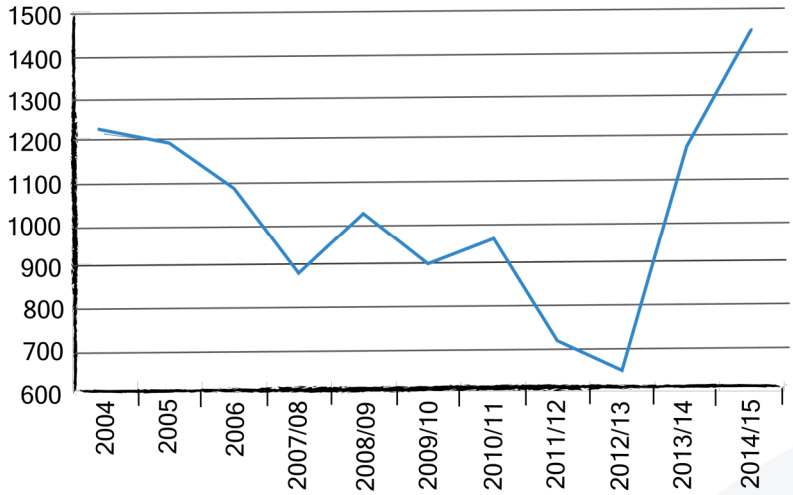


Figure102. The figure below shows the total number of suspected ADR reports from Wales over 11 years

There has been an encouraging increase in the number of reports from Wales in 2013-14 due to the Champions Scheme, increasing by 81% (1,177) compared to the previous year (649). This represents the highest number of reports in a year since 2005. The highest number of reports was from hospital pharmacists, who displayed a 129% increase on the number of reports made in 2012-13. This increase is closely associated with the launch of the Yellow Card Hospital Champion Scheme. Champions focussed their efforts in the next years to improving GP reporting.

The Yellow Card Hospital Champion Scheme has enabled YCC Wales to reach a wider audience across all Health Boards in Wales. In all, 438 extra healthcare professionals received training on the Yellow Card Scheme at 38 sessions. All champions gave positive feedback on their first year in the role and indicated that they wished to continue their participation in the Scheme.

In future, it would be valuable to include community based champions to ensure adequate coverage of colleagues in primary care. Phase two of the improvement work aims to develop the Scheme in this area. Including patients in the improvement work at an early stage is something that would also be beneficial in the future. The success of the initiative has shown implementation of similar Champion Schemes in other YCC regions.

Case study: A prescribing indicator in Wales

YCC Wales also was successful in launching Yellow Card reporting as a National Prescribing Indicator (NPI) for General Practitioners (GPs) and Health Boards in 2014/15 within their Devolved Administration region. The purpose of this indicator is to increase the number of Yellow Cards submitted in Wales particularly by GPs.

National Prescribing Indicators are endorsed as a means of promoting safe and cost-effective prescribing and allow health boards to compare current practice against an agreed standard of quality. The new NPI targets set for 2014–2015 were for:

- GP practices to submit 1 Yellow Card per 2,000 practice population for the year
- Each Health Board to submit at least one Yellow Card report per 2,000 Health Board population.

Yellow Card Champions supported communications and educating GPs about the new NPI. The introduction of this NPI in 2015 is associated with a corresponding 168% increase in submission of GP reports compared to the previous year. It has shown a reversal of the declining trend from GP reporting – GPs are now the highest reporting group in Wales. Work is ongoing to consider local incentive schemes to improve reporting rates further. All Health Boards saw an increase in the number of Yellow Cards submitted by GPs and by Health Boards in total. One Health Board, Abertawe Bro Morgannwg University Health Board, saw over 40% of their practices submit at least one Yellow Card by GPs per 2,000 practice population followed by 27% in Betsi Cadwaladr University Health Board.

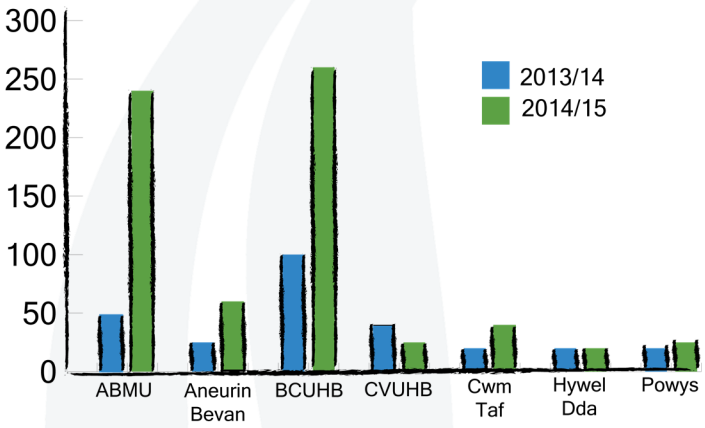


Figure103. Number of reports by GPs per 100,000 population by the top reporting Health Boards