**CHARTER AND TERMS OF REFERENCE FOR THE DATA AND SAFETY MONITORING BOARD (DSMB) FOR CLINICAL TRIALS OF HERBAL MEDICINES.**

**SIGNATURE PAGE**

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**Protocol Name:**

**Sponsor:**

**Protocol Number:**

**Trial Registration Number:**

**This document defines the terms of reference, composition, responsibilities, and mode of operation for the DSMB specifically constituted for Protocol number------**

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**A. INTRODUCTION**

Since the outbreak of new coronavirus, the WHO has supported African governments with early detection by providing COVID-19 testing kits to countries, training health workers and strengthening surveillance systems in communities. Forty-four (44) countries in the WHO African region can now test for COVIC-19.

According to Africa Centre for Disease Control and Prevention the confirmed cases of coronavirus were 1,228,971, deaths were 29,087 and 960,926 recoveries in Africa as at 30th August 20201 The exact factors responsible for the relatively low cases, low mortality and high recoveries are not known yet. Recently, Wu Yu and co-workers studied the effects of temperature and humidity on the daily new cases and new deaths of COVID-19 in 166 countries2. They reported that temperature and relative humidity were both negatively related to the daily new cases and daily new deaths of COVID-19 providing evidence that the COVID-19 pandemic may be partially suppressed with temperature and humidity increases. Nonetheless, the increasing number of confirmed cases in some countries, the weak health systems and availability of limited skilled manpower in Africa suggest the urgent need for rapid development of novel interventions.

Interestingly, global efforts to evaluate existing antivirals and therapeutic strategies to treat COVID-19 have intensified. One of the proactive approaches is the search for vaccines and effective and safe medicines for treatment and prevention against COVID-19. There are several publications regarding the immune boosting, anti-inflammatory and anti-viral effects of extracts of some African medicinal plants (eg *Sutherlandia frutescens, Sterculia setigera, Anacardium occidentale, Guiera senegalensis, Anogeissus schimperi*, *Moringa olefeira, Vernonia amygdala, Artemisia afra, Mushrooms, etc*). It is feasible that some African medicinal plants may provide either prophylactic or curative effect

1. <https://africacdc.org/covid-19>.

2. Yu Wu, Wenzhan, Jing, Jue, Liu and Qiuyue, Ma. **Effects of temperature and humidity on the daily new cases and new deaths of COVID-19 in 166 countries, April 2020, Science of the Total Environment 729, 139051**

on COVID-19[[1]](#footnote-1). It is therefore not surprising that more than 13 herbal medicines have already been developed by scientists working in collaboration with traditional health practitioners in Africa for the treatment of COVID-19. Some of these countries had approached the World Health Organization Regional Office for Africa (WHO-AFRO) for support *vis-à-vis* clinical evaluation of the herbal medicines. In response, the WHO-AFRO and Africa Centre for Disease Control and Prevention (Africa-CDC) developed a Standard Protocol which countries can adapt to their national regulatory requirements to validate the safety and efficacy of such herbal medicines. This Data Safety and Monitoring Board (DSMB) Charter has been developed by the WHO-AFRO and A-CDC as additional support to countries that will use the Standard Protocol.

A DSMB is a panel of experts, independent of the study investigators, who monitor the conduct of the trial, evaluating the efficacy and safety of the intervention periodically and providing unbiased advice to the investigators and sponsors.

The DSMB constitutes one of the most critical elements of a clinical trial. For this reason, it is important that all participants in and contributors to a trial understand the functions and responsibilities of the DSMB. Failure to understand the complexity of this group's mission can lead to substantial opportunities for confusion among investigators, sponsors, regulators, and the public, especially if the trial that it monitors must be modified or terminated early.

The DSMB has dual responsibilities to the study participants regarding their safety and sponsor *vis-à-vis* scientific credibility. DSMB has advisory role regarding review of protocol, solutions to identified problems, on-going interim reviews on safety and efficacy and recommendations on the overall performance of the trial. The DSMB occupies a unique and important place in studies requiring specialized monitoring for data and safety. Constituted and functioning under the authority of the sponsor, a DSMB is an independent advisory body responsible for assessing data during the course of a study. The DSMB’s recommendations provide the sponsor with an overall scientific, safety, and ethical appreciations of the study, and should assist the sponsor in maintaining the rigour of the study design, with appropriate attention paid to the protection of trial participants.

**B. OBJECTIVE OF THIS DOCUMENT**

This document defines the terms of reference, composition, responsibilities, and mode of operation for the DSMB specifically constituted by the WHO-AFRO and A-CDC for the clinical evaluation for safety and efficacy of herbal medicines against COVID-19.

**C. TERMS OF REFERENCE**

WHO-AFRO and Africa-CDC establish a DSMB to:

1. review safety data, all serious adverse and life-threatening events, as well as deaths, that may or may not be possibly attributable to the trial herbal medicine;
2. monitor trial progress, including recruitment and losses to follow-up;
3. monitor protocol compliance and assess the quality and completeness of study data;
4. advise the sponsor and researchers on the continuing safety of the trial participants and those yet to be recruited into the study.

**D. MEMBERSHIP OF THE DSMB**

The DSMB is an independent multidisciplinary group consisting of at least seven members with expertise in clinical medicine, biostatistics, medical ethics, clinical trial process, pharmacology, virology and patients’ advocate to represent the primary target population of the trial (one per study trial site). Members should not be affiliated with the sponsor, investigators, ethics committee, national medicine regulatory authority, and staff at the study site. Members should also not have vested conflicts of interest (e.g. a financial or other interests in an intervention or product similar to the intervention being studied). DSMB members will undergo training including introduction to the study and the Charter. The procedure for appointment to DSMB commences with screening of curriculum vitae of potential members. The screening will lead to selection of potential candidates based on the agreed roles and responsibilities of DSMB as indicated in this Charter. The selected candidates will then be contacted officially through letters of appointment. Thus, the procedure for appointment into the DSMB is through selection by the sponsor.  The procedure for identifying conflicts of interest (COI) and criteria for determining unacceptable conflicts of interest will be articulated by the sponsor. Furthermore, each DSMB member will be mandated to read and sign the conflict of interest form. Every potential member should report in writing, at the time of candidacy, all potential or real conflicts of interest to the sponsor. The performance of each member of the DSMB will determine renewal of his appointment, if necessary. In the event of resignation or withdrawal of a member, the procedure for appointment will be followed to replace him. Another condition of appointment concerns all reimbursements for work and expenses, if any, within or work-related, should be recorded and made available to the public upon request. Furthermore, a member should sign a confidentiality agreement regarding meeting deliberations, applications, information on research participants, and related matters.

The sponsor is responsible for the selection and appointment of DSMB members as well as for ensuring that the DSMB has the means and resources to function effectively so as to generate competent reviews and sound recommendations.

**E. DSMB STATISTICIAN**

The DSMB will obtain input from an independent DSMB statistician, who him-/herself is not a member of the DSMB.

* The DSMB statistician will provide unblinded analyses to the DSMB before each of the scheduled DSMB meetings, when requested to do so by the DSMB Chair.
* The DSMB statistician receives blinded datasets from the study trial statistician based at the study site.

The DSMB statistician can be requested by the DSMB to provide additional data analyses (blinded or unblinded), the results of which can support the decisions that are made by the DSMB.

**F. MODUS OPERANDI OF THE DSMB**

1. The members of the DSMB will serve for the duration of the study.
2. Nominees to DSMB membership will be required to complete a WHO declaration of interest form (Annex 1). Also, prior to confirmation by WHO-AFRO and A-CDC of their appointment as DSMB members, the nominees shall be required to sign a Confidentiality Undertaking (Annex 2).
3. A register of members' Interests and signed Confidentiality Undertaking will be maintained by the WHO-AFRO and Africa-CDC.
4. WHO-AFRO and Africa-CDC will make available resources (people, rooms, equipment, virtual meetings logistics, etc.) to the committee during the execution of work requested by the organization in line with this Charter. The WHO-AFRO and Africa-CDC will also provide daily subsistence allowances from their residence and to and from other locations on missions commissioned by the organization following WHO rules and procedures.
5. Membership may be terminated by the WHO Regional Director and Director Africa-CDC for any one of the following reasons:
   1. failure to attend two consecutive DSMB meetings without plausible reasons;
   2. change in affiliation resulting in a conflict of interest; and
   3. a lack of professionalism (for example, a breach of confidentiality).
6. Communication

The recommendations of the DSMB are communicated directly to the sponsor. It is the responsibility of the sponsor to notify the Principal Investigators (PI), national medicine regulatory authority, Ethics Committee, data managers, other relevant parties and ensure that the recommendations are acted upon by the various parties involved during the course of the study.

1. Audits

It is essential that all parties (including research participants, investigators, sponsors, ethics committees, regulatory authorities, and other study personnel) who are engaged in this study have confidence in the function and decisions of the DSMB. Nonetheless, the sponsor may arrange for audit/inspection of the DSMB once during the clinical study. However, due to the current pandemic, virtual video inspections should be organized for such inspections.

1. Statistical procedures

Statistical procedures to be utilized by the DSMB (including procedures for monitoring safety and efficacy outcomes, and/or ongoing benefit/risk[harm] analysis, as appropriate) will be discussed during initial meeting and agreed upon by the DSMB.

1. Data management and security

The mechanisms for data evaluation and secured storage including password for electronic storage will be discussed and agreed upon at the initial meeting of the DSMB. In view of the confidentiality of the data, the DSMB will also determine who should be authorized to have access to them at the initial meeting. However, it should be noted that the DSMB will not manage the study data. The data belongs to the investigators and sponsors who have invested in the study. The DSMB will periodically be unblinded or allowed to break the code for the purposes of an analysis especially when there are clusters of severe reactions.

1. Election of officers

The DSMB will elect their Chair, Vice-Chair and Secretary at the initial meeting. The procedure for electing officers should be through nomination by a member followed by secret balloting. The office holders are deemed by colleagues on the DSMB as capable to perform their roles effectively. Each office holder is expected to maintain that office until the end of the study except he decides to resign or he is withdrawn from the DSMB due to misconduct or beach of confidentiality clause. Except the DSMB decides otherwise, notification regarding recommendations is the responsibility of the Chair while minutes and agenda items are undertaken by the secretary. The DSMB will also determine the procedure for archiving all data until after the study when all data will be delivered to the sponsor through confidential channels.

1. Amendment of DSMB Charter

The Charter will be thoroughly reviewed at the initial meeting of the DSMB. All amendments to the Charter will be effected by unanimous vote by all the voting members of the DSMB. After reviewing the Charter, all DSMB members should agree to, and sign, the Charter at the time of their appointment to the DSMB. The members’ signatures’ indicate their intent to fulfil their DSMB responsibilities.

**G. CONFIDENTIALITY**

The DSMB shall maintain the confidentiality and privacy of all study-related data in a manner that is determined by them at their initial meeting. The confidentiality agreement signed by DSMB members is an undertaking to strictly bind them to adhere to all the provisions of this Charter.

**H. MEETING PROCEDURES**

* The DSMB should review the protocol, informed consent documents, the investigator’s brochure, relevant literature(s), and other research- related document(s). The DSMB should also consider prior ethics committee(s) reviews, as well as the requirements of applicable national laws and regulations. The statistical methodology described in the protocol and its role in the DSMB safety monitoring plan should be clarified at this initial meeting.
* DSMB members should receive orientation regarding the procedures outlined in this Charter, and training in relevant guidelines and SOPs. The DSMB may, in the context of this discussion, propose changes to the Charter. However, the sponsor is responsible for final decisions relating to this Charter.
* The frequency of DSMB meetings depends on several factors including the rate of enrollment, safety issues or unanticipated adverse events, availability of data, and, where relevant, scheduled interim analyses as well as the duration of the trial. The agenda for each meeting is the responsibility of the DSMB Chair and Secretary (selected among the DSMB members at their first meeting).
* It is the responsibility of the PI to ensure that both the DSMB and the national medicine regulatory authority as well as the Ethics Committee are apprised of all new safety information relevant to the investigational product and the study. This includes providing the DSMB with a copy of the Investigator’s Brochure (IB) in advance as well as promptly providing all IB revisions and all safety reports issued by the sponsor. Summary safety and enrollment data should be forwarded periodically to the DSMB every month. The DSMB should receive all protocol revisions and may receive other documents relating to the study.
* Reports are prepared by the study statistician. The study statistician should provide suggested formats or templates for data presentation for the initial meeting of the DSMB. The DSMB shall review and approve the data elements to be presented. At subsequent meetings, additions or modifications to these reports may be directed by the DSMB on a one-time or continuing basis. Written reports should be sent to DSMB members at least one week prior to the meeting.
* The initial meeting should include DSMB members, PI and trial sponsor or his/her representative. At this meeting, the DSMB should also develop procedures for conducting its business. Early safety review meeting examines the accumulated safety and enrollment data, review study progress, and discuss other factors (internal or external to the study) that might impact continuation of the study. Furthermore, safety information and factors relating to quality of trial conduct may be the focus of the meeting of the DSMB. In addition to scheduled meetings, the PI, sponsor or Ethics Committee can call for the DSMB meeting to discuss safety concerns.
* Meetings may be held by conference calls or videoconferences or face-to-face. In the event a DSMB member cannot attend a meeting, he/she may receive a copy of the closed session DSMB report (see below) and either participate by conference call or provide written comments to the DSMB Chair for consideration at the meeting.
* Meetings should be planned in accordance with this Charter. In addition, DSMB members should be given enough time to review the materials for the meeting. For example, background materials to be discussed at a DSMB meeting should reach the members at least a week before the scheduled meeting. The Minutes of all meetings should be documented, and finalized following an approval procedure determined by the DSMB at the initial meeting.
* . In view of the pandemic, the expected frequency of review meetings is bi-weekly for the first month and then monthly for 12 months. The meetings can be held in person or by teleconference. The meetings should review the efficacy and safety data generated during this period, and should include a progress report from the investigator, serious adverse events reports, and cumulative safety data. The DSMB should take into account the quality of conduct of the study and the accuracy of the data.
* The agenda for each DSMB meeting should be established based on the discussions and recommendations from previous meetings as well as according to events in, or related to, the study that may have occurred since the previous meeting. Procedures regarding the: responsibility for drafting, reviewing, and approving the agenda; issues to be reviewed; consultants and other participants; and the sequence of open and closed sessions should be determined at the initial meeting. The DSMB members will have access to the monitors’ and auditors’ reports as well as other documents relating to quality assurance activities.
* When significant trends in the data require further interpretation, the DSMB may request unblinding of the data. In such cases, it may only be immediately necessary to unblind the statistician or epidemiologist, for example, and not all the DSMB members. The unblinded person then reports to the other members if there is cause for concern. The unblinding procedures should be defined in advance and supported by documentation which indicates who has access to the unblinded data.
* When appropriate, a mechanism should be developed for timely reporting and assessment of serious adverse events, between regularly scheduled meetings of the DSMB, to ensure that participants are not put at undue risk. This is described in the SOPs..
* At the termination or conclusion of a study, the DSMB should meet to consider the efficacy and safety data generated from the study and provide a final recommendation to the sponsor. A final assessment report regarding the conduct of the study should also be prepared and given to the sponsors.

**I. MEETING FORMAT**

The recommended meeting format consists of three sessions: Open Session, Closed Session, and Closed Executive Session.

**Open Session**

Issues relating to the general conduct and progress of the study are discussed including adverse events and toxicity issues, accrual, demographic characteristics of enrollees in aggregate, disease status of enrollees, comparability of groups with respect to baseline factors, protocol compliance, site performance, quality control, and timeliness and completeness of follow-up. Any data provided must be presented without grouping by treatment assignment or otherwise by preserving the masking of all subjects. Outcome results must not be discussed during this session. Attendees include DSMB members, voting and *ex officio* members and ad hoc experts. The PI and the study biostatistician should be in attendance in order to present results and respond to questions. This session is open to study investigators, the national medicine regulatory authority and sponsor.

**Closed Session**

Grouped safety data and, if appropriate, efficacy data are reviewed with the study biostatistician for consultation at this session. Grouped data should be presented by coded treatment arm. This session is normally attended only by voting members. This final session involves only DSMB voting members to ensure complete objectivity as they discuss outcome results, make decisions, and formulate recommendations regarding the study. If treatment codes have been made accessible to the DSMB, then the DSMB may unmask the data based on mechanisms identified at the initial meeting. The DSMB should decide on the written recommendation it will present to the sponsors.

**Closed Executive Session**

A brief summary that describes the individual findings, overall safety assessment and DSMB recommendations should be forwarded to the sponsor within one week of the meeting by the DSMB Chair.

This session is attended by the DSMB Chair and the representative of the sponsor. A brief teleconference will be held between the DSMB Chair and the sponsor or his representative to discuss the recommendations of the DSMB.

**J. VOTING**

After a thorough discussion of DSMB members' opinions and rationale and an attempt to reach clarity regarding individual recommendations, the final recommendations of each DSMB member should be solicited during the Closed Session. A consensus opinion or recommendation among members is not required; each member may have individual opinions. The final recommendations are recorded and either identified as majority or minority positions or are accompanied by actual vote tallies for each divergent recommendation, i.e., as number of votes for or against a particular action, such as continuing or terminating a study, etc.

**K. QUORUM**

A quorum, as defined by the DSMB in the initial meeting, must be present either in person or by conference call. The DSMB quorum for this study is 80% of members. Such a quorum is empowered to review and make valid recommendations on this study. The quorum includes at least one physician with experience in the medical field of concern, and one statistician.

**L. CONFLICTS OF INTEREST (COI)**

* DSMB members will have no financial or intellectual conflict of interest that could prevent them from objectively reviewing the interim data and giving unbiased scientific advice to the study team.
* DSMB members will disclose any other potential conflicts that are considered relevant and sign a Conflict of Interest Declaration.
* The list of DSMB members and their potential conflicts of interest will be documented and maintained by the Sponsor. DSMB members will be invited to update their conflicts of interest at the beginning of each meeting.
* All appointed DSMB members, as well as the DSMB statistician, will sign a confidentiality and non-disclosure agreement as well as a conflict of interest declaration before the first DSMB meeting and at every meeting

**M. DSMB DECISIONS**

The possible recommendations open to the DSMB are:

* No action needed; trial continues as planned
* Early stopping due to clear harm of a treatment
* Sanctioning and/or proposing protocol changes. Any DSMB decision will be based on their review of the totality of evidence, including the emerging data from the trial. The PI will provide the DSMB with reports of related SAEs and Sustained Unexpected Serious Adverse Events (SUSARs) and 6-monthly line- listings of unrelated SAEs, and all other relevant data, including a summary of adverse events. The DSMB may also request additional data from the PI, PSRT Chair or Trial Steering Committee. Decision-making quorum The DSMB will have a quorum if at least 3 of the 4 DSMB members are present at a meeting. Every effort should be made for the DSMB to reach a unanimous decision through a vote if necessary. However, in the event of a split vote, majority vote will rule and a minority report should be appended. Absent member A DSMB member who will not be able to attend the meeting may pass comments on circulated reports or other documentation to the DSMB Chair for consideration during the discussions.
* If the DSMB recommends, and the sponsors agree, Trial Steering Committee, and other regulatory authorities as appropriate will be informed. Prior plans will be put into operation for the orderly conclusion of the trial, notification of study participants, and dissemination of the results.
* In the unlikely event that the DSMB and PI disagree about the proper course of action, every attempt will be made to reach a consensus through discussion. If, despite best efforts, significant differences of opinion persist, then additional input from independent experts selected by the Sponsor may be sought. Every attempt will be made to reach a consensus through this process.

**N. DOCUMENTATION AND ARCHIVING**

All documentation and communications of the DSMB should be dated, filed, and archived according to written procedures. A DSMB should develop the standard operating procedures (SOP) to define the archival and access procedures (including naming the persons responsible for archiving the materials and those authorized to access the archived materials) for the various documents, files, and archives. The SOPs should include special precautions concerning the filing and archiving of randomization codes or lists. The documents should be archived for the duration of this study. At the closure of the study, the archived materials should be forwarded to the sponsor.

Documents that should be filed and archived include, but are not limited to:

* The DSMB Charter.
* The curricula vitae of all DSMB members.
* A signed and dated statement from each DSMB member indicating that he/she understands his/her responsibilities and that he/she has no interests that conflict with the objective performance of his/her duties and responsibilities as a member of the DSMB.
* A record of all income and expenses of the DSMB, including payments and reimbursements made to the DSMB members.
* The agendas of DSMB meetings. The minutes of DSMB meetings.
* A copy of all materials received by the DSMB, including the sponsor’s reports.
* A copy of the recommendation(s) provided by the DSMB to the sponsor.
* A copy of all official DSMB correspondence.

**O. PUBLICATIONS ARISING FROM THE TRIAL**

The PI must have complete freedom to present and publish the results of the trial, free from any censorship or inappropriate delay. However, the sponsors must be informed and given the manuscript before publication. If DSMB members are to be acknowledged by name in trial publications then they should receive a draft of the trial manuscripts.

**P. INDEMNIFICATION OF THE DSMB**

DSMB members and their affiliated institutions should be protected from lawsuits (save for wilful misconduct). Accordingly, the Sponsor agrees to indemnify and hold harmless the DSMB and the academic institutions of its members from any and all third party claims, actions, lawsuits, losses, and reasonable expenses ("Claims"), including reasonable legal fees and expenses, related to services that the DSMB provides pursuant to this Charter, except with regard to claims brought by the Sponsors, and except to the extent finally determined to have resulted from the wilful misconduct or fraudulent acts of the DSMB relating to such services.

**R. . GLOSSARY**

The definitions provided within this glossary apply to terms as they are used in these guidelines. The terms may have different meanings in other contexts.

***Blinded/unblinded***

Data (or their format/presentation) are considered ‘blinded’ when those with access to the data are not informed of the significant characteristics associated with them. Often this refers to identification of the intervention associated with the data. Data (or their format/presentation) are considered ‘unblinded’ when those with access to them are informed of the significant characteristics (e.g. intervention) to which the data are associated.

***Charter***

A document prepared by the sponsor which establishes the role and responsibilities of the DSMB vis-à-vis the sponsor and other parties engaged in the study.

***Conflict of interest***

A conflict of interest arises when a member(s) of the DSMB holds interests with respect to specific applications for review that may jeopardize his/her (their) ability to provide a free and independent evaluation of the research. Conflicts of interests may arise when a DSMB member has financial, institutional, or social ties to the research.

***Data & Safety Monitoring Board (DSMB)***

An independent committee established by the sponsor to assess, at intervals, the ongoing scientific and ethical integrity of a study by reviewing and evaluating (unblinded) data and reports at regular intervals. The DSMB provides non-bonding recommendations to the sponsor regarding study modification, suspension, or termination. There is no fixed or harmonized international name for committees performing this function. Other names for

committees performing the same or similar functions include, but are not limited to: Data Monitoring Committee (DMC), Independent Data Monitoring Committee (IDMC), Monitoring Committee (MC), Data & Ethics Monitoring Committee (DEMC), Safety Monitoring Committee, Study Monitoring Committee.

***Ethics committee***

An independent body (an institutional, regional, national, or supranational board or committee) established to review independently proposed and ongoing research. Such committees are also known variously as Independent Ethics Committees (IECs), Institutional Review Boards (IRBs), Research Ethics Boards (REBs), Research Ethics Committees, and other designations.

***Investigator***

A qualified scientist who takes on the scientific and ethical responsibility, either on his/her own behalf or on behalf of an organization/firm, for the ethical and scientific integrity of a research project at a specific site or group of sites. In some instances, a coordinating or principal investigator may be appointed as the responsible leader of a team of co-investigators.

***Protocol***

A document that provides the background, rationale, and objective(s) of a health research project, and describes its design, methodology, and organization, including ethical and statistical considerations. Some of these considerations may be provided in other documents referred to in the protocol.

***Recommendation***

Non-binding decisions provided by the DSMB to the sponsor concerning the Board’s scientific and ethical appreciation of the study and regarding the continuation, modification, suspension, or termination of the study following review of the accumulated safety and efficacy data.

***Study participant***

An individual who participates in a research project, either as the direct recipient of an intervention (for example, study product or invasive procedure), as a control, or through observation. The individual may be a healthy person who volunteers to participate in the research, a person with a condition unrelated to the research being carried out and who volunteers to participate, or a person (usually a patient) whose condition is relevant to the use of the study product or questions being investigated.

***Standard operating procedures (SOPs)***

Detailed, written instructions to achieve uniformity of performance of a specific function.

***Sponsor***

An individual, company, institution, or organization that, either singularly or collectively, takes responsibility for the initiation, management, and/or financing of a health research project. The sponsor of a study may be composed of a number of individuals, companies, institutions, or organizations that share the responsibilities of the study. In this case, it is important that the protocol clearly defines how the sponsor responsibilities are distributed, the individual(s) or organization(s) responsible for establishing the DSMB, and to whom the DSMB reports.

**S. REFERENCES**

1. World Health Organization. Coronavirus Situation Report 192. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>, 31st July 2020.
2. Africa Centre for Disease Control and Prevention. Coronavirus (COVID-19) Report . <https://africacdc.org/covid-19/>, 31st July 2020.
3. [Liang-Tzung Lin](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lin%20LT%5BAuthor%5D&cauthor=true&cauthor_uid=24872930),[Wen-Chan Hsu](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hsu%20WC%5BAuthor%5D&cauthor=true&cauthor_uid=24872930),and  [Chun-Ching Lin](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lin%20CC%5BAuthor%5D&cauthor=true&cauthor_uid=24872930). Antiviral Natural Products and Herbal Medicines. [J Tradit Complement Med](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4032839/). 2014 Jan-Mar; 4(1): 24–35.

# Effects of temperature and humidity on the daily new

# cases and new deaths of COVID-19 in 166 countries Effects of temperature and humidity on the daily new cases and new deaths of COVID-19 in 166 countries. Yu, Wu, Wenzhan, Jing, Juel Liu, Qiuyue, Ma, Jie, Yaping, Wang, Min, Min Lu [Science of The Total Environment](https://www.sciencedirect.com/science/journal/00489697), Volume 729, 10 August 2020, 139051.

1. [Liang-Tzung Lin](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lin%20LT%5BAuthor%5D&cauthor=true&cauthor_uid=24872930),[Wen-Chan Hsu](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hsu%20WC%5BAuthor%5D&cauthor=true&cauthor_uid=24872930),and  [Chun-Ching Lin](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lin%20CC%5BAuthor%5D&cauthor=true&cauthor_uid=24872930). Antiviral Natural Products and Herbal Medicines. [J Tradit Complement Med](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4032839/). 2014 Jan-Mar; 4(1): 24–35. [↑](#footnote-ref-1)