epidemic regions. Using this dataset we investigated genetic diversity, patterns of distribution, and evolutionary history. **Results**: Our analysis indicates that the rabies virus in China is primarily defined by two clades that exhibit distinct population subdivision and translocation patterns and that contributed to the epidemic in different ways. The younger clade originated around 1992 and has properties that closely match the observed spread of the recent epidemic. The older clade originated around 1960 and has a dispersion pattern that suggests it represents a strain associated with a previous outbreak that remained at low levels throughout the country and reemerged in the current epidemic. **Conclusions**: Our findings provide new insight into factors associated with the recent epidemic and are relevant to determining an effective policy for controlling the virus.

**CO.44**

**PLAYING THE ODDS: PRIORITIZING HUMAN RABIES BIOLOGICS IN LIMITED SUPPLY SCENARIOS**

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Limitations in the availability and access to human rabies biologics in enzootic regions result in most rabies deaths in the developing world. Efforts to supply modern rabies vaccines and immune globulin (RIG) have improved availability, but cost and the lack of structured programs in many countries remain major obstacles to providing optimal care. Proposed policies to provide rabies post-exposure prophylaxis (PEP) at no cost to the patient through government programs are challenged by the limited supply of rabies biologics that providers are able to obtain. In many cases, the demand for biologics exceeds the limited supplies and national rabies programs are therefore forced to ration, resulting in delays or complete failures in provision of adequate PEP. Optimal PEP involves the use of rabies immune globulin and vaccine. While WHO recommendations for PEP are comprehensive, those recommendations offer no guidance on management of rabies exposures when there are limited supplies of biologics in the country nor if there is only vaccine available but no RIG. Complex operationalization issues, such as to how to approach prioritization when both nervous tissue and modern vaccines coexist in a country, or how to optimally integrate private distribution of rabies biologics, are not part of the WHO guidance documents. We present a proposal on how to develop recommendations and guidelines to deal with these scenarios accounting for local rabies epidemiology, patient age and body size, delays after exposure, and cultural and social issues. Several Old and New World country cases are presented to highlight how these challenging circumstances might be managed and overcome.

**CO.45**

**IMMUNE RESPONSE OF BALB/C MICE IMMUNIZED WITH VERO CELL RABIES VACCINE AND BpMPLA-SE ADJUVANT**

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The prophylaxis is an important strategy to control of human and animal rabies disease. The vaccine from Vero cellular culture for human use is efficacy and safety. However, because the technology used to produce this vaccine is expensive this product costs about ten dollars. This cost makes them impossible the use of this vaccine type in poor countries where the animal rabies control is inefficient and there many cases of human rabies. Rabies disease is responsible for about 55,000 deaths per year in the world. The objective of this study was evaluate the humoral immune response of mice (Balb/c) immunized with three different doses of Vero rabies vaccine associated with the BpMPLA-SE adjuvant. This adjuvant is a product obtained from Bordetella pertussis. Three groups of ten mice were immunized with two doses of 500μl (G1), 250μl (G2) or 125μl (G3) of Vero cell rabies vaccine (IB-lot 1103075) mixed with BpMPLA-SE (10μg/dose). Three groups control (Gc) received only rabies vaccine. The immunization occurred on days 0 and 21 and samples were taken ten days after the last dose injected and on days 60, 120 and 180 to determine the titer of neutralizing antibodies for rabies virus in BHK21 cells (RFFIT). The averages of the neutralizing antibodies titers found in the samples from each group ten days after finished the immunization were 39.2, 33.1, and 20.4 IU/ml for groups G1, G2 and G3 respectively. The results obtained on day 180 were 17.1 IU/ml (G1), 10.6 IU/ml (G2) and 9.8 (G3). In the control groups the averages of the antibodies titers were: 29.7 (Gc1), 26.9 (Gc2) and 22.2 IU/ml (Gc3) after immunization and 10.7 (Gc1), 9.5 (Gc2) and 8.5 IU/ml (Gc3) on day 180 (Gc3). These data show that the adjuvant BpMPLA-SE increased the humoral immune response for rabies vaccine in Balb/c mice independent of the volume of vaccine utilized to immunize the animals. The results found are very important to reduce the number of doses and the volume of Vero cell rabies vaccine utilized in the immunization against rabies. Financial Support: Butantan Foundation.

**CO.46**

**SAFETY AND IMMUNOGENICITY OF THE PURIFIED VERO RABIES VACCINE NEXT GENERATION IN CHINESE PEDIATRIC (≥ 10 YEARS) AND ADULT POPULATIONS**

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**Background**: The Purified Vero cell rabies Vaccine Next Generation (PVRV-NG) is a highly purified vaccine developed with innovative technology and human and animal origin-components-free medium. It was shown to be at least as immunogenic as Verorab® and presented a similar safety profile in a phase II clinical study conducted in France (pre exposure regimen). A phase III clinical study was performed in Chinese pediatric (≥ 10 years) and adult populations in simulated post-exposure regimen to further document PVRV-NG in comparison to Verorab®. **Methods**: This was a randomized, blind-observer, controlled study in healthy subjects aged 10 to 17 years (pediatric cohort) or ≥ 18 years (adult cohort). Participants received five doses by intramuscular route of PVRV-NG or Verorab™ (ratio 2:1 in each age group) at D0, D3, D7, D14 and D28 as per recommendation for post-exposure prophylaxis (Eisen schedule). No rabies immune-globulins were administered concomitantly with the first vaccine dose. Immunogenicity was evaluated at D0, D14 and D28 by measuring the level of rabies virus neutralizing antibodies (RVNA) using the rapid fluorescent focus inhibition test. Testings were performed at the National Institute for Food and Drug Control (Beijing). Safety was evaluated with a list of predefined solicited injection site and systemic reactions during the period between Do and D14 and during the seven days after the 2 last doses; any adverse events until 28 days after the final dose and any SAE until 6 months after the final dose were also recorded. **Results**: 816 participants were enrolled; 408 in each age group corresponding to 272 in PVRV-NG group and 136 in Verorab® group. The predefined criterion for noninferiority in terms of proportions of participants with RVNA titers ≥0.5 IU/mL at D14 (before the 4th injection) was met in the per-protocol analysis set and confirmed in the full-analysis set population.