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Ebola Outbreaks and the Pathogen Access Deadlock: Why the WHO Is Pressing to Finalize the Global Pandemic Agreement

Emerging Pathogens & Public Health * Virology * Epidemiology

Recurring filovirus emergencies across East and Central Africa -- including Uganda's 2025 Sudan virus disease outbreak and ongoing regional Orthoebolavirus spillovers -- have become the central empirical test case in Geneva, where World Health Organization (WHO) Director-General Tedros Adhanom Ghebreyesus is pressing member states to resolve the final Pathogen Access and Benefit-Sharing (PABS) deadlock holding up the operational WHO Pandemic Agreement [1, 2] .

Filovirus Spillover Reality Meets Diplomatic Deadlock

While international negotiators debate the legal architecture of post-COVID-19 pandemic preparedness, frontline public health laboratories in East and Central Africa continue to confront recurring zoonotic spillovers of high-consequence filoviruses [1, 2] . Following the historic adoption of the overarching WHO Pandemic Agreement framework at the 78th World Health Assembly in May 2025, full treaty operationalization has hinged on completing its most contested annex: the Pathogen Access and Benefit-Sharing (PABS) mechanism under Article 12 [2, 3] .

Speaking to member states and international outlets, WHO leadership has repeatedly pointed to active Ebola virus disease responses -- spanning both Sudan ebolavirus (SUDV) and Bundibugyo ebolavirus (BDBV) lineages -- to argue that treating genomic pathogen surveillance and medical countermeasure access as separate diplomatic tracks leaves the global health system vulnerable at the exact point where epidemic containment is cheapest and most effective: the primary spillover zone [1, 2] .

| Filovirus Species (Orthoebolavirus) | | Historical Case Fatality Ratio (CFR) | | GP Antigenic Cross-Protection | | Licensed Countermeasure Status | | Recent Clinical / Field Protocol |

| Zaire ebolavirus (EBOV) | | 60% - 90% (untreated) | | Minimal cross-neutralization vs. SUDV | | 2 WHO-prequalified vaccines (Ervebo rVSV-ZEBOV, Zabdeno/Mvabea) + 2 mAbs (Inmazeb, Ebanga) | | Standard ring vaccination & targeted monoclonal therapy |

| Sudan ebolavirus (SUDV) | | 40% - 65% | | Requires species-specific GP immunogen (~45% GP divergence) | | Investigational candidates only (rVSVDeltaG-SEBOV-GP, ChAdOx1-BiEBOV, cAd3-EBO S) | | TOKOMEZA SVD 4-day rapid ring vaccination trial (Uganda, Feb-Apr 2025) [4, 5] |

| Bundibugyo ebolavirus (BDBV) | | 25% - 51% | | Partial conserved receptor-binding epitopes; no licensed standalone vaccine | | Preclinical / early-stage multivalent filovirus constructs | | Rapid RT-qPCR & amplicon genomic sequencing + supportive critical care [1] |

Why Filovirus Molecular Diversity Demands Species-Specific Countermeasures

From a virological standpoint, 'Ebola' is not a single uniform antigen. The genus Orthoebolavirus (family Filoviridae) comprises enveloped, non-segmented, negative-sense single-stranded RNA viruses (approximately 19 kilobases in length) whose surface trimeric glycoprotein (GP 1,2) mediates attachment, macropinocytosis, and endosomal membrane fusion via the host intracellular receptor Niemann-Pick C1 (NPC1) [4, 6] .

Although the internal NPC1 receptor-binding pocket is structurally conserved across filoviruses, the exposed mucin-like domain and glycan cap of GP 1 diverge by roughly 40% to 45% at the amino acid level between Zaire ebolavirus (EBOV) and Sudan ebolavirus (SUDV) [4, 6] . Consequently, both the licensed recombinant vesicular stomatitis virus vaccine (Ervebo / rVSV-ZEBOV) and FDA-approved monoclonal antibody cocktails (Inmazeb and Ebanga) that transformed Zaire ebolavirus survival rates fail to neutralize Sudan or Bundibugyo virus strains [4, 5] .

When Uganda confirmed a Sudan virus disease (SVD) outbreak centered in Kampala on January 30, 2025, public health responders could not simply draw from routine commercial stockpiles [4] . Instead, the Ugandan Ministry of Health, the Makerere University Lung Institute, the WHO, and IAVI activated the TOKOMEZA SVD ring vaccination efficacy trial within 96 hours of outbreak declaration -- deploying pre-positioned investigational rVSVDeltaG-SEBOV-GP vaccine doses across 17 contact rings and containing the outbreak to 14 cases (12 confirmed, 2 probable) and 4 deaths before declaring transmission over on April 26, 2025 [4, 5] .

Genomic Surveillance Speed vs. Countermeasure Equity in PABS

The operational lesson from recent African filovirus responses is that local genomic capacity has accelerated dramatically. Portable nanopore and Illumina sequencing platforms deployed at national reference laboratories in Kampala, Kinshasa, and Entebbe now generate complete 19-kb filovirus consensus genomes within 24 to 48 hours of sample collection [1, 4] . These Digital Sequence Information (DSI) uploads immediately inform diagnostic PCR primer fidelity -- verifying that mutations have not eroded target binding sites in the viral nucleoprotein (NP), matrix protein (VP40), or RNA-dependent RNA polymerase (L) genes -- and allow structural biologists to map antigenic drift across GP 1,2 [4, 6] .

Yet this rapid open-science genomic sharing sits at the heart of the PABS controversy in Geneva [2, 3] . Under the status quo, frontline countries that shoulder the clinical, biosafety, and economic costs of detecting an outbreak and uploading pathogen sequences have no binding international guarantee that resulting diagnostics, vaccines, or monoclonal therapeutics will be allocated back to them during an emergency [2, 3] .

Inside the Article 12 PABS Architecture

To bridge this asymmetry, the WHO Pandemic Agreement's proposed PABS annex links rapid, unencumbered sharing of physical pathogen materials and Digital Sequence Information to legally binding benefit-sharing obligations by pharmaceutical

manufacturers that utilize the system [2, 3] :

* Real-Time Production Allocation: Participating manufacturers are called upon to reserve a baseline percentage -- negotiated around 20% of real-time pandemic-related production (typically structured as at least 10% donated free of charge and 10% supplied at affordable, non-profit prices) -- for distribution by the WHO based on epidemiological need and public health risk rather than ability to pay [2, 3] .

* Standardized Material & Sequence Traceability: Rather than requiring bilateral Nagoya Protocol negotiations that can delay sample transfer by weeks during a fast-moving hemorrhagic fever outbreak, a multilateral PABS portal establishes pre-agreed Standard Material Transfer Agreements (SMTAs) and database tags for DSI [3] .

* Regional Clinical Trial & Manufacturing Readiness: Building on the 4-day activation model demonstrated by Uganda's TOKOMEZA SVD trial, the agreement pairs pathogen access with technology transfer, regional fill-and-finish capacity, and pre-approved multi-country ring trial protocols for priority pathogen families (including Filoviridae , Coronaviridae , and Orthomyxoviridae) [4, 5] .

What Comes Next for Global Epidemic Preparedness

Epidemiological modeling of filovirus transmission consistently shows that every week of delay in ring vaccination or contact isolation allows secondary transmission chains (R 0 ~ 1.5-2.5 in unmitigated community and nosocomial settings) to branch across urban transport corridors [5, 6] . Whether the Intergovernmental Negotiating Body finalizes the PABS annex on schedule will determine if the next Sudan , Bundibugyo , or novel filovirus spillover is met with a predictable, treaty-backed supply of investigational and licensed countermeasures -- or relies once again on ad-hoc emergency donations [1, 2] .

References & Primary Sources

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