

SCIENTIFIC COMMITTEE MEETING

Ebola Vaccination Initiative Baltimore, Maryland, August 28, 2008

The first Scientific Committee meeting of the Great Ape Ebola Vaccination Initiative was organized by the Center for Biosecurity of the University of Pittsburgh Medical Center (UPMC) in conjunction with the World Wildlife Fund (WWF) and the Max Planck Institute for Evolutionary Anthropology. The Scientific Committee was convened in order to advise and make recommendations to the Ebola Vaccination Initiative regarding technical and pragmatic considerations for selecting, testing, developing, manufacturing and deploying an Ebola vaccine for the great apes. The Scientific Committee is comprised of experts in conservation, ape immunology, field ecology, vaccine development, microbiology, and Ebola pathology (see **Appendix A**).

Scientific Committee Meeting.....	1
Ebola: a major threat to gorilla survival.....	2
Concept of use for an ebola vaccine: oral baiting vs. darting.....	2
Discussion of available vaccine platforms for development.....	4
Ethical considerations	6
Recommended next steps and potential challenges.....	7
Appendix A: Scientific Committee Meeting Attendees.....	9
Appendix B: Gorilla populations and locations.....	11
Appendix C: Ebola/Marburg Vaccine Platforms.....	12
Appendix D: Impact of Ape Ecotourism	12

EBOLA: A MAJOR THREAT TO GORILLA SURVIVAL

Peter Walsh began with a presentation about the threat of Ebola to the African great apes, as well as the difficulties of working with animals in the dense forests of Central Africa. He estimates that Ebola has killed about one third of the wild gorilla population, and that the Ebola death toll could rise to one half of the world gorilla population in the next 7-10 years. He predicts that an epizootic wave of Ebola is moving through the Congo Basin at rate of 35-40 km/year, placing a recently reported trove of 125,000 gorillas¹ directly in the path of likely future Ebola outbreaks.

The following points were highlighted in the discussion that followed:

- The reservoir for Ebola virus is unknown, though fruit bats are strongly suspected.
- How Ebola virus is transmitted in great apes is unclear. Gorillas may contract Ebola from fruit that is contaminated by the saliva or feces of infected fruit bats. Gorillas may also, by virtue of their social structure and sharing food, spread the disease to other gorillas. It is not known whether there is transmission via the respiratory route for gorillas.
- It unknown whether Ebola outbreaks affecting great apes have occurred since the 2005 outbreak. There has been no systematic effort to search for Ebola outbreak activity in the past 3 years, although WCS has tested carcasses, none of which have been positive for Ebola virus.
- For carcass sampling, PCR testing is more indicative than testing for antibody titers, but virus isolation is the gold standard.
- There are no published data documenting whether wild apes have survived Ebola. The fatality rate among individually known gorillas has been very high (~95%; possibly even 100%) and it is assumed that wild apes incapacitated by Ebola would be vulnerable to many other threats. Trish Reed (WCS) briefly discussed ongoing work, looking for evidence of past Ebola infections in healthy gorillas. WCS has collected gorilla fecal samples in areas where outbreaks have occurred. Nancy Sullivan (NIH, and also on the Scientific Committee but not present at the meeting) assayed the fecal samples for antibodies to Ebola Zaire, and found cases of reactive antibodies (unpublished work). WCS is using fecal samples from zoo gorillas as a control population. It was suggested, however, that the laboratory assay should be double blinded, and that the control samples should be from wild (not zoo) gorillas for greater confidence. Other pathogens including measles, anthrax, and RSV have recently killed gorillas and chimpanzees. Transmission of respiratory viruses from tourists to habituated gorillas and chimpanzees is a particular concern.

CONCEPT OF USE FOR AN EBOLA VACCINE: ORAL BAITING VS. DARTING

The “field requirements” or concept-of-use for an Ebola vaccine were discussed next. The options included delivering vaccine by dart versus delivering an oral vaccine in baits, similar to those which were used to eradicate canine rabies virus from much of Europe. Darting and baiting

¹ By the Wildlife Conservation Society, on August 5, 2008

both present clear challenges for vaccine development and use in the field. The preferable method largely depends upon the ultimate goal of the vaccine project. If the goals are to provide protection for select populations, such as isolated populations in danger of extinction, or habituated populations of economic/scientific importance, then darting may be preferable (see **Appendix B for the numbers of habituated animals**). If the goal is to vaccinate large populations (e.g. in front of the wave of Ebola), then oral baiting may be preferable. Another suggestion was to reduce epizootic spillover, by vaccinating bat populations. However, as the Ebola virus reservoir is not definite, and vaccinating large populations of rapidly reproducing bats would be extremely difficult, was determined to be infeasible at this time.

Darting: Darting has been used to deliver vaccines to wild gorillas, and is more technically and politically tractable than oral baiting. In 1990, approximately 70 Mountain gorillas were vaccinated against measles using darts. Field and zoo veterinarians use darting to vaccinate gorillas, or sedate them for treatment. It is a dangerous job to dart a gorilla, but can be done if necessary. A vaccine that would need more than one dose would be very difficult to administer—Older darting technology is only effective within about 10 meters of a gorilla, but new technology may extend the range to several tens of meters (see section below on the biobullet, which may diminish some of the issues associated with darting). To minimize trauma, darts must travel at a low velocity, which leads the darts to be less accurate. This is complicated further by the low visibility across long distances in the forest. The estimated 250-300 Cross River gorillas² cannot be located easily, so it may not be possible to dart them.

Baiting: Oral baiting was used to eradicate rabies from large parts of Europe, but has never been attempted in the Congo Basin or for gorillas. Initial baiting trials performed by Peter Walsh using a fructose filled, fruit-flavored wax bait³ have been somewhat successful in captive animals. Preliminary trials on habituated gorillas in the Central African Republic produced limited success. Baiting has many inherent challenges, including the following:

- Stability of the vaccine formulation, especially if a live vector is used;
- Safety, especially the impact on non-target species from bait consumption or viral shedding;
- Acceptability to gorillas, as they are picky eaters;
- Need for testing non-target species that may also eat the vaccine;
- Tractability, as it would be difficult to know if gorillas were protected; and
- Dosing, because apes may eat more than one vaccine.

In studying an Ebola vaccination strategy in great apes, WCS came to the conclusion that an oral vaccination program would be most desirable because of the potential for vaccinating more apes.

Alternative Strategies considered by the committee:

² <http://www.iucnredlist.org/details/9404>

³ Manufactured by Impfstoffwerk Dessau-Tornau (IDT): Dessau, Germany.

- Postpone decision about darting or baiting, and concentrate on determining the most efficacious vaccine.
- Pursue two separate programs, for baiting and darting, though costs/development time increase. For an oral vaccine, it would take 2-5 years to develop a program. Using natural fruit could make a difference in acceptability to gorillas but would entail additional vaccine packaging challenges.
- BioBullet: Ballistic Technologies, Inc. created the BioBullet, which is a technique and equipment for vaccinating and treating wild animals without catching them⁴. Consists of hollow pellets made of hydroxypropylcellulose which dissolves in living tissue. The 25 caliber pellet is discharged from an air 'gun' and has low impact velocity and poor penetration. BioBullet was used to eradicate brucellosis in bison with little disturbance to bison behavior. Target accuracy is about 4in. at 50-100 m, a distance that exceeds the typical range of visibility in the Central African forest. Time release formulation might allow “prime and boost” strategy with only one vaccination.
- Aerosol vaccine: Increases the possibility of non-target species exposure if applied indiscriminately. But aerosol would degrade rapidly when exposed to UV light, so might reduce non-target exposure if applied selectively (e.g. with triggered traps). Not all sprays are the same – delivery method varies with droplet size, and the efficacy of an aerosol vaccine will be dependent on the formulation and droplet size of the vaccine.
- Bio Needles: are small hollow mini implants fabricated from biodegradable polymers which can be filled with antigen.² Bioneedles can be used for vaccination without syringes and needles and can be formulated to break down at different rates. They can degrade immediately (suitable for prime), or stable for weeks (booster).

DISCUSSION OF AVAILABLE VACCINE PLATFORMS FOR DEVELOPMENT

Vaccine Candidates: Keith Wells described six Ebola vaccine candidates in various stages of development for human use. These include a plasmid DNA platform, virus-like particles (VLP), and several vector-based approaches (VSV, adenovirus, alphavirus, parainfluenza, etc). There are also vaccine platforms that have been abandoned for human use, but could have potential for great apes. **(The complete list can be found in Appendix C)** Outstanding scientific questions were highlighted, including the need to determine the correlates of Ebola immunity in apes, proving safety and efficacy, determining the duration of immunity after vaccination, and determining the number of doses required for complete protection. After the August 28 Scientific Committee meeting, the National Institutes of Allergy and Infectious Disease (NIAID) announced two contracts on September 26, 2008 for development of a multivalent Ebola vaccine to:

1. Integrated BioTherapeutics, Inc. for its VLP Ebola virus candidate and
2. Crucell Holland BV for its adenovirus vector Ebola virus candidate.

⁴ <http://www.solidtechah.com/bds.php>

- **Target product profile:** Before deciding which vaccine to develop, the first step should be a product profile for both a parenteral and oral vaccine, determining the vaccine characteristics. Durability (how long will the immunity last?) of 5 years may be enough, but the vaccine must protect longer than a year. A multivalent vaccine may be important as Ebola vaccines are generally not cross-protective across strains. The product profile will be largely dependent on program objectives. For example, an important consideration is whether to vaccinate only accessible/habituated animals vs. wild. An oral vaccine would be at least 5 years down the road. Partial immunity is not ideal but not necessarily a wasted effort.
- **Costs:** Bob Nordren (Meriel) suggested that it might cost approx \$2.5 million over 18-28 months to get a vaccine ready to go to the field, including getting a conditional license, from time of proof of concept by vaccinating after challenge. It is relatively easy for industry to produce this size batch of vaccine. However, it may be difficult to engage commercial vaccine companies working on Ebola vaccine candidates (i.e. Crucell) due to the risk to their human vaccine candidates.
- **Regulations/ Licensing:** In the US, a vaccine would be licensed through USDA. It would be important to get a conditional license, which allows the vaccine to be used relatively freely in the target population (this would be a precursor prior to approaching African governments for an agreement to use the vaccine in their borders). To get a conditional license, the following criteria must be met: manufacturing process that is licensable; some safety data for licensed vaccines (20-30 gorillas in relatively high dose); reasonable efficacy shown (loose term up to interpretation and is influenced by degree of imminent threat).
- **Adenovirus vector:** The adenovirus vaccine platform has a well developed manufacturing process and the Ebola vaccine on the adenovirus platform has been effective in non-human primates in one dose. This vector also has potential for oral administration of vaccine, although oral delivery would require an enteric capsule. Pre-existing immunity to the adenovirus vector is a challenge, as 97% of wild mountain gorillas tested had adenovirus antibody titers. Unpublished data suggests that if a monkey has any antibodies for AD5, the vector does not work. In other literature with rodents, mucosal administration circumvents anti-vector immunity, but the adenovirus platform may not work well with mucosal administration. Number of doses (prime-boost) and dosing will be an issue. This platform has also recently come under intense scrutiny following the failure of the ad-vector HIV vaccine.
- **VSV:** The *Vesicular stomatitis virus* (VSV) can infect insects and mammals and is a virus in the same family as the Rabies virus. The Ebola vaccine using the VSV platform is a live vaccine, is better for mucosal administration, and is likely to receive Department of Defense (DoD) funding through the Defense Threat Reduction Agency (DTRA). In macaques, the VSV Ebola vaccine conferred one-dose protection and showed potential for post-exposure application. Not as dangerous if you dart, but there are global opposition groups, i.e. groups opposed to genetically modified organisms
- **VLP:** The virus-like particle (VLP) is a particle that self-assembles from specific virus structural proteins expressed in insect or mammalian cells. Because VLPs lack nucleic acids,

they cannot replicate and are considered to be a safer option. The vaccine platform has precedence for use in humans with the Gardasil vaccine. The VLP Ebola vaccine has conferred protection in cynomolgus macaques using VLPs containing GP, NP, VP40 matrix protein after challenge with 1000 pfu four weeks later. There is an intellectual property issue with this platform that could be problematic. The Wisconsin Alumni Research Foundation owns the patent. VLP vaccines may also require multiple doses and questions regarding efficacy remain.

- **Background on NIAID contracts:** On September 30, 2008, NIAID and BARDA awarded 2 contracts for development of a multivalent Ebola and Marburg vaccine to Crucell Holland BV and Integrated BioTherapeutics, Inc. The requirements of these contracts are that the vaccine protect against the four strains (Zaire, Sudan, Ivory Coast, Reston) of Ebola and against one strain of Marburg (Ci67, Musoke, other). The vaccine must also confer protection in, at most, 2 doses. Crucell is working with the Vaccine Research Center (VRC) at NIH, using an adenovirus vector platform for delivery of the vaccine. Its award is for \$29.8 million with options that could add \$40.5 million to the contract. Integrated BioTherapeutics is using a virus-like particle (VLP) vaccine platform and is working with collaborators at the United States Army Research Institute of Infectious Diseases (USAMRIID). The award for Integrated BioTherapeutics was \$22.5 million with options that could increase the contract by \$42.7 million.⁵

ETHICAL CONSIDERATIONS

Vaccinating great apes in a politically and environmentally complex region raises a number of ethical considerations. At the Scientific Committee meeting, a discussion of these issues was designed to anticipate some of the ethical questions that would be raised.

- Why vaccinate gorillas and not people? The requirements for human vaccination are more stringent; great ape vaccination may be a stepping stone towards eventual approval of a human vaccine; precedence of vaccination against other veterinary diseases that also affect humans, i.e. vaccination of livestock in Africa for Rift Valley Fever virus.
- Animal rights issues (perception of testing human vaccine on gorillas); in particular, the project needs to be cognizant of GMO (vaccine) release, and need to prove safety and efficacy (though efficacy will be difficult to prove without testing).
- Influence of cultural differences on perception of what is being done: Must be cognizant of perceptions of witchcraft, especially in an outbreak area. Some area populations have very little understanding of vaccination and/or Ebola.
- What happens if a gorilla dies after vaccination? What happens if gorillas die of an unrelated event during the vaccination program?

⁵ Rambhia, K. NIAID, BARDA Award Anthrax Vaccine Contracts, Ebola/Marburg Contracts. Biosecurity Briefing. October 6, 2008. http://www.upmc-biosecurity.org/website/biosecurity_briefing/index.html#bb2. Accessed October 9, 2008.

- Should we vaccinate? Should we allow the natural course of disease? Why interfere when it is not a human induced disease? Ebola is a naturally occurring disease. The great apes are the closest relatives to humans, and also have economic value for ecotourism (See Appendix D for ecotourism data) (esp. Uganda, Rwanda, DRC).

RECOMMENDED NEXT STEPS AND POTENTIAL CHALLENGES

The meeting concluded with a group effort to synthesize the most important questions that will need to be addressed in moving this initiative forward. Each Scientific Committee member offered insights on the initiative. Some of these recommended next steps may be contradictory, but are recorded here for further discussion and research.

- Priority targets should be accessible/habituated animals.
- One dose vaccine and delivering preferentially with dart like mechanism is the fastest track to vaccination.
- Determine if there are separate regulations for pediatric animals in USDA regulations
- Will the vaccinators pose a risk of exposing gorillas to new diseases when they get close enough to vaccinate gorillas?
- Oral bait is the best option for large numbers of animals. While testing vaccine for gorillas, testing for non-target species must also be going on.
- Parallel strategy development is a possibility—the group can do something quickly to protect apes at high risk of contracting Ebola or those of special concern due to their unique ecological, taxonomic, scientific or economic importance, but the program can also develop a longer term strategy for larger populations. Have a plan “B” to achieve goals (worse case scenarios may become the best possible option)
- Correlates of immunity for protection against Ebola would be very valuable.
- Studies that correlate results of immunity with gorillas, chimpanzees, and macaques will be helpful for feasibility studies.
- Can studies be done in chimps? Southwest Foundation quotes about \$100K for vaccine tests on six chimpanzees: currently in touch with other labs for better pricing/cost sharing. The most valuable thing is to own data regarding VSV in chimps, 3-6 chimps which would lead to critical decision for industry to fund vaccine candidate.
- Find an industrial partner (critical to success)
- One Health Initiative has interest in this problem and this is being explored by the Center for Biosecurity.
- Field front: determine if Gorillas are dying and track Ebola. More dung data is needed to determine preexisting immunity to vaccine vectors– in the field.
- 3 candidates: VLP, VSV, Adenovirus – conduct captive tests and gather concrete data with these three (chose these three because they cover the spectrum from extreme to extreme, i.e. stability, safety).
- Metrics for down-select process for vaccine candidates should be addressed in the future

- Contingency plan – Ebola is dangerous: need action soon in case of event
- Must make outreach to African partners soon
- Need to clearly refine the goals of the project
- Role for traditional conservation policies, i.e. develop robust populations that can withstand Ebola
- Multivalent and combine other diseases in same vaccination so that if the Ebola component is not effect, the efforts are not wasted. Think about a multivalent vaccine and keep other diseases in mind, such as respiratory diseases
- No possible ways to do challenge studies on vaccinated gorillas. Because challenge studies in non-human primates are done in BSL4 labs and designed to advance human vaccines – be in close communications with them to get the information needed for down-selecting vaccine candidates for gorillas

APPENDIX A: SCIENTIFIC COMMITTEE MEETING ATTENDEES

Allard Blom, PhD

Director, Congo Basin,
Namibia and Madagascar
World Wildlife Fund

Nidhi Bouri

Analyst
Center for Biosecurity of UPMC

Michael R. Cranfield, DVM

Director, MGVP, Inc. (Mountain Gorilla
Veterinary Project)
Director of Research and Conservation
Maryland Zoo in Baltimore

Andrew P. Dobson, PhD

Professor
Ecology and Evolutionary Biology
Princeton University

Diane M. Doran-Sheehy, PhD

Professor and Chair
Department of Anthropology
SUNY at Stony Brook

Thomas Fuerst, PhD

Senior Science Advisor
Office of Biomedical Advanced Research
and Development Authority (BARDA)
Office of the Assistant Secretary for
Preparedness and Response (ASPR)
U.S. Department of Health and Human
Services

Thomas W. Geisbert, PhD

Associate Director
National Emerging Infectious Diseases
Laboratories Institute
Professor, Department of Microbiology
Professor, Department of Medicine
Boston University School of Medicine

Gigi Kwik Gronvall, PhD

Senior Associate
Center for Biosecurity of UPMC

Thomas V. Inglesby, MD

Chief Operating Officer, Deputy Director
Center for Biosecurity of UPMC

Damien Joly, PhD

Wildlife Epidemiologist
Associate Director for Wildlife Health
Monitoring and Epidemiology
Global Health Programs
Wildlife Conservation Society

Brandi Klotz

Senior Administrative Assistant
Congo Basin, Namibia, Madagascar
World Wildlife Fund (WWF)

Michael G. Kurilla, MD, PhD

Director, Office of BioDefense Research
Affairs
Associate Director for BioDefense Product
Development
DMID, NIAID, NIH, DHHS

Myron M. Levine, MD, DTPH

Head, Division of Geographic Medicine
Grollman Distinguished Professor and
Director
University of Maryland School of Medicine
Center for Vaccine Development

Tom Monath, MD

Partner
Kleiner Perkins Caufield & Byers

Robert M. Nordgren, MS, PhD

Head, Research and Technology Acquisition
Merial, Ltd.

Anne Pusey, PhD

Professor
Department of Ecology, Evolution and
Behavior
University of Minnesota

Patricia (Trish) Reed, DVM

Field Veterinarian, Congo
Wildlife Conservation Society

Kunal Rambhia

Analyst
Center for Biosecurity of UPMC

Jean-Francois Saluzzo, PhD

Senior Director, Expert Virology Global
Manufacturing Technology
Campus Merieux, Sanofi Pasteur

Alan Schmaljohn, PhD

Professor of Microbiology and Immunology
University of Maryland School of Medicine

Christine SooHoo, MS

Analyst, Center for Biosecurity of UPMC

Peter Walsh, PhD

Max Planck Institute for Evolutionary
Anthropology, Department of Primatology

Keith Wells, PhD

Senior Consultant
The Biologics Consulting Group
Massachusetts Office

APPENDIX B: GORILLA POPULATIONS AND LOCATIONS

	<u>Western lowland gorilla</u> (G. GORILLA GORILLA)	<u>Eastern lowland gorilla</u> (G. GORILLA GRAUERI)	<u>Mountain gorilla</u> (G. GORILLA BERINGEI)
Location	Lowland rainforests from Cameroon to the Congo River	Lowland rainforests of the eastern Democratic Republic of the Congo (Kinshasa)	Mountain rainforests and bamboo forests of the highland terrain north and east of Lake Kivu, near the borders of Uganda, Rwanda, and Congo (Kinshasa)
How Many	-Habituated: 50 gorillas in 3 groups -Total: Hundreds of thousands	-Habituated: 0 -Total: 5000	-Habituated: ~300 -Total: 700

6



⁶ Max Planck Institute for Evolutionary Anthropology: Department of Primatology: <http://www.eva.mpg.de/primat/files/gorillas01.htm>. Accessed October 20, 2008

APPENDIX C: EBOLA/MARBURG VACCINE PLATFORMS⁷

Vaccine type	Comments	Principal Concerns
killed filovirus	Early vaccine efforts and recent proofs of concept; inadequate efficacy in NHP	safety; potency; observed disease exacerbation
live attenuated filovirus	Only as proofs of concept with natural or passaged viruses; high risk could theoretically be mitigated by reverse genetics approach	live vaccine safety; incomplete attenuation or reversion
expressed protein, baculovirus	Incomplete efficacy in guinea pigs, no reported efficacy in NHP, may perform better if optimized	potency, adjuvant requirement; altered glycosylation
live vaccinia vectored	Proof of concept, deprioritized for human use along with other live pox-vectored vaccines	vaccinia safety; vector immunity ^d ; potency
DNA	Adequate in rodents; incomplete NHP efficacy with MARV and none reported with EBOV; touted for immunological priming	potency
defective adenovirus	Excellent rodent and NHP efficacy at high doses (e.g. 10 IU). First demo of NHP efficacy and single-shot efficacy with EBOV in NHP	vector immunity, safety at doses high enough to achieve potency
virus-like particles	Efficacy in both rodents and NHP	potency; adjuvant requirement
live recombinant vesicular stomatitis virus, VSV	Excellent rodent and NHP efficacy with both MARV and EBOV. Single shot vaccine, rapid immunity. No overt illness from live vaccine itself. In recombinant, filovirus GP replaces VSV GP	live vaccine; balance of safety & potency; environmental release
live recombinant parainfluenza	Good efficacy against Ebola in guinea pigs and NHP, contains both parainfluenza and EBOV glycoproteins	live vaccine; balance of safety & potency; environmental release
defective VEE replicon	Excellent rodent efficacy, first demo of NHP efficacy against MARV, potency of 10 IU near "tipping point" in NHP	vector immunity; safety at doses high enough to achieve potency

APPENDIX D: IMPACT OF APE ECOTOURISM

⁷ Adapted from Nat Rev Immunol [2007] 7:556-567.

	Rwanda ⁸	Uganda ⁹	DRC ¹⁰
Quick Facts:	GDP (2007 est.): \$2.8 billion. <i>Per capita income</i> (2006 est.): \$260.	GDP (nominal, 2006/2007): \$10.8 billion. <i>Per capita GDP</i> (2007): \$900	GDP (2007): \$9.85 billion. <i>Per capita GDP</i> (2007): \$300.
What is the current impact of ecotourism on the economy?	Tourism (mainly ecotourism) is the <u>third</u> most significant industry to Rwanda's economy (after agriculture and minerals and before exports)	More than 70% of Uganda's tourism revenue comes from gorilla tourism (Visitors increased from 2,250 in 1995 to 3,450 in 1998)	-Ecotourism has a role in the economy- but depends on the perceived security of the area -Social structure of gorillas in this area is different; it is more difficult and more expensive to habituate groups
How much revenue is Gorilla Tourism generating?	- Gorilla tourism alone generated about \$7 million in 2007 - In 2000 only 3,700 tourist totals visited Rwanda; by 2008, over 38,000 visited, generating \$42.3 million (mainly going to Northern Rwanda for gorilla tourism) - Number of foreign tourists and prices have consistently increased - Average gorilla trek and permit (across the region)= US\$500	- Gorilla tourism attracted net foreign exchange earnings of about \$7.70 million (1994-98) - Gorilla tourism is also estimated to have generated \$15.40 million of sales in the Ugandan economy; contributed \$4.77 million in government tax revenues; supported close to 1,700 person years of jobs; and contributed to national income of \$6.93 million.	-While there are not exact economic figures available for the DRC, gorilla ecotourism has a role in their economy -Comparatively, the DRC does not generate as much income from gorilla tourism as Rwanda or Uganda, or as much as it could (mainly due to difference in gorilla accessibility and lack of infrastructure)
Specific Challenges to Development of Ecotourism Industry:	- Preserving scarce land and environment; gorillas are being forced out of their habitat since land is needed for food production - Generating rural employment - Lack of internal capacity and development (infrastructure, resources, etc.)	- Gorilla trafficking - Controversy over fee-sharing agreements between parks and local communities (a decrease in revenue sharing with communities has resulted in less support from communities to expand industry)	- Political conflict (resulting in economic instability, poor governance, and corrupt practices) - Concerns over recurring encroachments, poaching, deforestation, population growth, and the refugee related problems that have arisen due to civil unrest/militia activity

⁸ Vieta, F. Ecotourism propels development. *Africa Recovery*. 13(1). June 1999.

<http://www.un.org/ecosocdev/geninfo/afrec/subjindx/131envir.htm>. Accessed September 8, 2008.

⁹ Moyini, Y. Analysis of the economic significance of gorilla tourism in Uganda. International Gorilla Conservation Programme. <http://www.igcp.org/pdf/MoyiniUganda.pdf>. Accessed September 8, 2008.

¹⁰ Kirby, Alex. Hope rises for mountain gorillas. BBC Online News. October 17, 2002.

<http://news.bbc.co.uk/2/hi/science/nature/2332527.stm>. Accessed September 20, 2008.