



# **WHO Advisory Committee on Variola Virus Research**

Report of the Tenth Meeting

Geneva, Switzerland  
19–20 November 2008

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## **Executive summary**

The major accomplishments in the variola virus research programme were as follows:

- Combinations of chimeric chimpanzee/human monoclonal antibodies fully protected mice challenged with vaccinia virus. The combinations were also active therapeutically, with protection against death even when administered three days after challenge.
- Submission for regulatory approval of the therapeutic agent ST-246 was aimed for 2010. Alternative formulations of ST-246, such as capsules for adults, oral suspensions for children and older people, and intravenous injectable forms for emergency situations are being investigated. WHO would act as a facilitator between potential users and SIGA Technologies for the availability of ST-246 in the case of a requirement for emergency compassionate use.
- The Committee considered that it would be premature to establish a WHO stockpile of any drug that did not yet have approval for use by drug regulatory authorities.
- Two diagnostic assays designed for field use based on real-time polymerase chain reaction (PCR) technology are currently being evaluated. It is anticipated that the assays will become available to Member States through international networks of commercial products.
- Two protein-based "point-of-care" diagnostic assays are in development.
- Discussions pointed out that currently available technology could allow the recreation of a full-length variola virus genome by chemical synthesis.

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## **1. Report from the Secretariat**

- 1.1. The WHO Advisory Committee on Variola virus Research met from 19 - 20 November 2008 with Dr David Evans as Chairman and Mr David FitzSimons as Rapporteur.
- 1.2. Dr Daniel Lavanchy recalled that the report of the ninth meeting had been noted by the Sixtieth World Health Assembly in May 2008. Over the past year, interest in antiviral drugs had subsequently increased and at the same time the need for transparency and for greater and equitable access to results was recognized. The mandate of the Committee was to consider research of public health importance.
- 1.3. A list of currently approved proposals was included in the documentation for participants, and the Committee updated the list. The review of research requested by Member States in 2010 expected that research projects that were currently ongoing would be concluded by that date, extension being considered after the review is finalized; that did not preclude submission of research proposals in the mean time or in the future but it did mean that clear goals were vital for assessing further research.

## **2. Update on variola virus strains held in the United States and Russian Federation repositories**

- 2.1. Dr I. Damon reported on the status of stocks held at the Centers for Disease Control and Prevention (CDC) in the United States of America and the time frames allotted for her research group to perform the WHO-approved research. She noted that the existing BSL-4 laboratory at the CDC is not scheduled to be re-opened until the end of 2008. The planned introduction of a new BSL-4 laboratory in 2009 will increase capacity for research. Since the previous report to the Committee, there have been no additions to or withdrawals from the long-term repository, but material was withdrawn from the laboratory stocks for work on agreed research protocols.
- 2.2. Dr A. Sergeev informed the Committee that, since November 2007, work at the State Research Centre of Virology and Biotechnology VECTOR in the Russian Federation has continued in four main areas: transfer of stocks from glass to polypropylene vials; study of viability of Asian strains of variola virus; antiviral agents; and neutralizing monoclonal antibodies. In particular, a new repository has been created in the same building where research is done, with high physical security, including automatic temperature controls and visual monitoring. No viable strain was detected among the Asian viruses studied. During the year, 200 working stocks of non-viable or duplicate material were destroyed, bringing the total number of vials in the repository to 691.

### 3. Update on prophylaxis and therapeutics

- 3.1. Dr B. Moss outlined progress in research into chimeric chimpanzee/human monoclonal antibodies. Combinations that targeted envelope and mature virion particle proteins fully protect mice infected intratracheally with the WR strain of vaccinia virus, with good dose-response values. The combinations were also active therapeutically, with protection against death even when administered three days after challenge, when mice had already suffered weight loss. The monoclonal antibodies acted synergistically, the combination of monoclonal antibodies Ch7D11 and Ch12F being the most potent.
- 3.2. Professor S. Shchelkunov, on behalf of Dr Tikunova who was unable to attend, described research on neutralizing antibodies against orthopoxviruses. Fully human recombinant antibodies were produced on the basis of mini-antibodies selected by a process of "biopanning" and shown to be specific for the H3L target protein. For the next year animal experiments are planned to analyse these antibodies in an animal model.
- 3.3. Professor S. Shchelkunov, on behalf of Dr Belanov who was also unable to attend, described recent advances in the development of antiviral agents against orthopoxviruses. A series of adamantane derivatives, nucleoside analogues and heterocyclic compounds have been synthesized and tested for antiviral activity in cell culture against various orthopoxviruses. The most active were then tested against different strains of variola virus in cell culture. Of 84 compounds tested, 74 from all three groups proved to be active. In 2009 it is planned to extend this research to cowpox virus and ectromelia virus in mice.
- 3.4. Dr J. Huggins reviewed developments in research of small-molecule antiviral agents. Safety concerns, in particular nephrotoxicity in the 300–600 subjects that would be required to establish safety of the four fold higher dose in man that corresponds to the efficacious dose in primates required to treat this acute infection, now preclude further work on cidofovir, even though the risk/benefit to a smallpox patient may be acceptable. The cidofovir lipid conjugated prodrug CMX001 that is designed to be administered orally has much greater activity but appears to be metabolized differently in primate models than in humans, making it impossible to evaluate CMX001 directly in non-human primate models even though it should be active in man, thus precluding evaluation under the Animal Efficacy Rule. A series of pyrimidine-5'-thionucleosides and in particular the 5-iodo compound show good oral activity against cowpox in mouse models and represent a new avenue for antiviral drug research and development.
- 3.5. ST-246 Advanced Development. Pharmacokinetic studies after oral administration of ST-246 to monkeys and man have established the appropriate equivalent primate dose to the proposed human dose of 400 mg/day. That dose is set at six-fold higher than the minimum effective equivalent primate dose. ST-246, at the primate dose equivalent to the proposed human dose, is efficacious in the monkeypox primate model, even when

treatment is initiated after onset of lesions in all animals, the time most patients would be expected to seek medical care. Recent FDA guidance on the studies required for ST-246 approval indicates that multiple additional variola primate and in vitro studies, requiring several years to complete, may be needed to provide the necessary information to allow drug approval, and also to provide critical information about how to implement a national intervention plan during a smallpox outbreak.

- 3.6. Dr D. Hruby outlined the timeline for the process of regulatory approval of ST-246, indicating that the aim was for making submissions in 2010 but this date is not fixed because of regulatory issues. Toxicity studies have been completed and all show no toxicity of note. The compound is easy to synthesize and stable, with a predicted shelf-life of at least three years. In clinical trials (whose data were unblinded earlier in 2008) no serious adverse event has been recorded with single or multiple doses. Experiments in numerous animal models all show protective efficacy against disease and death. Studies are in progress to see how vaccine and the antiviral agents can be used together. So far, results show no serious side effects and that the combination induces protective immunity in immunodeficient mice. Initial results in non-human primates indicate also good protection as well as decreased reactogenicity of vaccine and less viral shedding. Alternative formulations of ST-246 are being investigated, such as capsules for adults, oral suspensions for children and older people, and intravenous injectable forms for emergency situations. It was made available for emergency (compassionate) use for the treatment of a clinical case of eczema vaccinatum in 2007. Potential requests for its use should be directed to SIGA Technologies directly.

#### **4. Update on diagnostic assays**

- 4.1. Two presentations described developments in diagnostic assays. In a final report on work authorized until the end of 2008, Dr J. Huggins reported the evaluation of two assays designed for field use that were based on real-time polymerase chain reaction (PCR) technology with freeze-dried reagents and standardized protocols. One assay detected as few as 20 genome copies and differentiated variola virus from other orthopoxviruses, detecting virus in non-human primates infected with variola virus. The other assay, for differentiation between variola major and minor, was based on fluorescence and targeted noncoding sequences common to all variola strains that have been sequenced. Publications have described the probes and other information in sufficient detail to be replicated in other laboratories. Current collaboration with the private sector aims to stabilize reagents for the assays for room temperature storage. In response to a question Dr Huggins said that the system was a commercial product and underlined the utility of having a technology that was available to Member States through international networks.
- 4.2. Dr K. Karem described developments in protein-based diagnostic development under a protocol authorized until the end of 2007. Assays for viral nucleic acid had proven to be useful and specific, but examples existed where their utility had been compromised by delays between sample acquisition, testing and confirmation, and furthermore false-



positive PCR tests raised concerns. In addition, accessibility to the tests was not always feasible in the field. As a consequence, protein-based tests became desirable as a complement to nucleic acid assays. The protein-based assays were orthopoxvirus generic and not specific, thus needing confirmation by epidemiological data and PCR. "Point-of-care" assays needed to be simple to use, stable for long periods at room temperature, and should give rapid results. Two formats were being developed: for antigen and antibody detection. Pilot studies of a serological assay conducted in field conditions in the Democratic Republic of Congo during an outbreak of unknown rash illness confirmed the robustness of the assay and the absence of an orthopoxvirus infection. A virus-specific antigen-capture assay, using a commercially available polyclonal antibody, is being modified to increase sensitivity while an assay with killed antigen had a less dynamic range. Recent work with live variola virus revealed a significant loss of reactivity compared with gamma irradiated inactivated virus. A proposal for further research to explore the applications of this technology is being formulated. Further areas for potential research include proteomic arrays and vaccinia-specific epitopes. Participants commented on the potential of these diagnostic systems to field applications, as long as they were affordable and available, as an example of transfer of technology to the Democratic Republic of Congo.

## 5. Update on animal models

- 5.1. Dr P. Jahrling summarized five years of primate model development authorized by WHO to facilitate the evaluation and licensure of antiviral drugs and vaccines using the FDA Animal Efficacy Rule. Various combinations of primate species, variola strains, dose, and routes of exposure were evaluated. Uniform lethality was obtained when cynomolgus monkeys were exposed to a high dose ( $10^9$  pfu) of variola injected intravenously; 10-fold lower doses resulted in 30% mortality. These models simulated human smallpox but could be improved by developing more natural routes of exposure such as intratracheal or intrabronchial instillation with nebulizers. Additional enhancements could include evaluation of biomarkers and acquisition of clinical parameters using telemetry. Experimental infections of primates with variola and monkeypox viruses were compared with each other and with human data, where available, for tissue and cell tropisms, clinical changes, changes in gross pathology, comparison of histopathology, comparison of cytokines and soluble mediators, and comparison of host responses and viral gene expression using microarray technologies. Expression of more than 500 genes and significant key immune response pathways indicated that, although parallels exist, monkeypox may not be an adequate surrogate for variola. During the discussion, it was argued that monkeypox in monkeys did indeed offer a good model.
- 5.2. Significant progress has been made but further refinement of the animal models is desirable, including strategies to reduce the dose and to expose the animals via more natural routes. Promising antiviral drugs (e.g. ST-246), monoclonal antibody combinations and treatment strategies such as activated protein C and anti-cytokines should be tested for efficacy in the best available models.

## 6. Update on vaccines and vaccination

- 6.1. Dr I. Damon reviewed the experiments conducted in the maximum security BSL-4 laboratory at the Centers for Disease Control and Prevention (CDC) in the United States of America using live variola virus as the target of plaque reduction neutralization tests (PRNTs) in the evaluation of MVA and Dryvax vaccination regimens and presented additional statistical analyses. MVA vaccination regimens performed in a non-inferior manner and in some analyses the levels of variola neutralizing antibodies appeared higher than after vaccination with Dryvax. Additional analyses compared variola PRNTs performed at CDC with vaccinia Dryvax and MVA PRNTs obtained at the University of St Louis after vaccination with Dryvax or MVA. No linear correlation was found between aggregate PRNT responses against vaccinia Dryvax or MVA and variola virus (Solaiman). Additional analyses will further evaluate the role of the vaccination regimen. The data suggest that variola virus PRNT responses may be important for evaluating smallpox vaccines, especially if the vaccination regimen does not elicit the historical correlate of successful vaccination, that is take.
  
- 6.2. Dr H. Yokote gave an update of the attenuated vaccinia vaccine LC16m8, which has been licensed in Japan since 1975 and is being stockpiled. On the basis of studies in mice, it is expected that protective immunity may last for at least ten years in humans. Current research includes proteome arrays analysis, shows that both the antibodies from the LC16m8-inoculated and the Lister-inoculated mice recognized antigens from the extracellular enveloped virus (EEV) and intracellular mature virus (IMV). A study in SCID mice, which is an animal model of patients for whom vaccinia vaccine is contraindicated, showed that it is safer than the vaccine made from the parent Lister strain and preliminary data from studies in immunocompromised macaques suggest that it is safer than Dryvax. Results show that in mice protective immunity and neutralizing antibodies are long-lasting. Based on the animal studies, the risk of adverse events in an immunodeficient population is expected to be lower than with Lister or Dryvax vaccines. The Committee noted other advantages including the route of administration – the use of a bifurcated needle meant that the vaccine was simple to give in the field, and that only one dose was needed (compared with two for MVA). As in the smallpox immunization programmes, the visible take after vaccination meant that it was easy to track who had been vaccinated. During the discussion, the Committee recognized the advantages of LC16m8, and it was argued that LC16m8 had not received sufficient attention as a less reactogenic smallpox vaccine.

## 7. Regulatory issues

- 7.1. Dr M. Merchlinsky gave a brief overview of the current strategies being pursued to improve the safety of the smallpox vaccine while maintaining its efficacy. He pointed out that the US FDA's Center for Biologics and Research (CBER) requires that any

new vaccine candidate demonstrate efficacy in multiple animal models of smallpox, but that a model infection with variola virus would not be necessary. He noted that use of live variola virus would, however, be desirable, in terms of expediting the review process, for testing whether animals vaccinated with the new vaccines raised variola virus-neutralizing antibodies as well as the traditional vaccine. However, for the evaluation of new antiviral agents, demonstration of activity against live variola virus would be needed. It was argued on the other hand by one member of the Committee that the usefulness of non-variola animal models should not be underestimated and that they should be fully exploited. Other members stressed that a better understanding of the correlates of immunity or pathogenesis may be required for the evaluation of new vaccine candidates and therapeutics. When questioned about the timeline for full licensure of a new product, he replied that multiple years are required for even the most straightforward applications, and that in the case of a new product for variola a special advisory committee meeting would almost certainly be required, adding an additional year or more to final licensure.

## **8. Is there a need for stockpiling ST-246**

- 8.1. Dr D. Lavanchy informed the Committee that its previous report had generated interest among Member States, in particular about access to antiviral agents. Advice was therefore sought from the Committee as to whether it would recommend the stockpiling by WHO of any of the drugs that had so far showed promising activity in animal models of variola.
- 8.2. Dr D. Hruby indicated that SIGA Technologies had entered into discussions with some governments to provide ST-246 in case of the need for emergency use and would be willing to discuss such an agreement with WHO. After some discussion, the Committee considered that it would be premature to establish a WHO stockpile of any drug that did not yet have approval for use by drug regulatory authorities, and for which human safety and clinical data was still accruing. It was also mentioned that an in-depth evaluation of potential epidemiological scenarios would be required to estimate the need for drugs when they were approved. On the other hand it was pointed out by the Secretariat that in the event of an emergency requirement for compassionate use, WHO would attempt to facilitate contact between countries and manufacturers or other potential suppliers, as has happened in other contexts in the past.

## **9. Monkeypox**

- 9.1. Dr T. Muyembe described the natural history of human monkeypox in the Democratic Republic of Congo, based in a well-equipped referral hospital in the Kasai province, spared by years of civil conflict. In 2007–2008 more than 100 cases were seen and followed up clinically (number of lesions), haematologically, biochemically and by viral load. Some index patients handled sick or dead monkeys, and human-to-human transmission through close contact, especially in families, was observed. Contrary to

smallpox monkeypox transmission was limited to five generations or less and mortality was less than 5%. Monkeypox infections appear to have become more frequent in the country, particularly in the province of Kasai oriental, district of Sankuru.

## 10. Institute of Medicine (IOM) Report

- 10.1. The Committee was informed that the Institute of Medicine (IOM)<sup>1</sup> of the United States of America National Academy of Sciences has undertaken an assessment of future needs for variola virus research. It is currently in the process of producing a report incorporating an evaluation of its influential report in 1999 and considering whether there are unmet needs for research with live variola virus. The aim is to guide policy-makers and *not* to make any judgement on destruction or retention of stocks. The new report is expected to be published in mid-2009, and the Committee noted that it would potentially offer a valuable information resource for its own report to the World Health Assembly in 2011.

## 11. Synthesis of variola virus

- 11.1. Dr R. Drillien briefly overviewed new data in the literature suggesting that currently available technology could allow the recreation of a full-length variola virus genome by chemical synthesis, as has been done for other larger microorganisms, or from modification of existing poxviruses.
- 11.2. The Secretariat reminded the Committee that WHO had published guidelines on the use of fragments of variola virus DNA which strictly excluded the synthesis of the virus.<sup>2</sup> Members of the Committee were strongly encouraged to promulgate these guidelines widely, not just in the orthopoxvirus research community but widely among other researchers and policy-makers.

## 12. Review of research proposals

- 12.1. Dr D. Lavanchy, referring to the five-member Scientific Subcommittee for the review of research proposals, reported that the recently introduced questionnaire had facilitated the review process, but also that concern had been conveyed about delays in the process. He proposed that the Committee consider the addition of ad hoc substitutes, at the discretion of the Chairman of the Subcommittee. The Committee accepted the suggestion for expanding the Subcommittee to seven members but allowing decisions to be made by only five in order to improve the Subcommittee's functioning. The Advisory Committee approved the membership of the new subcommittee. The Secretariat would take into consideration other suggestions about the application of web-based tools to assist documentation and increase transparency

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<sup>1</sup> For details of membership of the Committee and outline of presentations, see [www.IOM.edu/CMS/3783/57706.aspx](http://www.IOM.edu/CMS/3783/57706.aspx).

<sup>2</sup> Weekly Epidemiological Report, 2008, Vol. 83, No 44, p.393.

and better focus, reflecting the mandate of the Advisory Committee, and exposition of proposals. One participant reiterated a plea for a broader remit for research in view of clinical and public health needs and in the context of advances in technology. The Secretariat emphasized that research must be essential to public health in order to meet the demands of the Member States.

### 13. 2011 Review and process

13.1. Dr D. Lavanchy recalled that the Health Assembly in resolution WHA60.1 requested the Director-General to undertake a major review in 2010 of the results of the research undertaken, currently under way, and the plans and requirements for further essential research for public health purposes so that the Sixty-fourth World Health Assembly in 2011 may reach global public consensus on the timing of the destruction of existing variola virus stocks. As a consequence the Committee decided to consider the following methods for the review

- Comprehensive review of the literature and of unpublished data concerning live variola virus research by a group of scientists endorsed by the Committee representing all areas of research and development on orthopoxviruses;
- Consideration by the Advisory Committee of the above mentioned reviews;
- External review of the above mentioned reviews by independent experts from outside the variola virus field;
- Preparation of a report of the major reviews for the final consideration by the Advisory Committee (September – November 2010)
- January 2011 - consideration of the report of the major review of the research mandated by resolution WHA60.1, including the recommendations of the WHO Advisory Committee on Variola Virus Research (WHA60.1 OP4(1)) by the Executive Board of WHO;
- May 2011 - consideration of that report and the Board's comments by the Health Assembly.

13.2. The Committee agreed the following proposals for the contents of the state-of-art review which should target a broad range of readers, including the general public:

- the current state of the variola virus stocks and repositories;
- diagnostics;
- genomics;

- vaccines;
- therapeutic agents;
- animal models and pathogenesis;
- benefits.

13.3. In addition, above mentioned comprehensive review should also address policy issues such as how to respond to and manage outbreaks, as well as advanced development and regulation of relevant biologics and drugs, with final conclusions and recommendations about the way forward. The Committee proposed to select lead authors for each research area, to include experts who are not variola virus researchers in the review process and to take into consideration the initiative recently launched by the IOM to review work on variola virus.

#### **14. Variola virus diagnostic network**

14.1. An ad hoc discussion was conducted regarding a WHO Secretariat proposed “Informal Network of Laboratories for Smallpox confirmatory diagnostics”. A series of member laboratories was proposed. Most felt such a network would be important, but additional details were requested on criteria for membership, quality management, and diagnostic testing to be employed. Specifically, the desire to limit culturing of infectious material was mentioned. There was additional discussion about how to formalize such a network, in particular the verification of smallpox diagnostic capabilities with the involvement of the two WHO Collaborating Centres for smallpox, but no consensus statement or criteria were determined.

## **Annex 1: Agenda**

### 10<sup>th</sup> Meeting of the WHO Advisory Committee on Variola Virus Research

19 and 20 November 2008

Salle A, WHO Headquarters, Geneva, Switzerland

### **Agenda**

#### **19 November 2008**

- |               |   |
|---------------|---|
| 9:00 – 9:15   | Opening – D. Heymann<br>Election of chair & rapporteur  |
| 9:15 – 9:30   | Report of the secretariat – D. Lavanchy   |
| 9:30 – 9:45   | Update on research proposals submitted to WHO – D. Lavanchy   |
| 9:45 – 10:00  | Update on variola virus strains held in the US repository – I. Damon  |
| 10:00 – 10:15 | Update on the current status of the collection of variola virus strains held in the Russian repository – A. Sergeev   |
| 10:15 – 10:30 | Prophylactic and therapeutic activities of chimeric chimpanzee/human and mouse/human monoclonal antibodies to vaccinia virus membrane proteins in a mouse model – B. Moss   |
| 10:30 – 11:00 | <b>Tea/Coffee Break</b>   |
| 11:00 – 11:15 | Evaluation of multiple variola assays utilizing the US Department of Defense fieldable diagnostic platforms (authorized until 2008 – final report) – J. W. Huggins  |
| 11:15 – 11:30 | Protein-based diagnostic development. Testing of non-human primate sera against intact variola virus and characterization of existing monoclonal antibodies (Authorized until the end of 2007– final report) – K. Karem |
| 11:30 – 11:45 | Development of therapeutic variola antibodies (authorized until 2009 if progress reported at the 2008 meeting – progress report) – N. Tikunova  |
| 11:45 – 12:00 | Discovery of antivirals for smallpox treatment and prevention (authorized until the end of 2009 – interim report) – S. Shchelkunov  |

- 12:00 – 13:15    **Lunch**
- 13:15 – 13:30    Antiviral therapy of smallpox and other pathogenic orthopoxvirus infections resulting from terrorist or biological warfare release (authorized until the end of 2009 – progress report) – J. W. Huggins
- 13:30 – 13:45    The use of live variola virus to support less reactogenic vaccine development. Proposal to evaluate the capacity of sera, generated through animal or human trials with less reactogenic smallpox vaccines, to neutralize IMV and EEV forms of live variola virus (approved 2008 – progress/final report) – I. K. Damon
- 13:45 – 14:00    Refinement of the primate model for human smallpox to facilitate licensure of antiviral drugs and other countermeasures (authorized until 2007 – final report) – P. Jahrling
- 14:00 – 14:15    Update on ST-246 drug development – D. Hruby
- 14:15 – 14:30    Results from the study of the natural history of human monkeypox in the Democratic Republic of Congo – T. Muyembe
- 14:30 – 14:45    Update on attenuated smallpox vaccine LC16m8 – H. Yokote
- 14:45 – 15:00    Discussion: correlates of immunity; what work requiring live variola virus is necessary for licensing of 3rd generation vaccines? – M. Merchlinsky
- 15:00 – 15:15    Discussion
- 15:15 – 15:45    **Tea/Coffee Break**
- 15:45 – 16:00    Needs for stockpiling anti-viral drugs by WHO? – D. Lavanchy
- 16:00 – 16:30    Discussion
- 16:30 – 16:45    Rules to establish task force and process for 2010 review – D. Lavanchy
- 16:45 – 17:30    Discussion
- 17:30 – 17:45    Review of research proposals : streamlining timelines, designation of secondees for the scientific subcommittee and proforma questions – D. Lavanchy
- 17:45 – 18:15    Discussion
- 
- 18:15 – 19:30    Social event at the WHO main cafeteria

**DAY 1 CLOSES**



**20 November 2008**

- 9:00 – 9:15 Information on IOM smallpox activities – D. Ulaeto
- 9:15 – 9:30 Discussion
- 9:30 – 9:45 Variola virus synthesis – R. Drillien
- 9:45 - 10:15 Discussion
- 10:15 – 10:45 **Tea/Coffee Break**
- 10:45 – 11:00 Miscellaneous
- 11:00 – 11:15 Discussion
- 11:15 – 12:00 General discussion and preparation of draft recommendations
- 12:00 – 13:30 **Lunch**
- 13:30 – 15:00 Final discussion of draft recommendations
- 15:00 – 15:30 Tea/Coffee Break**
- 15:30 – 17:30 **Monkeypox**
- 15:30 – 15:45 Opening – P. Formenty
- 15:45 – 16:00 Update on monkeypox activities – P. Formenty
- 16:00 – 16:15 The DRC monkeypox activities – J.J. Muyembe
- 16:15 – 16:30 Molecular investigation of monkeypoxvirus isolates from the Democratic Republic of Congo – H. Meyer
- 16:30 – 16:45 Molecular Biology of monkeypox strains: a tale of 2 clades – I. Damon
- 16:45 – 17:00 The Kole monkeypox project: case management of monkeypox – J. Huggins
- 17:00 – 17:15 A monkeypox outbreak in Bentiu Suda – P. Formenty
- 17:15 – 17:30 Summary and conclusions – P. Formenty

**MEETING CLOSES**

## **Annex 2: List of Participants**

### **10th Meeting of the WHO Advisory Committee on Variola Virus Research from 19 to 20 November 2008, Salle A, WHO Headquarters, Geneva**

#### **LIST OF PARTICIPANTS**

##### **TEMPORARY ADVISERS**

##### **MEMBERS OF THE ADVISORY COMMITTEE**

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