HPRA Safety Update

COVID-19 Vaccines, Overview of National Reporting Experience
Publication date: 19 May 2022 (Update #18)

Highlights from this update:

- As of 10 May, a total of 20,182 reports of suspected side effects were notified to the HPRA. The number of COVID-19 vaccines administered as of that date was reported as 8,091,610. This includes 240,443 administered as a single dose, 3,841,238 as a first dose and 3,787,797 as a second dose. Additionally, 2,893,322 booster doses and 117,901 third doses (for those with a weakened immune system) have been administered.[1,2]

- Whilst not experienced by everyone, all vaccines have some side effects, the vast majority of which are mild to moderate in nature. These side effects need to be continuously balanced against the benefits of vaccines, given the risk of COVID-19 illness and related complications, and as scientific evidence shows that they reduce deaths and hospitalisations due to COVID-19. Overall, the national reporting experience continues to support the favourable assessment that the benefits of COVID-19 vaccines outweigh the risks. An overview of national reports of suspected side effects received is provided in this safety update on page 6.

- The European Medicines Agency (EMA) published its latest COVID-19 vaccine safety updates on 13 April and 12 May. This publication describes safety issues under evaluation, as well as any new safety recommendations, however no updates to the product information for any of the authorised COVID-19 vaccines are currently warranted. The EMA published highlights from its monthly safety committee meetings on 08 April, which included information on mRNA COVID-19 vaccines, concluding that no updates to the product information were required.

- This is the final HPRA safety update to be published in the current format. An overview of national reports of suspected side effects will instead be given on the HPRA COVID-19 webpage and updated periodically, including links to any EMA safety updates. It is expected that the overview will be made available on 14 July.

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[1]*Health Service Executive Vaccination Programme overview as of Tuesday 10 May 2022* *https://www.hse.ie/eng/services/news/newsfeatures/covid19-updates/vaccination-programme-dashboard-as-of-10-of-may-2022.pdf*

[2]*Government of Ireland GeoHive Vaccinations* *https://covid-19.geohive.ie/pages/vaccinations*

CONTENTS

UNDERSTANDING THE DATA PRESENTED WITHIN THIS SAFETY UPDATE

This update includes an overview of reports of ***suspected side effects*** notified to the HPRA safety monitoring system and is provided as an enhanced transparency measure for members of the public and healthcare professionals. All vaccines have some side effects, the vast majority of which are mild to moderate in nature. These side effects need to be continuously balanced against the expected benefits in preventing COVID-19 illness.

Reports included in the overview are those notified to the HPRA on a voluntary basis by healthcare professionals and members of the public, with reporting of suspected side effects to COVID-19 vaccines (www.hpra.ie/report) encouraged. Any reports of Irish cases received by the HPRA from the company (i.e. the licence holder, to date, BioNTech, Moderna, AstraZeneca, Janssen, Novavax) responsible for the vaccine are also included within this update. This overview provides an up-to-date summary of national reporting experience.

However, it is important to understand that conclusions on the safety of a vaccine cannot be drawn based on the information provided, given well-established and known limitations in interpreting such data in isolation, examples of which are described below.

Causation

- The HPRA receives reports based on ***suspicion*** that an adverse experience may be associated with vaccination. This does not mean the vaccine ***caused*** the adverse experience**.** As such, these are referred to as ***'suspected'*** side effects.
- Reports may describe coincidental events, which have occurred post-vaccination, but would have occurred even if vaccination had not taken place (e.g. they may be due to an underlying medical condition, or be signs and symptoms of another illness).
- Each individual report is carefully reviewed, however, the totality of data from all sources (e.g. clinical and epidemiological studies and literature) must be considered as part of ongoing safety monitoring to ensure ***evidenced based conclusions*** are drawn.

Number/volume

- As the HPRA system is based on voluntary reporting, ***not all*** suspected side effects will be reported. As such, the number and types of reports notified can vary for a variety of reasons.
- An increased number of reports is expected for COVID-19 vaccines, given public interest as well as HPRA calls encouraging reporting. This is known as ***stimulated reporting***.
- A single report may describe more than one suspected side effect in an individual (e.g. headache and nausea reported together), therefore, the number of side effects may exceed the total number of reports received.

Comparisons

- The type and number of reports received for different COVID-19 vaccines are ***not directly comparable*** as, for example, the vaccines have not been used in the vaccination programme for the same length of time, and will have been administered to different numbers of people, with different underlying medical conditions and across different settings.
- Each vaccine is authorised on the basis that its benefits-risk profile has and continues to be favourable.

Changes to data over time

- The description of suspected side effects in this update reflects available information known at the time by the HPRA. These data may undergo changes as more information about individual reports becomes available through follow-up, and as more data are reported and evaluated.
- For these reasons, the information in this report is not sufficient in isolation to draw conclusions on the safety profile of a vaccine. Like all vaccines, some side effects are to be expected, with the vast majority mild or moderate in intensity and resolving within a few days. Vaccines are approved for use on the basis of robust scientific evidence that demonstrates their benefits outweigh any risks.

Always refer to the product information for information on the established safety profile, including known side effects of a COVID-19 vaccine.

This includes the Package Leaflet (for members of the public) and Summary of Product Characteristics (for healthcare professionals)

Product information for COVID-19 vaccines is accessible here.

AUTHORISED COVID-19 VACCINES

COVID-19 vaccines currently authorised for use in the European Union by the EMA include:

mRNA vaccines:

- Comirnaty® (licence holder: BioNTech Manufacturing GmbH) is authorised for use in individuals aged 5 years and older as a vaccination course consisting of two separate doses, with a third dose recommended for those who are severely immunocompromised. A booster dose may be administered three months after the second dose in individuals aged 12 years and older. For children aged 5 to 11 years of age, the dose of Comirnaty® is lower than that used in people aged 12 and above (10 microgram compared with 30 microgram). For further information on this vaccine click here.
- Spikevax® (*previously COVID-19 Vaccine Moderna®)* (licence holder: Moderna Biotech Spain, S.L.) is authorised for use in individuals aged 6 years and older as a vaccination course consisting of two separate doses, with a third dose recommended for those who are severely immunocompromised. A booster dose may be administered at least three months after the second dose, in individuals aged 18 years and older. For children aged 6 to 11 years of age, the dose of Spikevax® is lower than that used in people aged 12 and above (50 microgram compared with 100 microgram). For further information on this vaccine click here.

Adenoviral vector vaccines:

- Vaxzevria® (licence holder: AstraZeneca AB) is authorised for use in individuals 18 years of age and older as a vaccination course consisting of two separate doses. For further information on this vaccine click here.
- Jcovden® *(previously COVID-19 Vaccine Janssen®)* (license holder: Janssen-Cilag International NV) is authorised for use in individuals aged 18 years and older as a vaccination course consisting of a single dose administration. A booster dose may be administered at least two months after the primary vaccination course in individuals aged 18 years and older. For further information on the vaccine click here.

Recombinant adjuvanted spike protein vaccine:

- Nuvaxovid® (licence holder: Novavax CZ, a.s.) is authorised for use in individuals 18 years of age and older as a vaccination course consisting of two separate doses. For further information on this vaccine click here.

OVERVIEW OF SUSPECTED SIDE EFFECT REPORTS

Number of reports received

As of 10 May, the HPRA has received 20,182 reports describing suspected side effects[3,4] in association with COVID-19 vaccines, 2,268 of which were received in 2022. A breakdown of reports received by vaccine type is provided below:

mRNA vaccines (Comirnaty® and Spikevax®)	13,188
Adenoviral vector vaccines (Vaxzevria® and Jcovden® *[previously Janssen]*)	6,671
Recombinant adjuvanted spike protein vaccine (Nuvaxovid®)	<5
Brand unknown/not specified	321

Doses administered by vaccine type, as of 10 May, were reported as follows:[1]

- mRNA vaccines: 5,993,729 Comirnaty®, 647,051 Spikevax®.
- Adenoviral vector vaccines: 1,210,153 Vaxzevria®, 240,458 Jcovden® *[previously Janssen]*.
- Recombinant adjuvanted spike protein vaccine: 219 Nuvaxovid®

Further information on vaccination, including doses administered, is available from covid-19.geohive.ie.

Regularly reported suspected side effects

The most regularly reported suspected side effects notified to the HPRA include the following:[5]

mRNA vaccines (Comirnaty® and Spikevax®)
10% or more of reports describe side effects such as: ▪ Fever, pain (non-specific), tiredness ▪ Headache ▪ Nausea **1% to less than 10% of reports describe side effects such as:** ▪ Abdominal pain, diarrhoea, tingling sensation in mouth, vomiting ▪ Dizziness, drowsy, fainting/feeling faint, migraine, numbness/reduced sensations, tingling/pins and needles/tremor ▪ Back pain, joint/limb pain, muscle pain/weakness/spasm/stiffness, neck pain ▪ Blurred vision ▪ Chest discomfort/pain, chills, general discomfort, feeling unwell, feeling hot/cold, flu-like symptoms, lack of energy/feeling weak, swelling including of legs/arms/face, underarm pain ▪ Cough, shortness of breath, sore throat

[3]A single report may contain more than one suspected side effect for an individual (e.g. rash and hives reported together). Therefore, the total number of suspected side effects will exceed the total number of reports.
[4]In accordance with EU guidance, reports are valid if the minimum reporting criteria are met. These include an identifiable reporter, an identifiable patient, one or more suspected medicine known to have been administered and one or more suspected adverse reaction.
[5]Terms listed as frequently reported are presented according to standard coding classification system (MedDRA) adopted for use in the EU, and grouped by system organ class (SOC) and listed alphabetically. It should be noted that regular reporting of a side effect is not the same as the incidence of occurrence.

- Difficulty carrying out daily tasks (such as temporarily unable to attend work)
- Feeling anxious, insomnia/trouble sleeping
- Increased heart rate/racing heart, increased blood pressure
- Injection site redness, pain, itchiness, swelling, rash, difficulty moving injected arm
- Lack of appetite
- Menstrual disturbances
- Painful/swollen lymph nodes
- Skin red/red rash, sweating, general rash, itching, itchy rash, hives
- Subsequent diagnosis of COVID-19
- Tinnitus (ringing in the ears), vertigo-like symptoms

Adenoviral vector vaccines (Vaxzevria® and Jcovden® *[previously Janssen]*)

10% or more of reports describe side effects such as:

- Chills, fever, tiredness
- Dizziness, headache
- Joint pain, muscle pain, other pain (non-specific)
- Nausea

1% to less than 10% of reports received describe side effects such as:

- Abdominal discomfort/pain, diarrhoea, vomiting
- Back pain, bone pain, limb pain, muscle spasms/weakness/stiffness, neck pain
- Blurred vision, eye pain
- Chest discomfort/pain, general discomfort, feeling unwell/ill, feeling hot/cold, flu-like symptoms, lack of energy/weakness, swelling including of legs/arms
- Cough, shortness of breath, sore throat, nose bleed
- Difficulty carrying out daily tasks (such as temporarily unable to attend work, need to stay in bed)
- Drowsy, fainting, headache, migraine, numbness/reduced sensations, tingling/pins and needles, tremor
- Ear pain, tinnitus (ringing in the ears), vertigo-like symptoms
- Hives, skin red, general rash, sweating, itching
- Increased heart rate/racing heart, increased blood pressure
- Injection site pain, redness, swelling, bruising, difficulty moving injected arm
- Insomnia/trouble sleeping
- Lack of appetite
- Menstrual disturbances
- Swollen lymph nodes

The majority of regularly reported suspected side effects are consistent with the types of events typically observed following vaccination, including those described in the product information for the individual vaccines, and are mild to moderate in nature.

In reports evaluated which include information on outcome, approximately 40% of suspected side effects had resolved or were resolving at the time of reporting. For others, the suspected side effects had not yet resolved, or the outcome was reported as unknown, when initially reported. Information on reports with a fatal outcome is provided on page 9.

A full breakdown of all suspected side effects described in reports is provided on page 10. Further information on how reports received by the HPRA are processed, including how safety signals are evaluated, is given on page 14.

TOPICS OF INTEREST, INCLUDING EMA RECOMMENDATIONS

No new safety recommendations have been made by the EMA's safety committee since the last HPRA safety update.

The product information for each authorised vaccine is available from the HPRA website here. The product information includes the package leaflet, which provides up to date evidence based information on any expected side effects, as well as any relevant guidance.

In relation to the topics of interest included in the last safety update (#17), there are no significant updates. Topics re-included below are those with updated national reporting figures.

- Vaccination of children and adolescents (5 to 17 years of age)
- Booster or third dose
- Reports which included a fatal outcome

Vaccination of children and adolescents (5 to 17 years of age)

- As the national vaccination programme continues, the HPRA are closely monitoring reports of suspected side effects received in children (aged 5 to 11 years) and adolescents (aged 12 to 17 years).
- As of 10 May, the HPRA received 445 reports of suspected side effects following vaccination with Comirnaty® in this age category, 114 of which related to a child, with the remainder relating to an adolescent. As of that date, 875,000 doses had been administered to children and adolescents (5 to 17 years) as part of the national vaccination programme.[1]
- Overall, the reports received are consistent with the types of reports received for adults, with most being mild to moderate in nature. The most regularly reported include dizziness/fainting, headache, fever, nausea/vomiting, and tiredness. Of the reports received which include information on outcome, many of the suspected side effects had resolved or were resolving at the time of reporting. A breakdown of all suspected side effects by type is available on page 13.

Reports following a booster or third dose

- As the national vaccination programme continues, the HPRA are closely monitoring reports of suspected side effects received following a third dose (for people with a weakened immune system) or a booster dose.
- As of 10 May, the HPRA has received 1,809 reports of suspected side effects following either a third or booster dose, the vast majority of which were associated with Comirnaty® or Spikevax®. As of that date, 117,901 third doses[1] and 2,893,322 booster doses[2] had been administered as part of the national vaccination programme.
- Overall, the reports received are consistent with the types of reports received after the primary vaccination course with the majority mild to moderate in nature. The most regularly reported include headache, fever, nausea, pain, swollen lymph nodes and tiredness.

Reports which included a fatal outcome

- A total of 113 reports have been received describing an individual who was known to have been vaccinated and subsequently passed away. Of these, 96 were reported with an mRNA vaccine, 12 with adenoviral vector vaccines and the remaining five were reported with brand unknown/not specified. The majority of reports (approximately 70%) with a fatal outcome describe an individual aged 75 years and over, with the median age of the individuals being 80 years. Of those, 58 deaths occurred in males and 54 in females, with the sex not provided in one report. For a number of reports, the cause of death was unconfirmed at the time of reporting, with post mortem results awaited.
- Reports describing a death are carefully reviewed. It can be expected that fatalities due to progression of underlying disease or natural causes will continue to occur, including following vaccination. This does not mean that the vaccine caused the deaths.

BREAKDOWN OF SUSPECTED SIDE EFFECTS BY CATEGORY

A full breakdown of all suspected side effects described in reports received by the HPRA is provided below by vaccine type (i.e. mRNA and adenoviral vector vaccines) and by category (i.e. the related body system). Whilst the vast majority of reports notified to the HPRA describe expected events (i.e. known side effects of a vaccine or vaccination process), reports can also be received for events that are unexpected and/or are considered serious, as they required medical care or intervention. Such reports may describe events not caused by the vaccine and may have occurred coincidentally. However, all reports are carefully reviewed and if there is cause to do so, a further analysis is carried out to determine if a vaccine may have had a contributory role. If it is determined that a vaccine is a contributory factor, the public and healthcare professionals will be informed and the relevant product information will be updated.

Please read the following explanatory note in relation to understanding the data presented in the suspected side effect tables:

- A single report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, which may include more than one category, or more than one in a specific category. For example, a single report that describes chills, fatigue and nausea in an individual, includes three suspected side effects, two in general symptoms (chills and fatigue) and one in gastrointestinal (nausea). As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.
- The breakdown summary includes all suspected side effects as they are reported to the HPRA. This includes cases for which a diagnosis is reported as provisional, or for which there is more than one possible diagnosis at the time of reporting. In other cases, a diagnosis may not be available, and only signs and symptoms or laboratory test results are given. Reports are also received from members of the public, and the HPRA follows up to medically confirm these reports, where consent is provided and more information is required. For each report, all events are 'coded'[6] as suspected side effects in the national pharmacovigilance database using the exact information (verbatim) given in the report. The HPRA follows up with the reporter to collect any further information which may be relevant to the assessment of the case.
- The description of suspected side effects in this update, including the number and category, reflect available information known at the time by the HPRA. These data may undergo changes as more information about individual reports becomes available through follow-up, and as reports are further evaluated.
- Please refer to the section 'Understanding the data presented within this safety update' on page 3 with regard to further interpretation guidance. Background information on the evaluation of suspected side effect reports is available on page 14.

[6] *Medical Dictionary for Regulatory Activities (MedDRA) https://www.meddra.org/*

Of the 20,182 reports notified to the HPRA as of 10 May, over 85% have now been submitted to EMA's Eudravigilance database, and as such, additional anonymised information on these reports, is publicly available through the following link www.adrreports.eu. See page 14 for further details.

Suspected side effects to mRNA vaccines

A breakdown of suspected side effects described in the 13,188 reports notified to the HPRA is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

Category	Suspected side effects
General symptoms and local reactions *e.g. chills, fatigue, 'flu-like' feeling, fever, injection site pain or swelling*	15,177
Nervous system *e.g. dizziness, headache, lack of energy, pins & needles, fainting or feeling faint*	8,503
Muscles, tissue, bones or joints *e.g. general muscular pain or weakness*	5,846
Gastrointestinal *e.g. nausea, vomiting, diarrhoea*	4,134
Skin *e.g. rash, itchy rash*	3,370
Reproductive system, obstetrics or gynaecology related *e.g. menstrual disturbance*	2,235
Respiratory *e.g. cough, shortness of breath*	1,830
Behavioural, emotional and mental health *e.g. insomnia, trouble sleeping*	1,492
Social circumstances *e.g. need to rest in bed or take a break from normal daily activities*	1,189
Cardiac (heart) related *e.g. palpitations*	1,188
Procedural issues and complications *e.g. injection site bruising*	1,068
Blood and lymphatic system *e.g. swollen glands*	1,017
Eye *e.g. eye pain, vision blurred*	960
Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. high temperature (via thermometer), increased heart rate or blood pressure (via BP monitor)*	910
Infection *e.g. local or general such as influenza or cold sore*	766
Blood vessel related (i.e. veins/arteries) *e.g. pale complexion*	695
Ear related e*.g. earache, tinnitus*	579
Metabolism and nutrition disorders *e.g. decreased appetite*	404
Immune system related *e.g. hypersensitivity, allergic reaction*	214
Kidney related *e.g. change in frequency of urination*	125
Endocrine (hormone) *e.g. thyroid function change*	34
Liver related *e.g. jaundice, inflammation*	29
Cysts and polyps *e.g. benign skin growth*	17
Conditions present at birth	<5

Suspected side effects to adenoviral vector vaccines

A breakdown of suspected side effects described in the 6,671 reports notified to the HPRA is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

Category	Suspected side effects
General symptoms and local reactions *e.g. chills, fatigue, 'flu-like' feeling, fever, injection site pain or swelling*	11,362
Nervous system *e.g. dizziness, headache, lack of energy, pins & needles, fainting or feeling faint*	5,990
Muscles, tissue, bones or joints *e.g. general muscular pain or weakness*	4,117
Gastrointestinal *e.g. nausea, vomiting, diarrhoea*	3,110
Skin *e.g. rash, itchy rash*	1,748
Respiratory *e.g. cough, shortness of breath*	963
Behavioural, emotional and mental health *e.g. insomnia, trouble sleeping*	876
Social circumstances *e.g. need to rest in bed or take a break from normal daily activities*	701
Reproductive system, obstetrics or gynaecology related e.g. *menstruation disturbance*	527
Eye *e.g. eye pain, vision blurred*	513
Metabolism and nutrition disorders *e.g. decreased appetite*	485
Blood vessel related (i.e. veins/arteries) *e.g. pale complexion*	476
Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. high temperature (via thermometer), increased heart rate or blood pressure (via BP monitor)*	472
Cardiac (heart) related *e.g. palpitations*	411
Procedural issue or complications *e.g. injection site bruising*	386
Ear related e*.g. earache, tinnitus*	381
Infection *e.g. local or general such as influenza or cold sore*	284
Blood and lymphatic system *e.g. swollen glands*	195
Kidney related *e.g. increased frequency of urination*	74
Immune system related *e.g. hypersensitivity, allergic reactions*	72
Liver related *e.g. jaundice*	14
Endocrine (hormone) *e.g. thyroid function change*	9
Cysts and polyps *e.g. various*	5

Suspected side effects in children and adolescents (aged 5 to 17 years) following vaccination with an mRNA Vaccine

A breakdown of suspected side effects described in the 445 reports notified to the HPRA concerning children (aged 5 to 11 years) and adolescents (aged 12 to 17 years) following vaccination with an mRNA vaccine is provided below by category. Each report describes at least one suspected side effect for a vaccinated individual. Reports often describe several suspected side effects for an individual, including more than one in a specific category. As such, there are more suspected side effects in each category and overall, as compared to the number of reports received.

Category	Suspected side effects
General symptoms and local reactions *e.g. tiredness, weakness, chest pain, feeling hot*	395
Nervous system *e.g. dizziness, headache, fainting or feeling faint*	300
Gastrointestinal *e.g. nausea, vomiting, abdominal pain*	183
Skin *e.g. rash, sweating*	149
Muscles, tissue, bones or joints *e.g. limb, muscle, joint pain*	115
Respiratory *e.g. shortness of breath, nose bleed*	93
Behavioural, emotional and mental health *e.g. trouble sleeping*	56
Social circumstances *e.g. need to rest in bed or take a break from normal daily activities*	50
Cardiac (heart) related *e.g. palpitations/racing heart*	44
Reproductive system, obstetrics or gynaecology related *e.g. menstruation disturbance*	42
Blood vessel related (i.e. veins/arteries) *e.g. pale complexion*	41
Procedural issue or complications *e.g. injection site bruising*	41
Eye *e.g. vision blurred*	40
Infection *e.g. chest infection*	39
Abnormal clinical or laboratory result (i.e. where information is provided on results of relevant tests) *e.g. changes in heart rate*	35
Blood and lymphatic system *e.g. swollen glands*	24
Metabolism and nutrition disorders *e.g. decreased appetite*	18
Ear related e.*g. earache, tinnitus*	16
Immune system related *e.g. hypersensitivity, allergic reactions*	10
Kidney related *e.g. inflammation*	9
Liver related	<5

BACKGROUND INFORMATION ON THE EVALUATION OF SUSPECTED SIDE EFFECT REPORTS

As for all medicines and vaccines, suspected side effect reports in association with COVID-19 vaccines submitted to the HPRA are recorded and stored on the HPRA's national adverse reactions database. They are subsequently submitted (with any personal identifiers and contact details removed) to the EudraVigilance database operated and managed by the European Medicines Agency (EMA). EudraVigilance provides for the transfer of reports from national regulatory agencies such as the HPRA and marketing authorisation holders to the EMA. This supports early detection and monitoring of possible safety signals in relation to reported side effects.

The EMA also make available anonymised information on all reports, based on global safety experience, publically available through the following link www.adrreports.eu. The EMA also publish regular safety updates for COVID-19 vaccines, as well as highlights from meetings of the EMA's safety committee (Pharmacovigilance Risk Assessment Committee), which describe safety issues under review, as well as recommendations to revise product information. These are available via www.ema.europa.eu.

Information from side effect reports, together with additional safety data (e.g. from the scientific literature, cumulative safety data analysis, epidemiological studies etc.) are assessed on an on-going basis, in conjunction with our EU counterparts to consider their impact on the known safety profile of the COVID-19 vaccines and any need for regulatory changes to support safe and appropriate use.

Partially anonymised details of reports are also shared with other bodies also involved in safety monitoring of medicines, in accordance with the legislative provisions, including GDPR (please see the HPRA privacy statement here). These bodies include the World Health Organisation (WHO) and as appropriate, the company(ies) that hold the licence(s) for the medicine(s) concerned (i.e. marketing authorisation holders or 'MAHs'). Sharing of this information ensures that the information is available to all parties responsible for the ongoing safety monitoring of medicines.

Further information to support interpretation of the data provided in this update is available here.