**Letter of Agreement**
**Regarding**
**Data Sharing, Use and Publication of Results**
**Relating to:**

*"*Understanding the relation between Zika virus infection during pregnancy and adverse fetal, infant, and child outcomes: a protocol for a systematic review and individual participant data meta-analysis of longitudinal studies of pregnant women and their infants and children*" (the "**Protocol**")*

This Letter of Agreement is between the World Health Organization ("**WHO**") and [Eduardo Olivarez, Chief Administrative Officer] on behalf of [Hidalgo County Health & Human Services Department] (the "**Institution**"). WHO and the Institution are hereinafter referred to each as a "**Party**" and together as the "**Parties**".

## 1. Background and purpose

1.1 The Parties enter into this Letter of Agreement to collaborate regarding the activities and study described in the Protocol (the "**Research Activities**"), and pursuant to the terms of this Letter of Agreement, the Institution will provide one or more de-identified, participant-level data set(s), data dictionary(ies), and variable code list(s) (the "**Data**") to WHO for the performance of the Research Activities. This Letter of Agreement also addresses, among other things, the ownership, transfer, use and publication of results relating to the Data and the Research Activities.

1.2 The ZIKV IPD Consortium is a global collaboration of Zika Virus (ZIKV) researchers whose purpose is to use individual participant data meta-analysis (IPD-MA) to address extant questions related to the relation between ZIKV infection and adverse maternal and child health outcomes. WHO and the Institution are members of the ZIKV IPD Consortium.

1.3 All parties participating with WHO in the Research Activities by contributing data sets to WHO for analysis are also members of the ZIKV IPD Consortium, and each such party is required to enter into a Letter of Agreement with WHO materially similar to this Letter of Agreement to participate in the Research Activities.

1.4 Emory and Heidelberg Universities have been contracted by WHO to create the meta-analysis dataset of all submitted data by ZIKV IPD Consortium members to WHO in connection with the Research Activities (the "**Meta-Analysis Dataset**"). The Meta-Analysis Dataset will only include de-identified an anonymized information and will not contain any personally identifiable information or personal data.

## 2. Cooperation regarding the Research Activities

2.1 WHO and the Institution agree to collaborate on the Research Activities according to the terms of this Letter of Agreement and those set out in the Protocol, attached as **<u>Annex 1</u>**.

2.2 The date by which the Research Activities are expected be completed and any manuscripts prepared and submitted (the "**Completion Date**") will be agreed by the ZIKV IPD Consortium.

Unless otherwise agreed (see section 3.4.2, below), WHO will complete the Research Activities and destroy the Data received from the Institution and remove the Institution's data from the Meta-Analysis Dataset by the Completion Date and will provide certification of the destruction. The tentative Completion Date is 1 January 2026.

**3. Data and dataset ownership and use**

3.1 The Institution represents that it owns all rights in the Data and/or has the legal authority to share the Data.

3.2 Except as expressly provided in this Letter of Agreement, WHO does not hold, and is not granted under this Letter of Agreement, any rights in the Data, whether in implementing the Research Activities or otherwise.

3.3 Parties agree that the Data provided by Institution is public domain material. Institution shall maintain full rights to re-use the content and material it provides for any and all Institution purposes, and/or to share with other collaborators or requestors. Subject to the Institution's ownership or other rights in the Data and ability to re-use and share set out above, and the similar ownership or other rights of other members of the ZIKV IPD Consortium providing other data sets to WHO for the Research Activities, WHO will own all rights in the meta-analysis dataset and the analysis resulting from the Research Activities.

3.4 In addition to use in support of the Research Activities, and notwithstanding anything to the contrary in this Letter of Agreement, the Institution agrees and acknowledges that WHO is entitled to:

3.4.1 use, and allow third parties to use, the results of the Research Activities (including the Meta-Analysis Dataset) for normative guidance to countries until the agreed-upon Completion Date; and

3.4.2 if the Institution so agrees by signing below, allow the third parties (including, without limitation, Institutional members of the ZIKV IPD Consortium and institutions which have not committed data to the ZIKV IPD Consortium effort) to access the Meta-Analysis Dataset, subject to the following conditions:

3.4.2.1 The proposed recipient of the Meta-Analysis Dataset has provided to WHO a research protocol for which the proposed recipient is the sponsor, and the ZIKV IPD Consortium Data Access Committee (a group of cohort PIs and/or MoH officials who agree to oversee requests for access to the Meta-Analysis Dataset and associated codebooks) has decided that the research protocol is not duplicative of existing research protocols and is clinically relevant;

3.4.2.2 The proposed recipient of the Meta-Analysis Dataset has provided to WHO documentation of ethics committee review and approval of the aforementioned research protocol; and

3.4.2.3 The entry into a Data Access and Authorship Agreement between WHO and the proposed recipient of the Meta-Analysis Dataset which includes, without limitations terms for secure data transfer and storage, use of the Meta-Analysis Dataset by the recipient (only for conducting prespecified, approved-upon analyses), and authorship citation for the ZIKV IPD Consortium members who created the Meta-Analysis Dataset or whose data is included in the proposed analysis.

## 4. Undertakings of WHO

4.1 The WHO Research Ethics Review Committee has deemed this analysis exempt from Ethical Review.

4.2 In implementing the Research Activities, WHO will:

4.2.1 Not attempt to identify or contact research participants included in the Data;

4.2.2 Respect the confidentiality of the Data, including that WHO will take all reasonable measures to ensure that the Data will only be used for the Research Activities and will only be disclosed to those persons who need to receive the Data for the Research Activities;

4.2.3 WHO will transmit Data to the data synthesis groups at Emory and Heidelberg Universities securely, using secure file transfer protocol;

4.2.4 WHO will maintain the Data in a secure location on a password-protected, WHO-internal network protected by standard encoding and the WHO firewall for the duration of the project; and

4.2.5 WHO will require Emory and Heidelberg Universities to enter into a contractual commitment to maintain the Data in a secure location on a password-protected, internal network protected by standard encoding and by the Emory and Heidelberg University firewalls during the creation of the synthesized dataset (two years from the date that the data is received by WHO); and

4.2.6 Only perform analysis of the Data that addresses the objectives specified in the Protocol (with the exception of using the Data to provide normative guidance to countries, as cited in 3.4). Any additional analyses of the Data deemed necessary to meet the objectives of the Protocol will be performed by WHO only after it has received approval from the Institution and all other members of the ZIKV IPD Consortium whose data would be involved in such additional analyses, if any. Approval of any such additional analyses will be assumed if the Institution does not reply to WHO's request within 10 working days. Notwithstanding the foregoing, additional analyses of the Data which would address completely novel objectives not included in the Protocol must be affirmatively approved by the Institution.

4.3 With respect to preparation of the dataset for the Research Activities, WHO will assess the Data for irregularities and review the distribution of the Data with the Institution. Once the WHO has resolved any irregularities in the data with the Institution (i.e. discrepancies between the Data received and any published reports of the Data), WHO will return a copy of the Data to the Institution in the “cleaned” format. WHO will retain its copy of such “cleaned” Data for the purposes provided herein.

4.4 As part of its implementation of the Research Activities, WHO will:

4.4.1 Keep a detailed record of the formation of the Meta-Analysis Dataset;

4.4.2 Seek feedback on data synthesis questions (i.e., combining results from different diagnostic tests) from an expert panel of scientists and researchers decided upon by the ZIKV IPD Consortium;

4.4.3 Inform the Institution and other ZIKV IPD Consortium members of decisions made during the data synthesis process through monthly telephone or email updates; and

4.4.4 Share results of analyses with the Institution and all members of the ZIKV IPD-MA Consortium through monthly telephone or email updates.

4.5 With respect to the Meta-Analysis Dataset, WHO will:

4.5.1 Publish the requirements that need to be met to apply for and, pending approval, access the Meta-Analysis Dataset;

4.5.2 Keep a record of approved access to the Meta-Analysis Dataset;

4.5.3 Facilitate the ZIKV IPD Consortium Data Access Committee’s remotely hosted, quarterly meetings to review eligible requests to access the Meta-Analysis Dataset; and

4.5.4 Transmit the Meta-Analysis Dataset to approved users pursuant to the terms of this Agreement through a secure file transfer protocol.

**5. Undertakings of the Institution**

5.1 The Institution represents that:

5.1.1 It has obtained all rights and permissions necessary to transfer the Data to WHO and for WHO to implement the Research Activities and all other activities relating to the Data as described herein, including, without limitation, in Article 3.4;

5.1.2 The Data have been collected from clinical trials, observational studies, or surveillance systems that have been conducted in accordance with all applicable laws;

5.1.3 The individual(s) to whom the Data relate have provided their ‘informed consent’ to participate in the study wherein their data was collected if required by, and in accordance with, applicable laws.

5.2 Prior to transmitting the Data to WHO, the Institution will:

5.2.1 Verify whether approval from their local/relevant Ethics Review Committee is required for the use of the Data in the Research Activities, and if that approval is required, obtain it; and

5.2.2 Anonymize all participant-level data in the Data, pursuant to agreed standards, to remove all information in the Data that could be used to identify research participants.

5.3 The Institution will transmit the Data to WHO securely, using secure file transfer protocol.

5.4 The Institution will avoid providing to WHO or any other ZIKV IPD Consortium member any information relating to the Data or the Research Activities that relates to a natural person, which, either directly or indirectly, in combination with other information available or likely to be available to WHO, can identify such natural person.

5.5 The Institution will participate in the ZIKV IPD Consortium and the Research Activities pursuant to the Protocol, the terms of this Letter of Agreement, and any other participation modalities agreed by the ZIKV IPD Consortium members.

## 6. Authorship and publications

6.1 WHO will prepare manuscript(s) of the results of the Research Activities for publication, pursuant to the terms of the Protocol, and publish such manuscripts pursuant to WHO's rules and regulations, including its policy on open access, as contained at: http://www.who.int/about/policy/en/. WHO may further use the results of the Research Activities to update relevant WHO recommendations and develop any guidelines, including publication thereof, and may further publish those results.

6.2 WHO will provide all publications relating to the Research Activities, including all preliminary and final results of analyses performed by WHO in coordination with ZIKV IPD Consortium membership and all public reports of results or manuscripts, to all members ZIKV IPD Consortium (including the Institution) for review. WHO will provide such review publications at least fifteen (15) working days (seven (7) days for abstracts) before a proposed publication is submitted to any editor, publisher, referee or meeting organizer. In the absence of an objection by any member of the ZIKV IPD Consortium within that 15 day period (or 7 days as the case may be) concerning prejudice to its proprietary rights, the publication may proceed.

6.3 If a manuscript of the Research Activities is submitted for publication, WHO will in all events retain the Data until the peer review process is completed, and then for one year after publication to ensure sufficient time to address any required responses to the findings (e.g., letters to the editor).

6.4 WHO will ensure that all publications relating to the Research Activities will appropriately acknowledge WHO, the Institution, and all other participating institutions. The "ZIKV IPD Consortium" will be listed as the author of the manuscripts associated with Objectives 1-4 in the Protocol. Individual authors will be listed in alphabetical order at the end of the publication. The manuscripts associated with Objectives 3 and 4 will have separate groups for the writing committee and for institutions that contribute data to the analyses. The corresponding author will be a representative of WHO. The number of authors listed from each site will be decided by a majority vote that includes all sites or studies that contribute data to the proposed analyses.

## 7. Confidentiality and disclosure

7.1 As noted in Section 3.2, Data provided by Institution is public domain and may be re-used and shared by Institution, consistent with applicable law. However, Parties agree that either party may disclose or receive confidential information under this Letter of Agreement. All confidential information exchanged between the Parties must conspicuously bear the words "Confidential Information" or "Confidential." Confidential Information exchanged orally or through observation must be reduced to writing and marked "Confidential Information" or "Confidential" within 30 days after disclosure to be considered confidential information.

7.2 The results of the Research Activities will be disclosed pursuant to the agreed publication and dissemination means as set forth in the Protocol and this Letter of Agreement. The Parties shall maintain the confidentiality of all results relating from the Research Activities, including all preliminary results and draft manuscripts, to the extent allowed by law. Without limiting the foregoing, the Institution agrees, prior to publishing (including posting on the Internet), presenting in any public forum, or otherwise disseminating through any medium any results of the Research Activities, to ensure the ZIKV IPD Consortium membership has the opportunity to review the proposed publication, presentation or dissemination to assure that confidential information is used consistent with this Letter of Agreement and applicable law.

7.3 The obligations of confidentiality and restrictions on use contained in this Letter of Agreement will continue without termination, commencing on the date of disclosure.

7.4 The obligations of confidentiality and restrictions on use contained in this Letter of Agreement shall not apply to any confidential information (including the Data) which the disclosing Party is clearly able to demonstrate:

7.4.1 was lawfully in its possession and known to it prior to disclosure hereunder, as evidenced by documents antedating the date of disclosure;

7.4.2 was in the public domain or the subject of public knowledge at the time of disclosure by the disclosing Party;

7.4.3 becomes part of the public domain or the subject of public knowledge through no fault of the disclosing Party;

7.4.4 becomes available to the disclosing Party from a third party not in breach of a legal obligation of confidentiality in respect thereof;

7.4.5 was subsequently and independently developed by or on behalf of the disclosing Party, as shown by written records, by persons who had no knowledge of such confidential information; or

7.4.6 is required to be disclosed by law, provided that the disclosing Party will immediately notify the non-disclosing Party in writing of such obligation and shall provide adequate opportunity to the non-disclosing Party to object to such disclosure or request confidential treatment thereof.

**8. Other matters**

8.1 This Letter of Agreement will enter into force on the date of last signature and shall continue until completion of the Research Activities and all ancillary activities (which is anticipated to be on or near the Completion Date), unless earlier terminated pursuant to its terms.

8.2 Either Party may withdraw its agreement to participate in the Research Activities and thereby terminate this Letter of Agreement at any time by written notice to the other Party stating the basis for such termination, provided, however, that the Institution may not terminate its participation in the Research Activities or this Agreement, or withhold any consent required under this Agreement (including any consent to publication), on the basis of disapproval or disagreement with the results of the Research Activities, subject to the orderly conclusion of any activities then ongoing.

8.3 Neither Party shall use the other Party's name (or any abbreviation thereof) and/or emblem in any statement or material of an advertising or promotional nature, without the prior written approval of the other Party. The Parties acknowledge that, as Institution is an agency of the United States Government, Institution is subject to the United States Freedom of Information Act, 5 U.S.C. Section 552, as amended.

8.4 Any dispute relating to the interpretation or application of this Letter of Agreement shall, unless amicably settled, be subject to conciliation, to the extent consistent with applicable law.

8.5 Nothing contained herein shall be construed as a waiver of any of the privileges and immunities enjoyed by WHO under national or international law, and/or as submitting WHO to any national court jurisdiction.

**IN WITNESS WHEREOF**, the Parties have caused this Letter of Agreement to be executed by their duly authorized representatives on the date written below.

Agreed by **the World Health Organization:**

________________________________________________ __________________

Dr. Ian Askew Date
Director, Reproductive Health and Research
*(includes the UNDP/UNFPA/UNICEF/WHO/*
*World Bank Special Programme – HRP)*

**<u>Regarding data sharing between the WHO and the Institution for the analyses specified in the Protocol:</u>**

Agreed by **the Institution:**

________________________________________________ __________________

[Eduardo Olivarez] Date
[Chief Administrative Officer, Hidalgo County]

**<u>Regarding data sharing between the WHO and eligible third parties as outlined in Section 3.4.2 of this Letter of Agreement:</u>**

*Inclusion of the Data in the Meta-Analysis Dataset that can be accessed by eligible third parties (including, without limitation, Institutional members of the ZIKV IPD Consortium and institutions which have not committed data to the ZIKV IPD Consortium effort) for analyses other than those described in the Protocol, subject to the conditions outlined in **Section 3.4.2** of this Letter of Agreement*

Agreed by **the Institution**:

________________________________________________ __________________

[Eduardo Olivarez,] Date
[Chief Administrative Officer]

**Annex 1:**

*"*Understanding the relation between Zika virus infection during pregnancy and adverse fetal, infant, and child outcomes: a protocol for a systematic review and individual participant data meta-analysis of longitudinal studies of pregnant women and their infants and children*" (the "**Protocol**")*