Reports of Suspected Adverse Reaction to COVID-19 Vaccines (01 March to 02 May 2021)

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About the report

- A summary is presented below of all received suspected adverse reaction reports following COVID-19 vaccination from 01 March 2021, the date when the first vaccine became available, up to 02 May 2021.
- Two (2) vaccines under Emergency Use Authorization (EUA) are currently being used in the vaccination program: the SARS-CoV-2 Vaccine (Vero Cell) Inactivated, [CoronaVac] and COVID-19 Vaccine AstraZeneca. Sputnik V Gam-COVID-Vac COVID-19 Vaccine will also be use in the next coming days/weeks.
- Data are based on VigiFlow, the national database of adverse reactions in the Philippines. It includes reports from hospitals, various epidemiology surveillance units (ESUs) of the Department of Health (DOH), patients/consumers, and EUA holders.
- Symptoms or diseases that occur after vaccination are reported if there is a *suspicion* of a possible link. However, it cannot be assumed that there is a causal relationship between the suspected adverse reaction and the vaccine.
- This report contains all suspected adverse reactions regardless of any possible causal relationship.
- Additional information may become available in individual case reports at any time which may change the assessment and figures presented.
- Adverse reaction reports are necessary for the safety assessment of the vaccines, making sure that the benefits always outweigh the risks.
- Reports are constantly reviewed and monitored for the possible emergence/identification of unknown adverse reactions also known as signal. If a signal is identified, investigations, regulatory actions, and timely communication is performed by the FDA.
- A weekly report is published to summarize reported adverse reactions to the COVID-19 vaccines.

Summary

This report is based on an assessment of adverse reaction reports received by 02 May 2021. As per benefit-risk assessment, these reports do not provide a basis for revising the current recommendations regarding use of the COVID-19 vaccines.

The reports received have no indications of new safety concern. The reported reactions are generally in line with what is described in the product information and labels. Most of the reports are minor adverse reactions which include body pain, chills, fatigue, fever, headache, nausea, and pain in the injection sites. These usually appear on the first or second day of vaccination and may last for 2-3 days. Most people tolerate these adverse reactions while others experience greater discomfort.

CoronaVac is used for elderly population aged 60 years old and above. The benefit on its use outweighs the risks considering the increasing need to protect the elderly population despite the limited availability of vaccines. The FDA posed no objection on its use in elderly.

Considering the post-authorization experience on the use of COVID-19 vaccine AstraZeneca, information on the very rare and serious adverse events of thrombosis and thrombocytopenia, and in some cases accompanied by bleeding has been revised under the special warning and precautions for use. The vaccine is now contraindicated for patients who have experienced major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine.

COVID-19 vaccines with Emergency Use Authorization in the Philippines

At present, there are six (6) COVID-19 vaccines granted emergency use authorization:

- Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)
- ChAdOx1-S [recombinant] (COVID-19 Vaccine AstraZeneca)
- SARS-CoV-2 Vaccine (Vero Cell), Inactivated (CoronaVac)
- Gam-COVID-Vac (Sputnik V)
- Ad26.COV2-S [recombinant] (Janssen COVID-19 Vaccine)
- Whole Virion Inactivated Corona Virus (Covaxin)

Various vaccine platforms have been approved for use in the Philippines. Pfizer-BioNTech COVID-19 vaccine is a mRNA vaccine; COVID-19 Vaccine AstraZeneca and Janssen COVID-19 Vaccine are non-replicating viral vector vaccines, Sputnik V uses the same technology having two (2) different (dose) components of viral vectors; and CoronaVac and Covaxin are inactivated vaccines. All are administered in two doses within an interval of a few weeks except for Janssen COVID-19 Vaccine which is administered as a single-dose.

Statistics regarding reports of suspected adverse reactions

As of 02 May 2021, more than 1.6 million individuals have received their first dose of COVID-19 vaccines either CoronaVac or COVID-19 vaccine AstraZeneca. Almost 290,000 individuals have received their second dose of CoronaVac. An aggregate of 29,925 suspected adverse reaction reports were received, evaluated, and analyzed by the FDA.

Demographics

The figures provide a descriptive overview of the population reporting adverse reactions from COVID-19 vaccines. Figure 1. and Figure 2. shows the distribution of reports by age and gender.

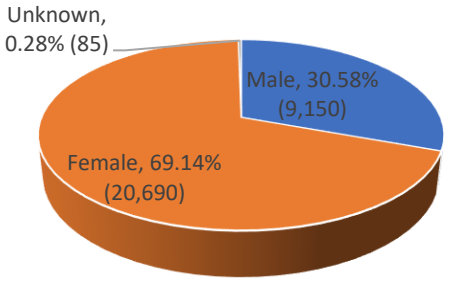

Figure 1. Report distribution by gender

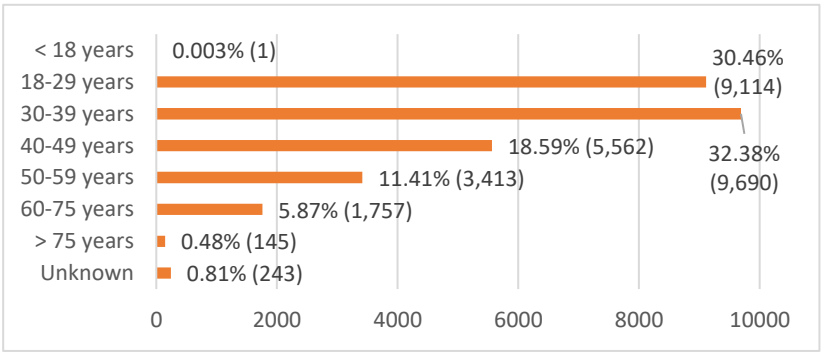

Figure 2. Report distribution by age

The early phase of the vaccination program is intended for the frontline health workers, thus, the high number in the female and younger population might be associated with the data that our health system is dominated by female (75%) and young adults under the age of 35 (65%).[1] An increasing number of reports from the age group 40 years and above were observed in the last few weeks. This may be attributed to the coverage of priority groups of senior citizen and individuals with comorbidities.

[1] *Human Resource for Health in the Time of the COVID-19 Pandemic: Does the Philippines Have Enough?* https://www.drdf.org.ph/sites/default/files/pdf/COVID-19-Research-Brief-08.pdf

Distribution of reports of adverse reactions for each vaccine

Data shown below are cumulative reports from the start of the vaccination program on 01 March 2021 up until 02 May 2021.

Table 1. Distribution of reports of adverse reactions for each vaccine

Vaccine	Number vaccinated with first dose[b]	Number vaccinated with second dose[b]	Total number of reports[a]	Reports of non-serious events	Reports of serious events
CoronaVac	1,131,187	289,541	10,523	10,321	202
AstraZeneca	527,477	0	19,402	19,161	241
TOTAL	**1,658,664**	**289,541**	**29,925**	**29.484**	**441**

Data source: [a]VigiFlow, [b]NVOC daily report as 6PM, 25 April 2021
Notes: Additional information may become available in individual cases which may change the figures presented
[c]Data concerning various vaccines are not directly comparable. COVID-19 vaccines profile varies, they have not been used for equal periods of time and they have been administered to number of people with different profiles including various age and sex.

Reports of suspected serious adverse reaction

Adverse reactions experienced after vaccination are considered serious when it resulted to any of the following criteria:

- In-patient hospitalization/prolongation of existing hospitalization
- Significant disability/incapacity
- Life-threatening (e.g. anaphylaxis) and death
- Birth defect or congenital malformations
- Considered to be medically important event

Hypersensitivity including severe allergic reactions
Severe allergic reactions have been reported on the use of COVID-19 vaccines including CoronaVac and AstraZeneca. It is very rare (0.002% for CoronaVac and 0.001% for AstraZeneca from local data) and occurs only in a few vaccinated individuals. It typically occurs in people with a history of severe vaccine reactions. Severe allergic reactions generally occur soon after vaccination and is usually managed with Epinephrine in combination with other medicines. Thus, vaccinees are observed for at least 15 minutes after receiving the vaccine. Epinephrine is readily available in all vaccination sites.

Hypersensitivity including severe allergic reactions to COVID-19 vaccine AstraZeneca have been identified to be biologically possible. AstraZeneca revised the labeling of their product to reflect the changes that the second dose of the vaccine should not be given to those who have experienced a severe hypersensitivity reaction to the first dose of COVID-19 vaccine AstraZeneca.

Increased blood pressure
Blood pressure increased has been continuously reported as the top adverse reaction to inactivated vaccine and still included as one of the top ten reported reactions to viral vector vaccine. Monitoring blood pressure is part of the screening processes for COVID-19 vaccination program in the Philippines.

According to Sison, Divinagracia & Nailes (2019), the latest data on prevalence of hypertension is 28%; 9% of which are unaware that they have hypertension. The BP control rate of 20% may be attributed to the increasing reports of blood pressure increased. Anxiety during vaccination may also cause elevation in blood pressure levels.[2]

An updated joint statement from the Philippine Heart Association and Philippine Society of Hypertension on elevated blood pressure readings during COVID-19 vaccination was released last 14 April 2021 revising their recommendations on the screening process, observation period, and other information related to COVID-19 vaccination.

[2] *Immunization stress-related response (ISRR) - A synopsis*
https://www.who.int/immunization/sage/meetings/2019/april/2_A_synopsis_of_ISRR_Draft_SAGE.PDF?ua=1

Thrombocytopenia and coagulation disorders
The European Medicines Agency's (EMA) safety committee had concluded that unusual blood clots with low platelets should be listed as a very rare side effect of COVID-19 vaccine AstraZeneca. AstraZeneca revised their label reflecting the information on thrombocytopenia and coagulation disorders.

COVID-19 Vaccine AstraZeneca is now contraindicated to patients who have experienced major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine.

Information on thrombocytopenia and coagulation disorders were discussed in the label under special warnings and precautions for use.

Since this is a very rare event, the benefits of the vaccine continue to outweigh the known and potential risks. Considering the new safety information as well as the points and recommendations raised by the World Health Organization, and various independent expert panels, the FDA recommended the continuation of inoculation of the COVID-19 vaccine AstraZeneca.

Reports involving death
As of 02 May 2021, 61 fatal events were received. Most of these events occurred in people with multiple existing comorbidities. There were cases of confirmed COVID-19 infections leading to severe cases with fatal outcome. Another cause of deaths was cardiovascular disease which belongs to the three leading causes of death in the Philippines (PSA 2020). An independent committee assessed 26 of these events as coincidental events or not related to the vaccine, two (2) cases were indeterminate, and two (2) were unclassifiable. Other cases are still under investigation and are continuously being reviewed.

To date, there were no reports of fatal events directly associated with the use of the vaccines currently in use.

Confirmed COVID-19 infections
Reports included 93 confirmed COVID-19 infections. Most of the reported infections were asymptomatic cases. There were 12 severe cases with a fatal outcome which, upon assessment, were not related to the use of the vaccine. These cases were attributable to the number of daily COVID-19 infections.

The vaccines currently being used in the COVID-19 vaccination program are non-replicating viral vector and inactivated vaccines. It does not contain any live virus and does not cause COVID-19 infection in vaccine recipients.

Number of suspected adverse reactions per category

A total of 29,952 case reports containing 74,157 suspected adverse reactions were received from the start of the vaccination program. Multiple suspected adverse reactions may be reported in a single case. Suspected adverse reactions were coded using the Medical

Dictionary for Regulatory Activities (MedDRA) terminology to allow international comparison of reports.

The data presented below are categorized by System Organ Class (SOC), the highest in the hierarchy of MedDRA. They are grouped by manifestation site (e.g. gastrointestinal, cardiac) and etiology (e.g. infections, examinations).

Reactions to inactivated vaccine

- CoronaVac

Classification	Number of suspected reactions
General symptoms & reactions in the administration site *E.g. Pain and reaction in the injection site, chills, discomfort*	4,213
Cardiac symptoms *E.g. Palpitations, bradycardia*	387
Ear symptoms *E.g. Ear swelling, vertigo*	13
Examinations *E.g. Increased blood pressure, increased heart rate*	3,099
Eye symptoms *E.g. Eye itchiness, blurred vision*	98
Gastrointestinal symptoms *E.g. Abdominal pain, diarrhea, nausea, vomiting*	1,194
Hepatobiliary symptoms *E.g. Jaundice*	1
Immune system symptoms *E.g. Allergic reactions*	98
Infections *E.g. Cold symptoms*	423
Metabolism and nutrition-related symptoms *E.g. Decreased appetite*	57
Musculoskeletal symptoms *E.g. Back pain, joint pain, pain in extremities*	795
Neurological symptoms *E.g. Dizziness, headache, syncope*	3,350
Procedural symptoms *E.g. Procedural hypertension, vaccination adverse reaction*	337
Psychiatric symptoms *E.g. Feeling anxious*	39
Renal and urinary symptoms *E.g. Urine coloring yellow, urine frequency*	9
Reproductive symptoms *E.g. Vaginal bleeding, vaginal spotting*	6
Respiratory symptoms *E.g. Cough, nasal congestion, throat irritation*	1,124
Skin symptoms *E.g. Cold sweat, rash, redness*	1,822
Symptoms in blood and lymphatic system *E.g. Pain in the lymph nodes*	18
Vascular symptoms *E.g. Flushes, low blood pressure*	622

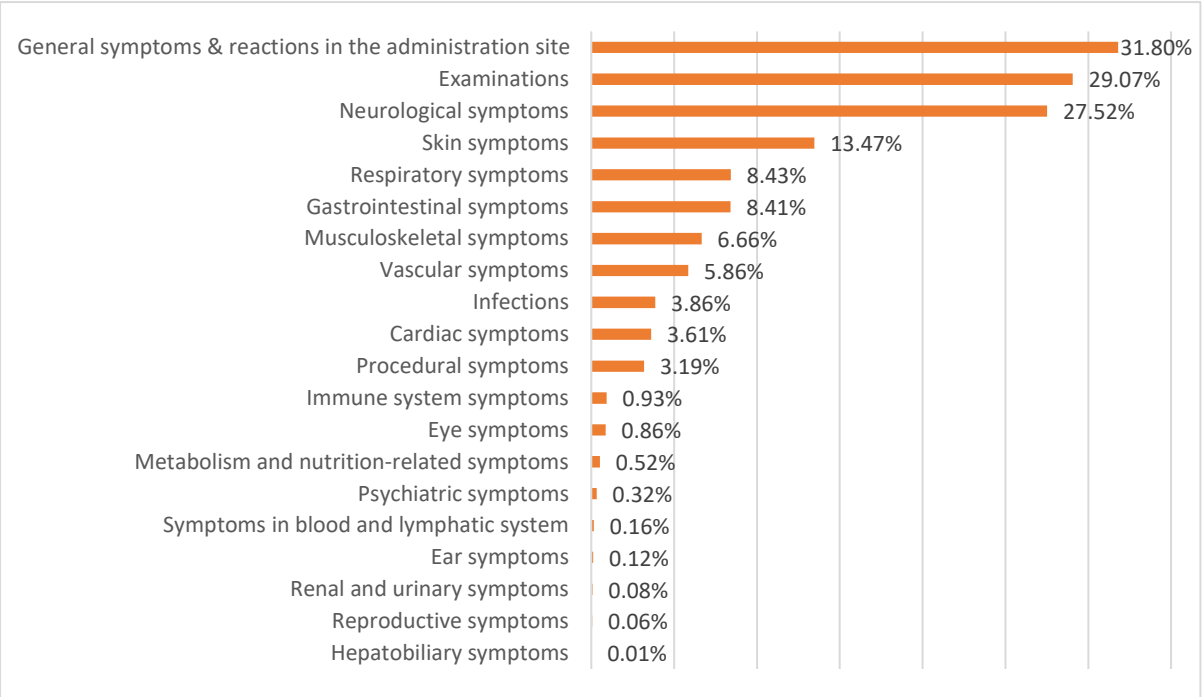

Figure 3. Suspected adverse reaction distribution by SOC for inactivated vaccine

As shown in Figure 3, the SOC containing the greatest number of events were general symptoms and reactions in the administration site (4,213), followed by neurological symptoms (3,350), examinations (3,099), skin symptoms (1,822), gastrointestinal symptoms (1,194), respiratory symptoms (1,124), musculoskeletal symptoms (795), vascular symptoms (622), cardiac symptoms (387) and infections (423).

The top reported events are:

- blood pressure increased (28.58%)
- headache (16.62%)
- vaccination/injection site pain (16.00%)
- dizziness (9.21%)
- rash (8.44%)
- pyrexia (7.99%)
- pruritus (5.28%)
- nausea (4.18%)
- hypertension (3.87%)
- fatigue (3.78%)

Reactions to non-replicating viral vector vaccine

- COVID-19 vaccine AstraZeneca

Classification	Number of suspected reactions
General symptoms & reactions in the administration site *E.g. Pain and reaction in the injection site, chills, discomfort*	26,569
Cardiac symptoms *E.g. Palpitations, bradycardia*	337
Ear symptoms *E.g. Ear swelling, vertigo*	23

Examinations *E.g. Increased blood pressure, increased heart rate*	1,652
Eye symptoms *E.g. Eye itchiness, blurred vision*	251
Gastrointestinal symptoms *E.g. Abdominal pain, diarrhea, nausea, vomiting*	2,753
Hepatobiliary symptoms *E.g. Jaundice*	1
Immune system symptoms *E.g. Allergic reactions*	163
Infections *E.g. Cold symptoms*	696
Metabolism and nutrition-related symptoms *E.g. Decreased appetite*	395
Musculoskeletal symptoms *E.g. Back pain, joint pain, pain in extremities*	6,607
Neurological symptoms *E.g. Dizziness, headache, syncope*	10,436
Procedural symptoms *E.g. Procedural hypertension, vaccination adverse reaction*	3,123
Psychiatric symptoms *E.g. Feeling anxious*	34
Renal and urinary symptoms *E.g. Urine coloring yellow, urine frequency*	6
Reproductive symptoms *E.g. Vaginal bleeding, vaginal spotting*	14
Respiratory symptoms *E.g. Cough, nasal congestion, throat irritation*	1,186
Skin symptoms *E.g. Cold sweat, rash, redness*	1,741
Symptoms in blood and lymphatic system *E.g. Pain in the lymph nodes*	29
Vascular symptoms *E.g. Flushes, low blood pressure*	436

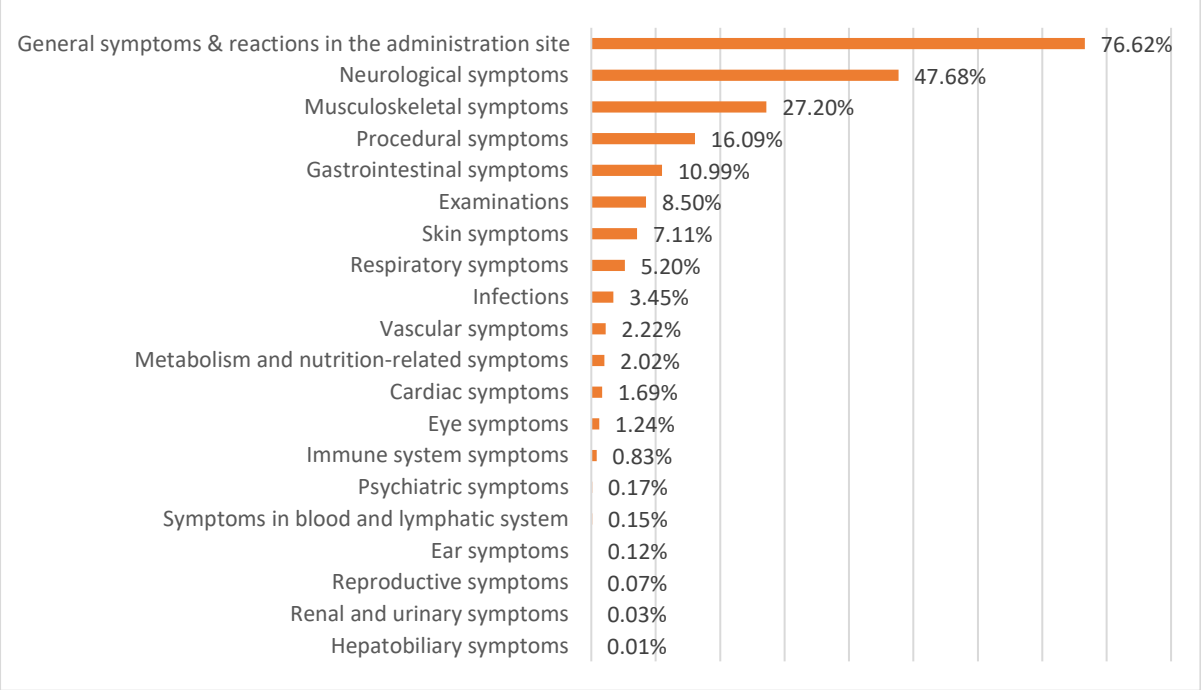

Figure 4. Suspected adverse reaction distribution by SOC for viral vector vaccine

As shown in Figure 4, the SOC containing the greatest number of events were General symptoms and reactions in the administration site (26,569), followed by neurological symptoms (10,436), musculoskeletal symptoms (6,607), procedural symptoms (3,123), gastrointestinal symptoms (2,753), skin symptoms (1,741), examinations (1,652) and respiratory symptoms (1,186).

The top reported events are:

- pyrexia (47.23%)
- headache (41.82%)
- malaise (27.98%)
- vaccination/injection site pain (27.01%)
- myalgia (21.18%)
- chills (20.02%)
- fatigue (15.02%)
- arthralgia (10.49%)
- blood pressure increased (8.18%)
- pain (6.94%)

Outcome of suspected adverse reactions

The outcome of cases of suspected adverse reactions to COVID-19 vaccines is shown in Figure 5. Overall, most of the reported cases have *recovered/resolved*, although there were few cases who have *recovered but with sequalae*. Almost 10% of cases are *recovering/resolving* while less than 1% have *not recovered/not resolved* at the time of reporting. A proportion of 0.20% were reported with fatal outcome as discussed in the section Reports involving death.

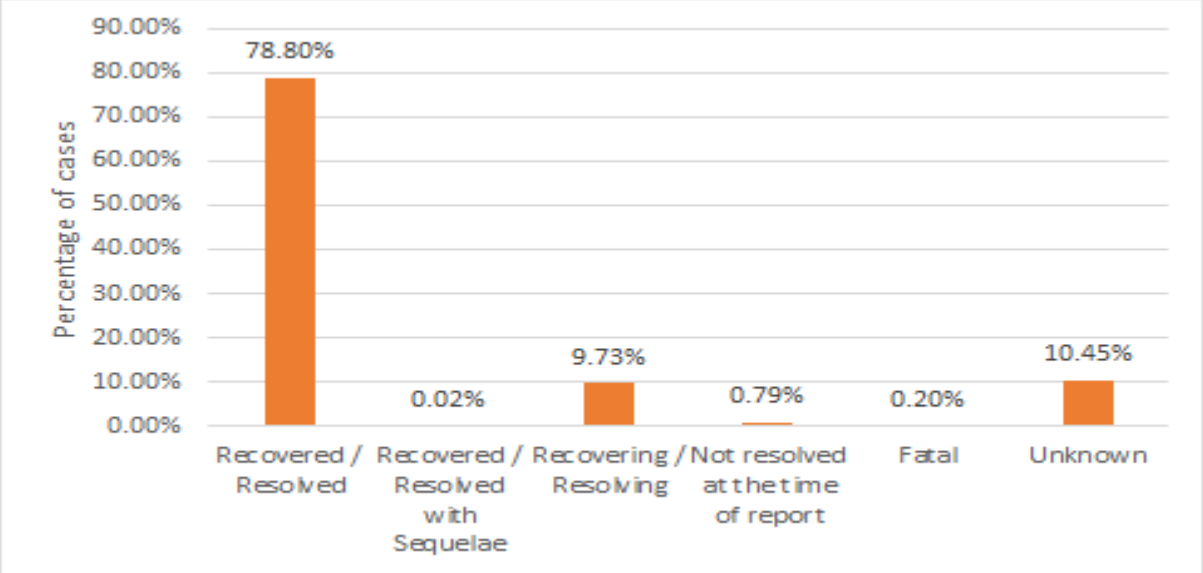

Figure 5. Case outcome

Reporting of suspected adverse reactions following vaccination

Individuals who received their COVID-19 vaccination shots can report any suspected adverse reaction to any of the following:

- Immunization site where you were vaccinated
- Directly to the vaccine manufacturer or emergency use authorization holder
    - Sinovac
    - AstraZeneca
- FDA online reporting system

Kindly **report only to one** of the above to avoid duplication of reports.