South African Health Products Regulatory Authority (SAHPRA)

Chief Executive Officer: Dr Boitumelo Semete-Makokotlela

By email: Boitumelo.Semete@sahpra.org.za

25 October 2022

Dear Dr Semete-Makokotlela,

Referral of matter to SAHPRA for review of Sisonke's compliance with the Medicines Act:

1. We refer to the above matter, our correspondence, and meetings in 2021 and 2022.

2. As you are aware, we lodged several access to information requests related to the allocation of Covid-19 vaccines during a time of scarcity and in a pandemic under the Sisonke study and programme.[1]

3. We wish to thank you and your offices for your cooperation in responding to our request (your ref: 'HJI PAIA Request').[2]

4. It is common cause that on 17 February 2021, the Sisonke study commenced.

    a. The Sisonke study was approved as a 'phase 3B clinical trial' in a pandemic and it saved many health workers' lives. It also marked the beginning of South Africa's Covid-19 national vaccine programme.
    b. It provided the Johnson & Johnson vaccine to healthcare workers at a number of research sites across South Africa when the country had no immediate and alternative supplies of vaccines (after the decision by the South African government to pause the roll out of the Astra-Zeneca vaccine).
    c. On 16 May 2021, when announcing details about the second phase of the national vaccine rollout, the then Minister of Health, Dr Zweli Mkhize announced that 'left-over' vaccines from the Sisonke study will not form part of the national vaccine roll-out, but that it will be used by the South African Medical Research Council (SAMRC) "to conduct important studies and programmes that will help us to understand how the vaccines work for population groups such as persons living with HIV and other co-morbidities,

[1] Open-label, Single-arm Phase 3B Implementation Study to Monitor the Effectiveness of the Single-dose Ad26.COV2. S COVID-19 Vaccine Among Health Care Workers in South Africa (VAC31518COV3012). Subsequently amended, with SAHPRA approval.

[2] HJI submitted formal requests for access to information under the Promotion of Access to Information Act (PAIA). PAIA requests were lodged with SAHPRA (information was furnished by early 2022); the SAMRC; the National Departments of Health (NDoH) and Sports, Arts and Culture (DSAC).

elite athletes, pregnant and lactating women and other special groups".[3] (emphasis added).

5. The scope of the Sisonke programme was then reported to have been widened to provide for the early vaccination of certain so-called *"elite athletes"* ahead of their respective age cohorts, commencing with the Olympic team travelling for the Tokyo Olympics (which SAHPRA approved).

6. Through access to information requests we have established from the SAMRC's response (see below), that other athletes (from rugby, cricket, and soccer teams) as well as government officials from the Department of International Relations and Cooperation (DIRCO) were also included in this early vaccination 'group', where they received left over product.[4] The scientific, ethical, and public health rationale for the inclusion of these groups (athletes and DIRCO officials) in the Sisonke programme / study remains unknown and is of particular concern because:

    a. to date, despite lodging multiple access to information requests, the *rationale* to include them, and the *approval* for same, has not been fully shared (see below); and
    b. their vaccination occurred during and at a time of gross global vaccine inequity where there was also domestic scarcity.

7. In respect of our request for information from SAHPRA, thankfully your offices responded and confirmed that it provided approval for the vaccination of the 'Olympic squad' (athletes and support staff) for the purposes of participating in the Olympic Games in Tokyo. *(See SAHPRA letter to HJI dated 15 February 2022* ***Annexure A1*** *in the annexure folder* ***Annex Bundle A*** *to this lette*r).

    a. The aforementioned letter states:

    'Please find the list of categories of athletes duly authorised by SAHPRA for vaccination as follows:

    - *Athletes*
    - *Coaches*
    - *Physiotherapists*
    - *Doctors*
    - *Other specific technical/essential members of the support team that accompanies the athletes.*

[3] "The former Health Minister, Dr Zweli Mkhize officially launched Phase 2 of the country's vaccination campaign." 16 May 2021, available https://youtu.be/IQkRcSUdSwA (at 4:20).
[4] We established this by submitting multiple requests for information to several stakeholders including formal requests for access to information under the Promotion of Access to Information Act (PAIA). PAIA requests were made to SAHPRA (information was furnished by early 2022); the SAMRC; the National Departments of Health (NDoH) and Sports, Arts and Culture (DSAC).

SAHPRA is not aware, nor did it authorise any additional categories of persons to be vaccinated under the Sisonke Programme'. (emphasis added)

b. From SAHPRA's response dated 15 December 2021 to the HJI (*Reference: **Annexure A2a***) we were unable to locate in the annexures regulatory approval for **any other** categories of athletes / sports people / government officials. The annexures thereto include:
   i. the 'eligibility waiver' request from the SAMRC; (***Annexure A2b***);
   ii. National Department of Health letter of support; (***Annexure A2c***);
   iii. redacted email thread of members of the SAHPRA Clinical Trials Unit (***Annexure A2d***); and
   iv. SAHPRA's response to the SAMRC (***Annexure A2e***).

8. The SAMRC, NDoH and DSAC did not initially respond to HJI's access to information requests and the subsequent internal appeals under PAIA, thus, on 7 April 2022, the HJI launched an application in the High Court of South Africa (Case no 19342/2022) citing the SAMRC, NDoH and DSAC as Respondents. *Reference: **Annexure B** (HJI Founding Affidavit).*

   a. The HJI, acting in the public interest (to ensure proper and public health-based decision making around the allocation of scare vaccine supplies) sought to establish how, when and on whose authority the vaccination of several groups (athletes and sports officials) - ahead of their age cohorts - took place in a pandemic and why. Had the information (which constitutes a very simple request) been shared and provided at the outset by the SAMRC, NDoH and DSAC, then the application could have been avoided.

9. Following the launch of the court application referred to above, the SAMRC wrote to us, as follows:

   a. SAMRC Letter to HJI, 3 May 2022 (***Annexure C1***) with Annexures (***Annexure Bundle C2***):
      i. ***Annexure C2d*** indicates that "*1000 vaccines for sports people and accompanying staff"* and *"*320" as a *"DIRCO allocation"* under Sisonke were used, and as follows:

         - "Sportsperson and accompanying staff allocation (no spouses were allocated vaccines): 1000
            - Olympians: 428
            - Para-Olympians: 88
            - ***Rugby: 286***
            - ***Cricket: 105***
            - ***Soccer: 93***
         - ***DIRCO allocation: 320***
         - Health Care Worker mop-up: 8758". (emphasis added)

Note: Our understanding is that SAHPRA only approved vaccinating the **Olympic squad** under the Sisonke programme as a special consideration. In our correspondence with the SAMRC, we also requested the details of the sporting codes that benefited from early vaccination, but this was not shared with us (including details on race, gender, age, disability, occupation, international or domestic teams, etc).

b. SAMRC Letter to HJI, 15 June 2022 (***Annexure C3***):

   i. The SAMRC requested that HJI withdraw the matter on the basis that they have provided the information that HJI required and also proposed that we have a "round table conference" to discuss this matter. Our legal representatives have attempted to arrange a discussion with the SAMRC, but they have not responded.
   ii. The SAMRC attached various ethics committee approvals related to the Sisonke *study protocol* changes, and also SAHPRA's waiver of the eligibility criteria requirements, dated 19 May 2021 (which relates to the Olympic squad/team) (see ***Annexure bundle C2*** and ***Annexures C2e*** in particular).

10. We received answering affidavits from the NDoH (29 July 2022 – ***Annexure D***) and DSAC (14 July 2022 – ***Annexure E***).

a. Both the NDoH and DSAC have stated on oath that they supported the early vaccination of the Olympic squad at the request of the South African Sports Confederation and Olympic Committee (SASCOC)[5], which request SAHPRA subsequently approved, and they claimed that they have no knowledge of the circumstances related to the request to vaccinate other sports teams / officials and / or government officials.
b. Attached to the respective NDoH and DSAC Answering Affidavits, are letters from the Director-General of Health to SAHPRA (dated 18 May 2021 – ***Annexure D***) and from SASCOC to the Director-General of DSAC (dated 3 May 2022 – ***Annexure E***).
   No other letters are attached.
c. After several months of trying to collate information on what transpired in the allocation of vaccines in and via the Sisonke study / programme, especially to meet equity considerations in a pandemic, we are of the view that based on all the information provided to the HJI thus far, by SAHPRA, the SAMRC, DSAC and NDoH - that none of the relevant institutions / departments / bodies can point us to the relevant outstanding requests and regulatory approvals, and thus, it is likely that such approvals were not obtained / do not exist. If so, it behoves SAHPRA to establish *inter alia* why not, and to take the necessary remedial measures.
d. This is because it is our understanding from SAHPRA's correspondence to the HJI, that at the very least, SAHPRA approval was required for the use

[5] The NDoH noted that the Department was approached by the DSAC, who received a request from SASCOC.

of ‘left-over investigational product from the Sisonke 1 trial’ (see SAHPRA letter to the HJI dated 15 December 2021, ***Annexure A2a***).

11. Based on the scope, functions, and duties of SAHPRA[6] - including being the regulatory body entrusted with ensuring ‘good and sound’ practice in clinical trials and studies - we are of the view that your offices should consider all the information before it, and all relevant supporting documentation (including the Annexures to this letter) to establish the true state of affairs; and whether *inter alia* the provisions of the Medicines Act; and relevant sections of the *South African Good Clinical Practice: Clinical Trial Guidelines (2020)* have been complied with.

12. We believe that such a review should also include interviews with all relevant personnel and stakeholders. The outcome of the review should also be placed in the public domain in the interests of transparency and accountability. Here, we note that *accountability, transparency, and responsiveness* are key values and indicators included in the WHO’s *Global Benchmarking Tool*[7] and are also reflected in SAHPRA’s ‘Core Values’, including in its goals for attaining *Maturity Level 4 (*now that it has successfully attained *Maturity Level 3* status).[8]

13. In reviewing this matter, we trust that SAHPRA will also consider strengthening applicable clinical trial frameworks / best practices going forward - including developing / amending such *Guidelines* for the future, drawing on the lessons of the Covid-19 pandemic and also from the circumstances of the Sisonke study / programme.

14. In this respect, we recommend a consideration of at least the following issues and concerns:

    a. Including equity as a key factor in allocation frameworks in any trial, study (similar), or for any (clinically approved and recommended) left-over investigational product during times of global and local scarcity, and for any future pandemics, including requiring approval from an ethics committee for the re-direction of any such products.
    b. Consideration of how best to avoid the potential of undue influence by well-resourced sporting codes and / or government departments and / or other bodies and individuals – where such influence is often directed at researchers as well as regulatory bodies – in other words, providing guidelines on how to record, declare and manage actual and perceived conflicts of interest and / or any undue influence, particularly in times of a public health crisis.

[6] To ‘ensure that compliance with existing legislation is being promoted and controlled through a process of active inspection and investigation; and ensure that clinical trial protocols are being assessed according to prescr bed ethical and professional criteria and defined standards’ (Section 2B(1) of the Medicines and Related Substances Act, Act 101 of 1965, as amended).
[7] WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems of medical products, revision VI. Geneva: World Health Organization; 2021.
[8] SAHPRA Annual report 2020-2021, Available https://www.sahpra.org.za/wp-content/uploads/2021/10/SAHPRA-202021-Annual-Report.pdf and SAHPRA Annual Performance Plan 2020-2021, Available https://www.sahpra.org.za/wp-content/uploads/2022/03/SAHPRA-Annual-Performance-Plan-2020-2021.pdf

c. Ensuring that there is a robust and pandemic worthy 'Research/er Code of Ethical Conduct' located within the current '*South African Good Clinical Practice: Clinical Trial Guidelines* (2020)' that at least considers and includes:

    i. The role of the research community, research, statutory and regulatory bodies in respecting and promoting the important role of civil society organisations in asking questions in the public interest about decisions underpinning clinical studies/ trials / programmes and outcomes.
    ii. Proactive disclosure standards and rules, so that going forward there is greater transparency and accountability on the part of all researchers and clinical trial leads (if civil society organisations are always required to file legal papers to obtain related details and copies of regulatory approval decisions or are discouraged at times through bullying tactics (the details of which we can share with your offices) to refrain from asking any questions, that is not ideal). Such measures will also help to foster public trust in future research studies/trial and in related decision making, and ideally should be an ethical requirement too.

ci. Mandate the proactive and public disclosure in real time of trial / study applications, review status, approvals, requests for waivers or amendments including for eligibility and even for left over investigational product. This should include disclosure of all requests made by third parties to the research teams / leads and even to SAHPRA – even if such a request is from a political party, pharmaceutical company, medical association, sporting body - such as SASCOC, Cricket SA, the South African Football Association, SA Rugby, trade unions, government departments, etc.). A public registry would not only support transparency and accountability aspirations but would also increase public trust in SAHPRA decision making processes and in the project of science by evidence.

We look forward to hearing from your offices shortly on the next steps. If you have any queries or require any additional information, please do not hesitate to contact us.

Yours sincerely,

[redacted] [redacted]

Fatima Hassan and Dr Marlise Richter

Health Justice Initiative
marlise@healthjusticeinitiative.org.za

Attachments: *https://bit.ly/3TCt2FK (special e-folder of all annexures referred to above, for SAHPRA use)*