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Protocol for Dengue in Brazil epidemiological trends literature search and analysis.

**Protocol for Dengue in Brazil epidemiological trends  
literature search and analysis**

**Dated: 21 November 2011**

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## 1. Purpose of the protocol

- This protocol summarises the methodology and approach for a literature analysis and review to characterise the epidemiology of Dengue disease in Brazil. The protocol will be registered and on PROSPERO<sup>1</sup> (*See LRG and the literature analysis protocol, page 5*)

## 2. Aims and objectives of the literature analysis and review

- The objectives of the analysis and review are to:
  1. Describe the epidemiological trends of Dengue disease in Brazil from 2000 to the current date in the context of the regional trends
  2. Identify gaps in epidemiological knowledge and future research needs, in preparation for the introduction of a vaccination programme for Dengue disease.

## 3. Version control

- All documents will be marked clearly with a unique, consecutive identification number.
- The identification number will be included in the electronic file name, and also on the header and front page of each document.

Version	Date	Amendments	Notes
D 1	25 July 2011	Draft protocol for comment by Literature Review Group	

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<sup>1</sup> PROSPERO. An international database of prospectively registered systematic reviews in health and social care. <http://www.crd.york.ac.uk/prospero/>

#### 4. Individuals with responsibility for the literature review (Literature Review Group; LRG)

Name	Location
Lucia Bricks	sanofi pasteur, Brazil
Germano Ferreira	sanofi pasteur, Lyon
Graham Joint	Communigen
João Bosco Siqueira, Jr.	Universidade Federal de Goiás, Instituto de Patologia Tropical e Saúde Pública, Departamento de Saúde Coletiva, Goiania, Brazil
Maria da Gloria Teixeira	Instituto de Saúde Coletiva, Universidade Federal da Bahia, Salvador, Brazil

#### 5. Literature analysis

- The literature analysis will employ well-defined methods to identify and select relevant research (*See Search strategy, page 5*).
- Articles identified through the analysis will be critically appraised and studies will be selected according to predetermined inclusion criteria (*See Search limits, page 7*).
- Due to the expected heterogeneity of eligible studies in terms of selection, numbers and classification of cases, a meta-analysis will **not** be conducted.

## 6. Literature review

- The literature review will be developed following a search of the existing literature on the epidemiology of Dengue disease in Brazil.
- The literature review will address, primarily:
  - 1) General epidemiology indicators (incidence, attack rate, seroprevalence); Intensity of epidemics; frequency of hospitalization; severe Dengue fever (including Dengue haemorrhagic fever/Dengue shock syndrome)
  - 2) Populations and sub-groups at increased risk for Dengue disease and severe Dengue disease (e.g. age group, age and demographic shift in severe Dengue, monotypic immunity)
  - 3) Geographical expansion of Dengue disease cases, epidemics and outbreaks
  - 4) Expansion of vector infestation; effectiveness and limitations of vector control measures (e.g. acquired resistance to commonly used insecticides; cumulative toxicity of frequent use to human populations)
  - 5) Trends of serotype introduction in susceptible populations; historical outbreak records and impact (e.g. increasing length of the outbreak duration, number of people affected, impact on the health systems)
- Secondly, data on the following topics will be reviewed, if available (but may not be included in the general literature search criteria):
  - i. Description of existing surveillance systems, outbreak response capability and diagnostic capacity
  - ii. Other epidemiological information (e.g. trends in imported cases; cross-border/regional trends and dynamics)

## 7. LRG and the literature analysis protocol

- The LRG will guide the literature analysis process, prepare and approve this protocol (including refining the search strategies/methodology) and develop the literature review.
- A predetermined search strategy (*See Identifying search terms, page 7*) will be developed by the LRG.
- To demonstrate transparency, the literature analysis will be registered with PROSPERO and the current protocol will be linked to the registration process.

## 8. Search strategy

- The search strategy will enable a comprehensive literature analysis to be carried out which will be designed to find a high proportion of relevant studies.
- Classifications employed in recent review articles and identified during testing of search terms in PubMed will be used to refine the search terms.

### 8.1 Sources

- Data will be gathered from various sources, including, but not limited to the following:

#### i. On-line databases for medical literature

- Bibliographic references to scientific articles published in health sciences journals will be gathered from online databases and libraries.
- A proposed list of databases will be reviewed by the LRG and the approved list will be stated in the protocol.
- Where databases have no formal classification system, such as ‘subject headings’ or ‘descriptors’ a set of ‘free text’ terms will be devised and agreed by the LRG.
- A cross-check of the utility of these non-Medical Subject Heading (MeSH) terms will be conducted in PubMed and compared against the results of the findings using MeSH terms.
- If required, the overall search strategy will be modified by the LRG and stated in a protocol amendment.

#### *Relevant electronic databases include:*

- United States National Library of Medicine and the National Institutes of Health Medical Database (PubMed).<sup>2</sup>
- Scientific Electronic Library Online (SciELO) – a consolidated electronic publication project that makes available the full text articles from more than 290 scientific journals of Brazil, Chile, Cuba, Spain, Venezuela and other Latin American countries.<sup>3</sup>
- Latin American and Caribbean Health Sciences Database (LILACS) – part of the Virtual Health Library (VHL), an initiative by Brazil-based BIREME (the Latin American and Caribbean Center on Health Sciences Information).<sup>4</sup>
- CAPES database of postgraduate research and theses from various Brazilian Universities.<sup>5</sup>

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<sup>2</sup> PubMed: Available at: <http://www.ncbi.nlm.nih.gov/pubmed/>

<sup>3</sup> SciELO: Available at: <http://www.scielo.org/php/index.php?lang=en>

<sup>4</sup> LILACS: Available at: [http://bases.bireme.br/cgi-](http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&base=LILACS&lang=i)

[bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&base=LILACS&lang=i](http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&base=LILACS&lang=i)

**ii. National and international reports and guidelines**

- Reports and guidelines published by relevant national and international organisations will be gathered from online sources.
- A proposed list of organisations will be reviewed by the LRG and the approved list will be added as a further appendix to this protocol.

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<sup>5</sup><http://capesdw.capes.gov.br/capesdw/>

*Relevant electronic databases include:*

- World Health Organization (WHO) Library database (WHOLIS)<sup>6</sup>.
- Pan American Health Organization (PAHO) Headquarters Library database<sup>7</sup>.
- BIOETHICS – Documentation Center Database from PAHO/WHO Bioethics Unit.
- CidSaúde – database of literature about the implementation and development of the Cidades Saudáveis em Municípios Brasileiros Project.
- Brazilian Ministry of Health official bulletins<sup>8</sup>

**iii. Congress materials**

- Literature relating to key congresses (see *Appendix A1, page 10*) such as conference papers and posters, etc will be sought to complement data gathered in the literature and from organisational searches.

**iv. Grey materials**

- Grey literature such as lay publications will be sought to complement data gathered in the literature and from organisational searches.
- A Google search will be used to identify other research reports published by national and international organisations. In addition, websites suggested by members of the LRG will be accessed as necessary, and added as amendments to this protocol.

**8.2 Identifying search terms**

- A draft list of search terms will be prepared by the LRG from a list of MeSH terms (See *Appendix A2, page 13*) to cover epidemiology, population, intervention and outcome corresponding to the review parameters.
- Search terms will include MeSH terms/subjects (including synonyms, abbreviations, spelling variants and closely related words) and free text terms.
- MeSH terms will be grouped and linked by ‘AND’ or ‘OR’ to make searches reproducible.
- The final full search strategy will be added as an amendment to this protocol.

**8.3 Search limits**

**i. Language**

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<sup>6</sup>WHOLIS: Available at: <http://www.who.int/publications/en/>

<sup>7</sup><http://new.paho.org/>

<sup>8</sup>[www.saude.gov.br/svs](http://www.saude.gov.br/svs)



- Only studies published in English, Portuguese or Spanish will be included.
  - If abstracts are unavailable in English, members of the LRG who speak Portuguese or Spanish will assess the suitability of the data against the inclusion criteria. The full text of the non-English articles selected will be translated into English where necessary, for inclusion in the analysis.

**ii. Date range**

- Date limits will be set at 1 January 2000 to the date that searching begins.
  - The date of the initial search will be entered into this protocol as an amendment.
  - To inform and provide background to the data analysis, epidemiological data on Dengue epidemics prior to 2000 will be reviewed where considered necessary by the LRG.
  - A search of the CAPES database was conducted on 27 October 2011 following recommendations from the LRG.

**iii. Study design**

- No limits by study design. Although data from reviews and/or meta-analyses will not necessarily be included, reference lists of these papers will be hand searched (See Section 8.4, *Search results, below*) to identify any references that may meet the selection criteria but that have been missed by the electronic searches.
- Single case reports will be excluded.

**iv. Evidence**

- No limits by evidence type (research based evidence, clinical practice guidelines, expert opinion, case studies, editorials, letters to editors, etc).
- Unpublished reports will be included if they are identified in an agreed database (e.g. LILACS, WHOLIS, SciELO, etc) or referenced in a publication identified in the initial literature analysis.

**v. Sex and Age**

- No limits by sex or age.

**vi. Ethnicity**

- Inclusion of both indigenous and non-indigenous populations.

#### 8.4 Search results

- The bibliographies of retrieved papers (including reviews and/or meta-analyses) that meet the inclusion criteria will be hand-searched to identify any references that may meet the selection criteria but that have been missed by the electronic searches.
- Reference handling and data extraction are described in *Appendix A3, page 14*.
- Such references will be included in the final search selection providing that they meet the inclusion criteria.
- On completion of the database searches, publications identified by the approved search strategy and/or by the LRG will be included in the literature review based on the criteria described in *Search limits (page 7)*.
- Duplicate publication of data could lead to over-sampling. This may arise with use of meta-analyses and other reviews. In such cases the original, primary publication will be used and **not** the meta-analyses or reviews.

#### 9. Assessment of level of evidence

- Although it is possible to judge the quality of epidemiological studies in general terms, the broad range of study types (case studies, surveys, etc.) encompass such a wide variation that it may be difficult to assign articles to precise quality criteria. Nonetheless, a judgment about the overall quality of studies is desirable.
- The requirement for a quality assessment tool for the studies will be discussed within the LRG.
- A template for assessing the evidence presented will be developed (See *Appendix A5, page 17*), ranking studies as high, medium or low quality according to predefined criteria, such as study population or methodology (e.g. laboratory confirmed, type of analysis, etc), surveillance type (e.g. passive, active/sentinel etc), study design (e.g. prospective cohort, randomized controlled, etc) and evidence type (analytical case control, systematic review, etc). The design of the final table will be published in an amendment to this protocol.

## 10. APPENDICES

### A1. Key congresses for review: searches will cover 2008 onwards.

Congress	Frequency	No. Attending	Association	Abstracts; website address
American Society for Tropical Medicine and Hygiene (ASTMH)	Annual	3100	American Society of Tropical Medicine and Hygiene	Abstracts published on website; <a href="http://www.astmh.org/Home.htm">http://www.astmh.org/Home.htm</a>
European Congress for Clinical Microbiology and Infectious Diseases (ECCMID)	Annual	8000	European Society of Clinical Microbiology and Infectious Diseases	Abstracts published on website and on CD-ROM Clinical Microbiology and Infection; <a href="http://www.congrex.ch/eccmid2012/">http://www.congrex.ch/eccmid2012/</a>
European Congress for Chemotherapy and Infection (ECC)	Annual	3000	Federation of the European Societies for Chemotherapy and for Infection (FESCI)	Abstract book; <a href="http://www.fesci.net/">http://www.fesci.net/</a>
European Society for Pediatric Infectious Diseases (ISPID)	Annual	3000	European Society for Pediatric Infectious Diseases (ESPID)	Abstract book; <a href="http://www2.kenes.com/espид2011/Pages/Home.aspx">http://www2.kenes.com/espид2011/Pages/Home.aspx</a>
Infectious Diseases Society of America (IDSA)	Annual	4000	Infectious Diseases Society of America	Journal of Infectious Diseases; <a href="http://www.idsa2011.org/">http://www.idsa2011.org/</a>

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<b>Name</b>	<b>Frequency</b>	<b>No. Attending</b>	<b>Association</b>	<b>Abstracts; website address</b>
International Congress of Chemotherapy and Infection (ICC)	Biennial	3000	International Society of Chemotherapy (ISC)	Abstract book; <a href="http://www.eccmid-icc2011.org">http://www.eccmid-icc2011.org</a>
International Conference on Emerging Infectious Diseases (ICEID)	Biennial	2500	American Society for Microbiology (ASM)	Abstract book; <a href="http://www.iceid.org/">http://www.iceid.org/</a>
International Congress on Infectious Diseases (ICID)	Biennial	3000	International Society for Infectious Diseases (ISID)	International Journal of Infectious Diseases; <a href="http://www.isid.org/icid/">http://www.isid.org/icid/</a>
Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)	Annual	10,000	American Society of Microbiology (ASM)	Abstract book; <a href="http://www.icaac.org/">http://www.icaac.org/</a>
International Meeting on Emerging Diseases and Surveillance	Biennial	600	International Society on Infectious Diseases (ISPID)	Abstracts not available; <a href="http://imed.isid.org/">http://imed.isid.org/</a>
ISID – Neglected Tropical Diseases Meeting	Biennial	NA	International Society for Infectious Diseases (ISID)	Abstracts not available; <a href="http://ntd.isid.org/">http://ntd.isid.org/</a>

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<b>Name</b>	<b>Frequency</b>	<b>No. Attending</b>	<b>Association</b>	<b>Abstracts; website address</b>
World Congress of the World Society for Pediatric Infectious Diseases (WSPID)	Biennial	2300	World Society for Pediatric Infectious Diseases (WSPID)	Abstract book; <a href="http://www2.kenes.com/wspid/Pages/home.aspx">http://www2.kenes.com/wspid/Pages/home.aspx</a>

## **A2. Proposed MeSH level headings**

### **MeSH search terms, including but not limited to the following:**

- Brazil
- Communicable diseases (communicable disease control, communicable diseases, emerging, contact tracing)
- Dengue (Dengue complications, Dengue death, Dengue fever, Dengue haemorrhagic fever, Dengue shock syndrome, Dengue vaccines, Dengue virus)
- Diagnosis
- Disease notification
- Disease outbreak
- Disease transmission, communicable
- Disease transmission, infectious
- Disease vectors
- Effectiveness (comparative effectiveness research, treatment outcome, program evaluation)
- Epidemiology
- South America
- Surveillance (sentinel, population)
- Vaccinations

### **A3. Reference handling and data extraction**

#### **Retrieval**

- Papers identified as satisfying the inclusion criteria of the literature analysis will be retrieved electronically or in paper form, either directly from the journal website, or from sanofi pasteur.
- Other retrieval methods (e.g. from the British Library) will be used, as necessary.
- It is currently assumed that approximately **40** references will be eligible for inclusion in the analysis and reporting stages.

#### **Logging**

All references identified in the review entered in a Reference Manager database in which they will be assigned a unique identification number.

#### **Data extraction**

- The inclusion criteria for the literature analysis are wide and it is estimated that the searches will identify between 500 and 2000 articles for the selection process.
- It is possible, therefore, that the searches will generate more than the targeted number of studies for analysis (approximately 40). In this case, the search limits (see *Section 8.3*) will be re-examined with the LRG and, if necessary, amended prior to data extraction being undertaken.
- A data extraction form will be reviewed and approved by the LRG. In discussion with the LRG, a process for data validation and the method for resolution of disagreements will be agreed.
- The data extraction form will contain a set of fields for each study, including information such as: bibliographic information, study objectives, design, study population characteristics and study outcomes.

#### **Data synthesis and reporting**

- The results of the studies included in the literature review will be collated and summarised. If sufficient data are available, the results will be tabulated.
- The synthesis of findings will be reported according to a conceptual framework, which will be developed by the LRG. The synthesis will make it possible for readers to access evidence in relation to the parameters stated in the review objectives.

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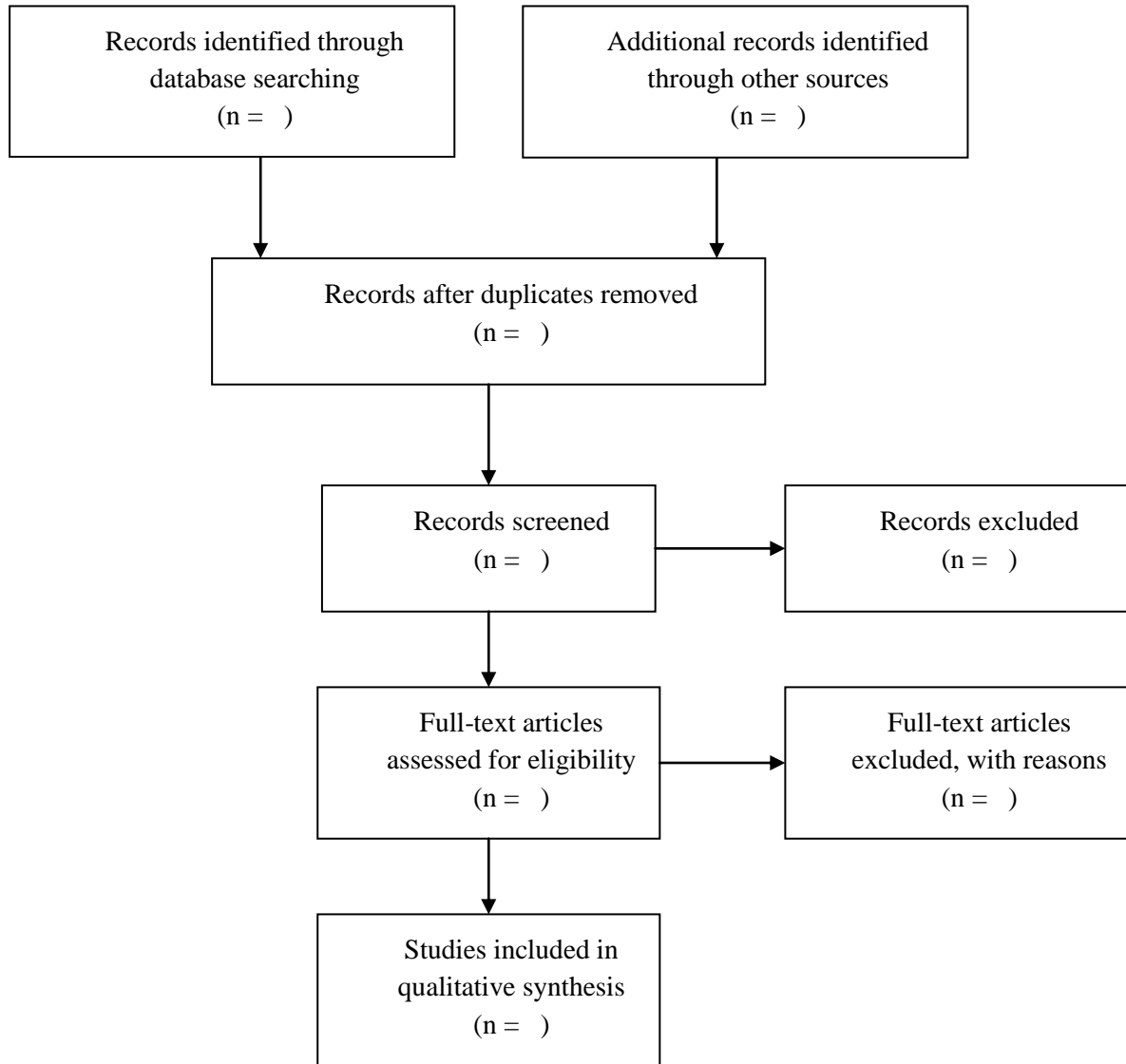
- The report will follow the relevant recommendations for reporting systematic reviews analysis developed by the PRISMA group.<sup>9</sup> A flow chart showing the number of studies/papers remaining at each stage will be used to document the study selection process (See *Appendix A4, page 16*).
- In addition to the initial report, other planned publications and authors of the publications will be identified within the LRG.

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<sup>9</sup> Preferred Reporting Items for Systematic Reviews and Meta-Analyses. <http://prisma-statement.org/>



#### A4. PRISMA Flow Diagram<sup>10</sup>



<sup>10</sup> Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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### A5. Evidence assessment template

RefMan identificati on no.	First author	Citation details	Funding/CI	Region (if known)	City/Geographical area	Evidence type (eg. clinical study, case report, etc)	Study design	Date range/ year	No. patients/p opulation studied	Male: Female	Age range	Notes	Corresponding author

Year	N	DF cases			DHF cases [confirmed]			DHF/ DF ratio	Mortality		Serotypes (%)				Sero- typing method (if known)	Prev- alence	Att- ack rate	Oth- er (eg Ro)	Not- es (1)	Not- es (2)	Geograph- ical scope
		Numb er [virolo gically confir med] {m:f}	Incid- ence rate	Hospitalisatio ns	Numb- er	Incid- ence rate	Hospitalis- ations		Number of deaths	Mort- ality rate [% of DHF cases]	1	2	3	4							