AUDA-NEPAD
AFRICAN UNION DEVELOPMENT AGENCY

SMART SAFETY SURVEILLANCE

Spotlight

The Smart Safety Surveillance Newsletter in Africa

Edition 2 **November 2021**

In this edition:

1. Overview of AU-3S progress in 2021

AU-3S is a long-term programme with the goal of strengthening the safety surveillance of medical products across Africa for priority health products. The programme aims to tackle continental challenges such as low adverse event reporting rates, siloed pharmacovigilance (PV) systems, and limitations in safety expertise. With COVID-19 reinforcing the need for strong African PV, AU-3S is currently supporting the safety surveillance of COVID-19 vaccines in 4 pilot countries. These countries are Ethiopia, Ghana, Nigeria, and South Africa – comprising around 30% of Africa's population. The UK's Medicines and Healthcare products Regulatory Agency (MHRA) is the technical partner for the programme. For more information about the AU-3S programme and an explanation of our solutions, see Edition 1 of Spotlight (which can be accessed here) or visit the AU-3S website.

2021 has seen the acceleration of the AU-3S programme towards its objectives through the COVID-19 response, which served as a "proof of concept" of the AU-3S solutions. AU-3S successfully launched 4 solutions, covering both in-country and cross-country areas:

- Expanded electronic vaccine data collection through the Med Safety App
- Developed the interim cross-country data integration and signal detection (DISD) system
- Launched the AU-3S Joint Signal Management Group for aggregate signal reports
- Facilitated capability strengthening trainings with the MHRA

By delivering these solutions, the AU-3S's COVID-19 response has delivered significant impact to date:

- Digital health ecosystem that enables real time data access and downstream analysis: Through the COVID-19 response, over 400 million Africans are covered by digital safety surveillance tools. Around 32,000 new users of the Med Safety App were added in 2021, and over 8,500 total reports have been submitted through the App – see Updates on e-reporting using the Med Safety App. AU-3S continues to support countries to decentralise data entry of paper forms, to reduce workload and ensure the NRAs have near-real time visibility of AEFI reports.
- First African-owned cross-country safety data integration and analysis platform: The interim DISD system has enabled the integration of safety data from all 4 pilot countries and signal detection on African-owned data – the first of its kind on the continent. As of 18 November, the system contains more than 20,300 AEFI reports. To read more about the current status of the DISD system and to understand the end-to-end data flows, see data flow from AU-3S DISD system to the JSM Group.
- African-led evidence-based decision making on their own African data: Both the AU-3S Joint Signal Management (JSM) Secretariat and Group are now fully operational and have held 32 and 7 meetings, respectively. More than 1,600 different vaccine-event combinations have been reviewed. Based on the analysis of this DISD system data, the AU-3S JSM reiterates that the benefits of the AstraZeneca, Janssen, Pfizer, and Moderna COVID-19 vaccines outweigh the risks of vaccination. See further information in Update on AU-3S JSM Group.
- End-to-end safety strengthening and collaboration across EPI programmes and NRAs: To advance the knowledge and capabilities on the continent, AU-3S facilitated 14 trainings hosted by the MHRA. An average of 100 attendees participated in each session and reported

a 95% satisfaction rate. E-learning modules are publicly available on the AU-3S website.

- Critical safety coordination and alignment across country and global stakeholders: More than 125 in-country and cross-country experience sharing sessions were held by AU-3S. Information was shared in over 100 continental guidance documents, publications, videos, templates and other media. In addition, AU-3S had around 60 additional touchpoints with other continental initiatives and stakeholders.

Because COVID-19 vaccine supply to African countries has been constrained so far, the total number of AEFIs reported in AU-3S pilot countries has remained relatively low. However, during this period, all 4 countries have managed to strongly increase their AEFI reporting rate (x3 at a minimum) in comparison to their baseline reporting rate. The COVID-19 vaccination effort in Africa is now entering a new chapter. While only 6.6% of the African population is vaccinated to date, a significant influx of vaccine supply is expected in the coming months. Accordingly, we expect a three to sixfold increase in AEFIs by the end of the year in AU-3S countries.

AU-3S has created a public health impact on the continent. Importantly, African data and African regulators have confirmed the safety of COVID-19 vaccines in their own populations, based on analysis to date. An approach and tools for safety surveillance have been developed and can be scaled across countries and other priority health products. Furthermore, AU-3S's approach is an example of a model that can be leveraged for LMIC safety response in future pandemics: the improved collaboration between NRAs and EPI programmes can enable future vaccination programmes. These measures are able to boost patient confidence that African regulators are safeguarding their health.

All the strong progress and impact made by the AU-3S programme was driven largely by the collaboration with partners and advisors. The involvement of the 4 pilot countries – Ethiopia, Ghana, Nigeria and South Africa; partners – WHO-AFRO and WHO-EMRO; collaborative forums – African COVID-19 Vaccine Deployment Readiness and Execution Taskforce (ACREDT) and the Africa CDC-led African Vaccine Delivery Alliance (AVDA); technical advisor – UK's MHRA; advisor – US FDA; and funding from the Bill and Melinda Gates Foundation (BMGF) has contributed towards AU-3S's ambition to advance the safety surveillance of medical products in Africa.

While work remains to fully embed and continuously improve these solutions, AU-3S is looking to start expanding its reach early next year. The AU-3S team, together with current and future programme partners, looks forward to continuing to support safety surveillance in Africa.

> ***"Thank you to each and every individual for your commitment to the AU-3S programme over and above the routine work that we know you do at the national level. We appreciate all of the feedback that you have shared to help us best mould the next phase of the AU-3S programme"***
>
> **- Hudu Mogtari, Programme Lead of AU-3S**

2. Updates on e-reporting using the Med Safety App

How is electronic reporting using the Med Safety App progressing?

As outlined in the first edition of the Spotlight newsletter, the AU-3S team and the MHRA facilitated the development of a vaccine reporting form for use in the Med Safety App. This enables e-reporting of adverse events following immunisation (AEFIs) by both healthcare professionals and the general public. While this form was initially only rolled-out to the 4 AU-3S pilot countries, it has since been made available to all other countries using the Med Safety App.

There has been significant uptake of the Med Safety App due to both the COVID-19 need and communication efforts made by the countries (see "How have the AU-3S pilot countries been promoting the use of the Med Safety App?"). Since the start of 2021, there have been approximately 27,000 new users of the App across all AU-3S pilot countries. This represents about a 13x average increase in monthly Med Safety App active users relative to 2020 for these geographies. To date, a total of approximately 8,500 COVID-19 vaccine AEFIs have been directly reported using the Med Safety App for AU-3S programme geographies. With support from AU-3S, each pilot country is working towards making the Med Safety App the primary tool for safety reporting. Target setting and monthly tracking is being conducted to help countries increase the share of total safety reports submitted via the App.

How have AU-3S pilot countries been promoting the use of the Med Safety App?

Since the launch of the AEFI form, the AU-3S team has been working closely with in-country communication teams from each of the pilot countries to promote the use of the App. This work has involved the development of tailored communications plans and the production of promotional content. Notably, the AU-3S team has developed 3 videos which: (i) provide an overview of the App, (ii) show how one can navigate the entire App, and (iii) outline step-by-step instructions for how to report an AEFI using the App. These videos can be customised to country specific requirements, such as regulatory authority branding and language translation. A detailed Med Safety App guideline and set of FAQs have also been prepared to support any country to use the App successfully. For further information and access to materials, kindly visit the AU-3S website. Furthermore, Med Safety App trainings have been delivered as part of national COVID-19 vaccine rollout programmes. These trainings have been targeted at healthcare professionals.

> ***"Previously, we only had paper forms to report AEFIs. The Med Safety App improved our visibility and gave us real-time access to AEFI reports to inform our regulatory decisions. AU-3S provided us with multiple materials to help us with our national communications about safety surveillance."***
>
> **- Prof. Moji Adeyeye, Director General of NAFDAC**

3. Success of the Med Safety App in Nigeria

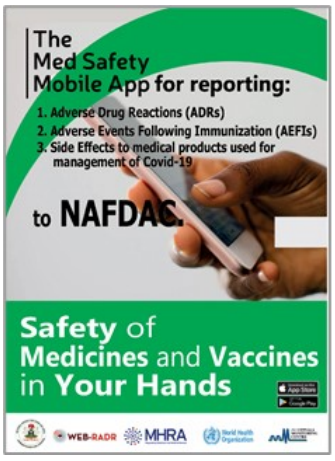
Starting from this edition of Spotlight, there will be a standing 'focus article' that features progress on a particular topic from one of the AU-3S programme countries. This edition focuses on Nigeria and its progress towards improved levels of electronic reporting. Key insights and outcomes from other AU-3S programme countries over a range of topics will be shared in subsequent editions of this newsletter series.

Note: This article was jointly prepared by AU-3S and the National Agency for Food and Drug Administration and Control (NAFDAC)

Usage of the Med Safety App has increased significantly in Nigeria, driven by NAFDAC's practical training sessions with healthcare professionals, and a strong communication plan developed in collaboration with the National Primary Health Care Development Agency (NPHCDA).

Trainings to healthcare professionals have been a core priority to drive up usage of the Med Safety App, and to improve data quality. NAFDAC found that an effective training technique is for participants to download the App during the training and practice entering a "case study" AEFI case report in the session. This allows NAFDAC staff to quickly assist any individuals having challenges with downloading and/or using the App. This approach was shared with the other AU-3S pilot countries who are now using and benefiting from it. NAFDAC is now providing trainings to national and state level EPI staff to promote use of the drop-down fields in the App for drug name and reaction term, rather than use free text, which causes dropouts from the interim DISD system.

From a communications perspective, press articles and interviews have played an important role in spreading awareness about the Med Safety App and how it should be used. For example, here are 3 articles from completely different contexts where the use of the App has been promoted to the Nigerian public: link, link, and link. A number of posters and electronic flyers have also been prepared and distributed to raise awareness – see illustrative screenshots below. Recently, Nigeria has also focused on engaging with professional bodies on historically low levels of incidence reporting relative to other countries. Here, the Med Safety App is being highlighted as a tool to improve the quality and quantity of reporting from healthcare professionals and the public so that the NAFDAC can focus more on signal detection activities.



Based on the forementioned initiatives, amongst others, Nigeria has seen approximately 1,500 new users and about 2,900 active users on average per month since the start of 2021. A significant spike in these two metrics can be seen during the month where the majority of above-mentioned trainings were held. This has helped the reporting situation evolve from <1% of reports being submitted electronically in 2020 to about 30% as of July 2021. Nigeria has committed to working towards a target of 90% electronic reporting via the Med Safety App – starting with COVID-19 vaccines. AU-3S is assisting with progress towards and tracking of this monthly target. Working towards improved levels of e-reporting in Nigeria is expected to improve timely access to data, strengthen signal detection and enable easier case follow-ups and/or causality assessments.

Overall, Nigeria has seen a sizeable increase in the level of AEFI reporting relative to previous immunisation campaigns – which has been largely enabled by both healthcare professional and public reporting using the Med Safety App. During Nigeria's measles vaccination campaign in 2019, a reporting rate of about 50 AEFIs per 100,000 doses administered was observed. Since the COVID-19 vaccination rollout in Nigeria commenced in March 2021, the average monthly reporting rate has been about 150 AEFIs per 100,000 doses administered. This represents an approximately 3x increase vs. 'baseline' reporting rate values that Nigeria had anticipated. NAFDAC hopes that this momentum will continue in the years to come and looks forward to e-reporting becoming the primary channel for safety reporting.

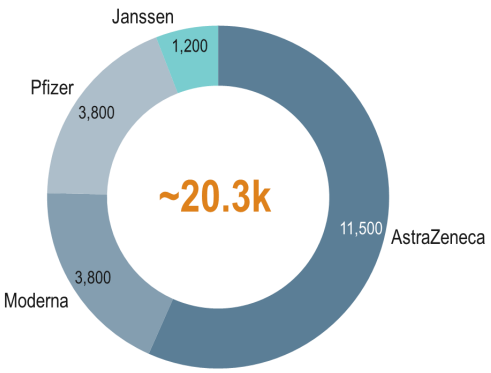
4. Data flow from AU-3S DISD system to the JSM Group

What is the current status?

In the last 3 months significant progress has been made in data flow to the AU-3S DISD system. In the 4 pilot countries, all electronic AEFI data is now routinely flowing directly into the DISD system. The AU-3S team is also working with the countries to ensure that the non-electronic data also goes into the DISD system, and to help promote the use of electronic data collection tools over paper forms.

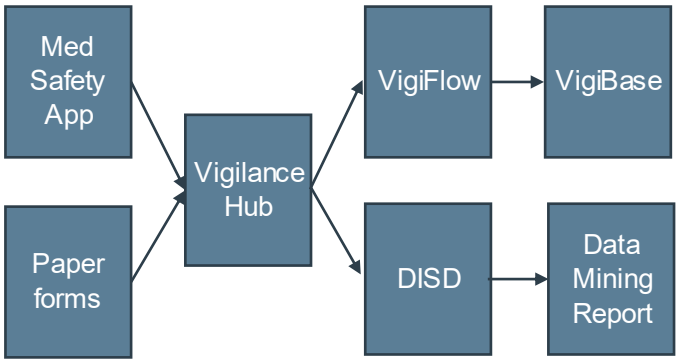
The DISD system now contains data from AstraZeneca, Pfizer, Janssen and Moderna vaccines, and data from Sinopharm and Sputnik is expected in the next few weeks as the vaccines start to be used by the pilot countries. As of 18 November 2021, the DISD system contains more than 20,300 AEFI reports.

Number of AEFI reports in AU-3S's DISD system by vaccine as of 18 November 2021



What is the data flow process?

When an AEFI report is submitted in the Med Safety App the report appears in the back end of the App, the Vigilance Hub. From the Vigilance Hub it goes simultaneously into both the DISD system and VigiFlow, where it is then available for the country to share with the Uppsala Monitoring Centre (UMC) through VigiBase. Any updating to cases or re-coding of the data in the Vigilance Hub will automatically update the case in the DISD system and VigiFlow.



As paper forms are still the most common data collection tool in African countries, the pilot countries are focusing on decentralising data entry into the Vigilance Hub, to reduce the workload at the national level. To do this the regional officers of the NRA and the EPI programme have been provided with access to the Vigilance Hub to enable the entry of data from paper forms. Once this data is in the Vigilance Hub it flows automatically into the DISD system and VigiFlow.

However, data flow from VigiFlow back into Vigilance Hub is not automated. As a result, the AU-3S team has been working with UMC to develop an XML download from VigiFlow that can then be readily uploaded into the Vigilance Hub. This means that any cases which have gone straight into VigiFlow can be added to the Vigilance Hub and thus be included in the DISD system. The Vigilance Hub maintains the VigiFlow case reference numbers, so no duplication of data occurs in either system.

> ***"The AU-3S Vigilance Hub has helped us reduce the need for manual sharing of reports between our NRA and EPI as data can now be accessed at a central point."***
>
> **- Mafora Matlala, Head of PV Unit at SAHPRA**

How is the data in the DISD system analysed?

A fortnightly data mining run is performed in the DISD system. This data mining run analyses all the combined country data and produces a report summarising the number of reports per vaccine-event combination that have occurred for each vaccine. Statistical disproportionality methods are used to indicate vaccine-event combinations where the observed rate of reporting is greater than the expected rate of reporting. The disproportionality analysis is calculated based on the UK background data for vaccines. The UK data will be used until sufficient African data has been collected by AU-3S to determine African specific background rates.

The AU-3S JSM Secretariat (including pilot country representatives) reviews each vaccine-event combination in the data mining report. The JSM Secretariat focuses on events that are not already listed as known possible adverse events from the vaccines. These include unlisted adverse events of special interest (AESIs) and other serious or unexpected events.

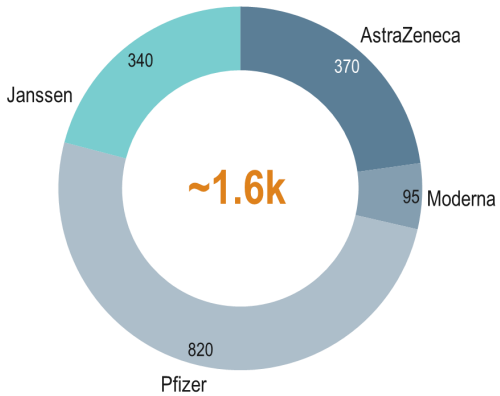
For these events, the JSM Secretariat reviews available information in individual cases and may go back to the national committee of the relevant country to determine if a causality assessment has occurred or if there are any results from case investigations. Based on this information and the number of cases, the JSM Secretariat will determine which vaccine-event combinations to take to the JSM Group for further discussion as a potential signal or an item of interest.

5. Update on AU-3S JSM Group

The JSM Group has met monthly since its inception in April, under the helm of its elected Chair, Prof Hannelie Meyer. Prof Meyer has worked extensively on immunisation-related activities and serves as the current head of the South African Vaccination and Immunisation Centre (SAVIC) at Sefako Makgatho Health Sciences University, and as chair of South Africa's National Immunisation Safety Expert Committee (NISEC).

So far, more than 1,600 different vaccine-event combinations have been recorded from the data in the interim DISD system, across the AstraZeneca, Pfizer, Janssen and Moderna COVID-19 vaccines. These vaccine-event combinations occurred from a total of over 41 million COVID-19 vaccine doses administered by the AU-3S countries. The majority of which were Pfizer, administered in 2 countries, followed by AstraZeneca, administered in 3 countries, then Janssen, administered in 3 countries, and finally Moderna, administered in 1 country. The JSM Secretariat has spent many hours reviewing these cases for information on new or changed risks, and to date, the AU-3S JSM Group has not identified any new signals. For all 3 vaccines, the top 3 AEFIs are the same: headache, pyrexia, and local reaction – these terms, or closely-related ones, are listed in the vaccines' product information.

Number of vaccine-event combinations in AU-3S's DISD system by vaccine as of 18 November 2021



A number of adverse events of special interest (AESIs) have also been reported. The AU-3S JSM Group uses the Brighton Collaboration's list of AESIs, including events that are seen with COVID-19 disease, and those that have a proven or theoretical association with immunisation in general, or a specific and relevant vaccine platform. Cases of these AESIs have been brought to the attention of the AU-3S JSM Group, and further follow-up is being done in-country where required.

Looking ahead, the AU-3S JSM Group is looking at ways to improve data quality, and also how to share its findings more widely. Given the data received and analysed to date, the AU-3S JSM Group would like to emphasise that the benefits of the AstraZeneca, Janssen, Pfizer and Moderna COVID-19 vaccines outweigh the risks of vaccination.

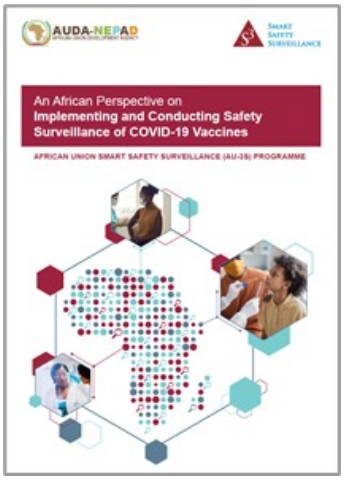
> ***"I have found the AU-3S JSM Group to be very useful for us who were still growing in PV. There's a lot to learn and it's helpful to see what other countries are doing and/or struggling with."***
>
> **- Victoria Sekiti, Medicine Control Officer at SAHPRA**

6. AU-3S capacity strengthening trainings

AU-3S's capacity strengthening series, conducted by the UK Medicines and Healthcare products Regulatory Agency (MHRA), has now been concluded. This is after 5 modules of successful trainings with country representatives from Ethiopia, Ghana, Nigeria, and South Africa. The trainings aimed to strengthen countries' safety surveillance capabilities across a comprehensive range of topics. They are recommended to anyone involved or interested in effectively monitoring the safety of medical products. The training recordings and associated materials have now been made available via the AUDA-NEPAD e-learning portal. To access as a first-time user, select the option titled "Click here to login as guest". Once completed, navigate to the AU-3S Capacity Strengthening page by selecting the appropriate tile.

7. Update on publication on safety surveillance in Africa

AUDA-NEPAD has released a publication that provides a series of reflections and guidance for successfully implementing safety surveillance in the African context. "An African Perspective on Implementing and Conducting Safety Surveillance of COVID-19 Vaccines" can be found in the 'Research Publications' section of the AUDA-NEPAD website (link) or via the 'Publications' section of the AU-3S website. The publication explores the importance of pharmacovigilance for COVID-19 vaccines, considering challenges in the African context. Recommendations for successful safety surveillance implementation are provided, with helpful tools, materials and initiatives outlined where relevant.



> ***"I believe the learnings, best practices, relevant tools, and materials developed under the AU-3S Programme, and recommendations provided in this publication will go a long way to assist African countries to successfully implement safety surveillance on the continent."***
>
> **- Margareth Sigonda, Head African Medicines Regulatory Harmonisation Initiative (AMRH)**

8. Links to additional safety-related resources

See what our team and JSM Group experts are reading! Relevant links to COVID-19 vaccines safety related resources on key topics over the past few months can be found below.

Guillain-Barré Syndrome (GBS)

WHO, August 2021 – WHO GACVS on GBS and Janssen + AstraZeneca vaccines: Link

Thrombosis / Thrombocytopenia

- **EMA, August 2021** Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 5 August 2021. COVID-19 Vaccine Janssen: update on safety issues. PRAC recommended updating the product information of COVID-19 Vaccine Janssen to include immune thrombocytopenia as an adverse reaction. Accessible: Link

COVID-19 variants

- **Reuters, August 2021**
    - South African study shows high COVID protection from J&J shot. Accessible: Link

Mixing of vaccines

- **Reuters, August 2021**
    - Combining AstraZeneca and mRNA COVID-19 vaccines is effective - Danish study. Accessible: Link

General / Other

- **August 2021**
- Breakthrough infections – Janssen Link
- Breakthrough infections – USA Link
- COVID-19 mRNA vaccines blunt breakthrough infection severity – USA Link
- Patients with suspected allergic reactions to COVID-19 vaccines can be safely re-vaccinated after diagnostic work-up Link
- **September 2021**
- FDA grants full approval to the Pfizer-BioNTech COVID-19 vaccine Link
- Long COVID is significantly reduced by double vaccination Link
- Risk of blood clots after vaccination not as high as the risk from COVID-19 Link
- Heart problem more common after COVID-19 than after vaccination Link
- 3rd COVID-19 vaccine dose for severely immunosuppressed over 12s Link
- Single dose of Janssen COVID-19 vaccine elicits sustained antibody responses with substantial increase following late boosting Link
- A nationwide study from Israel shows waning immunity of the Pfizer COVID-19 vaccine Link
- EU looking into new possible side effects of mRNA COVID-19 shots Link
- PRAC link dizziness and tinnitus to Janssen COVID-19 Vaccine Link
- PRAC continues to closely review reports of Guillain-Barré syndrome with AstraZeneca COVID-19 vaccine Link
- No causal association between COVID-19 vaccines and menstrual disorders Link
- **October 2021**
- Pfizer: vaccine effectiveness against new COVID-19 cases and complications of breakthrough cases Link
- AstraZeneca & Pfizer: duration of protection of COVID-19 vaccines against clinical disease Link
- CDC recommends Pfizer COVID-19 vaccine booster shot Link
- Venous thromboembolism (VTE) and immune thrombocytopenia (ITP) added as side-effects of Janssen vaccine Link
- Approval of Sinopharm COVID-19 vaccine for children aged 3 – 11 Link
- **November 2021**
- PRAC is assessing further data on risk of myocarditis & pericarditis with mRNA vaccines Link

The African Union Development Agency - NEPAD (AUDA-NEPAD) was established in 2018 as part of the global reforms geared at improving the African Union's impact and operational efficiency

The African Union's Smart Safety Surveillance (AU-3S) programme was launched in 2020, with the long-term goal of strengthening the safety surveillance of medical products across Africa

Spotlight: The Smart Safety Surveillance Newsletter in Africa is a newsletter published by AU-3S which provides an update on safety surveillance in Africa and key progress made by the AU-3S programme

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