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**TO: DDG: CHIEF OF OPERATIONS**  
**CHIEF DIRECTORS**  
**DIRECTORS**  
**HEADS OF INSTITUTIONS**  
**HEAD OF HEALTH: CITY OF CAPE TOWN**

**CIRCULAR H112 /2022**

**AMENDED THRESHOLD FOR REFLEX LABORATORY-BASED CRYPTOCOCCAL ANTIGEN SCREENING FOR HIV-  
POSITIVE PATIENTS FROM CD4 <100 cells/ $\mu$ l TO CD4  $\leq$ 200 cells/ $\mu$ l**

**Background**

Cryptococcal meningitis (CM), which is a serious opportunistic fungal infection, is the second leading cause of mortality in people living with HIV (PLHIV). The presence of cryptococcal antigen (CrAg) in blood is highly predictive of CM and mortality, and screening at-risk PLHIV for CrAg offers an opportunity to detect cryptococcal disease early and start appropriate antifungal treatment. Since 2016, South Africa has implemented reflex CrAg screening for any PLHIV with a CD4 count < 100 cells/ $\mu$ L. However, cryptococcal antigenaemia also occurs in a proportion of individuals with CD4 counts between 100-200 cells/ $\mu$ L, and the World Health Organization (WHO) now conditionally recommends CrAg screening in this range. In November 2020, a National survey was conducted to assess CrAg prevalence, number of additional CrAg tests required and the potential case-finding yield for routine CrAg screening at a CD4 threshold of  $\leq$ 200 cells/ $\mu$ L. Nationally, screening at a CD4 count of  $\leq$ 200 cells/ $\mu$ L (versus at a CD4 count of <100 cells/ $\mu$ L) increased overall case-finding by 36%, with this percentage increase most pronounced at primary health clinics and community health centers (41%) compared to hospitals (28%). Based on a recent National Health Laboratory Service (NHLS) review, the Western Cape (WC) can anticipate approximately 360 additional lumbar punctures to be done annually with implementation of this amended threshold for screening.

**Implementation of amended criteria**

The NHLS will implement the amended criteria for reflex testing for CrAg at all CD4 laboratories in the Western Cape from **15 August 2022**. This means that **all** blood specimens submitted for CD4 counts (from patients of all ages) will automatically be tested for CrAg with the Lateral Flow Assay if the CD4 count result is  $\leq$ 200 cells/ $\mu$ l. The result of the test will be provided on the CD4 test report.

### Special considerations

1. Although the CrAg test is an accurate diagnostic tool, there is insufficient data to recommend screening in HIV-infected children or early adolescents (<15 years). However, reflex laboratory-based screening will include all ages. Children and early adolescents who screen CrAg positive and have not been previously treated for CM, must be discussed with a paediatrician and referred to hospital for confirmation of the diagnosis by lumbar puncture if advised to do so.
2. Adults with a positive result, must be referred for a lumbar puncture regardless of whether or not symptoms of CM are present.
3. If HIV positive and not on ART, only delay initiation of ART in clients with clinically suspected CM as per ART guideline.

### Follow-Up of Laboratory Results of CD4 Counts And Reflex CrAg Test

Facility managers should ensure that all staff is made aware of the changes to the cryptococcal screening procedure, and that the result of the laboratory-based reflex CrAg test is noted in the folders of patients with CD4 counts  $\leq 200$  cells/ $\mu$ l. Clinicians should consult an Infectious Disease Specialist if they are uncertain of how to manage specific cases. Patients with positive CrAg results should be recalled and referred for lumbar puncture investigation timeously.

Yours sincerely,

pp *HD Gouman*

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**JO ARENDSE**

**CHIEF DIRECTOR: ECSS**

**DATE:** 05/08/2022

### References

1. *Ending Cryptococcal Meningitis Deaths by 2030- Strategic Framework.* <https://dndi.org/wp-content/uploads/2021/05/EndCryptococcalMeningitisDeaths2030-StrategicFramework-EN-2021.pdf>
2. *WHO Guidelines for the diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children: supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. March 2018.* <https://apps.who.int/iris/bitstream/handle/10665/260399/9789241550277-eng.pdf>