

Substandard and falsified vaccines and their detection

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Abstract

The COVID-19 pandemic has highlighted the neglected public health problem of substandard (due to incorrect temperature storage or manufacturing errors) and falsified/counterfeit (SF, due to fraud) vaccines in supply chains. There have been multiple reports of SF vaccines, both pre-pandemic and for COVID-19. Increasing reports are a public health concern and risk global vaccination implementation, for endemic diseases and preparations for the next pandemic.

There are currently no devices for inspectors to screen for SF vaccines in supply chains. Therefore, there is a vital need for research into innovative, accurate, affordable, rapid and user-friendly screening devices that can be effectively implemented to yield a step change in our ability to rapidly detect SF vaccines, at different levels in diverse supply chains, to protect vaccine-related global healthcare. We describe pilot research on promising tools to empower inspectors.

Substandard and falsified vaccines

There have been 184 public domain reports of diverted and SF COVID-19 vaccines from 48 countries involving thousands of vaccine doses; significant but neglected risks to global public health and to public confidence in vaccines (Fig 1). It has been estimated that 5 billion doses of vaccines were produced per year pre-pandemic. In the ten years before COVID-19 there were multiple examples of SF vaccines, including from China, Niger, Indonesia, Philippines and WHO have issued multiple alerts (<https://www.who.int/teams/regulation-prequalification/incidents-and-SF/full-list-of-who-medical-product-alerts>).

They are important public health risks, leaving patients unknowingly unprotected, risking further disease transmission, disease, disability and death. They will lead to economic harm for patients and their communities, governments and vaccine manufacturers. They also risk sparking loss of faith in vaccines and driving vaccine hesitancy.

The main drivers are presumed to be impaired access and cost with inadequate inspection and enforcement for falsified vaccines and errors in manufacturer and in maintaining the correct temperatures in supply chains for substandard vaccines. There is very limited public domain scientific investigation about what falsified vaccines actually contain, but liquids such as saline, amikacin, gentamicin, hyaluronic acid and water have all been described.

Interventions to reduce risk

Equitable access

Joined up stakeholder data sharing, across manufacturers, regulatory authorities, health ministries, enforcement, customs, donors, international organisations

Risk analysis – global and for countries to identify and rank risks to inform risk-based post-market surveillance
Authentication, such as bar code systems – but is the infrastructure there, especially in countries that have not implemented such systems pre-pandemic?

Vaccine vial monitors – but how widely used? Freeze/thaw?

Multiple reference labs for different vaccines

Screening devices for screening vaccines in supply chains – currently flying blind.

Public engagement in different communities. How will community engagement be conducted, reducing vaccine hesitancy risk in SF 'outbreaks'?

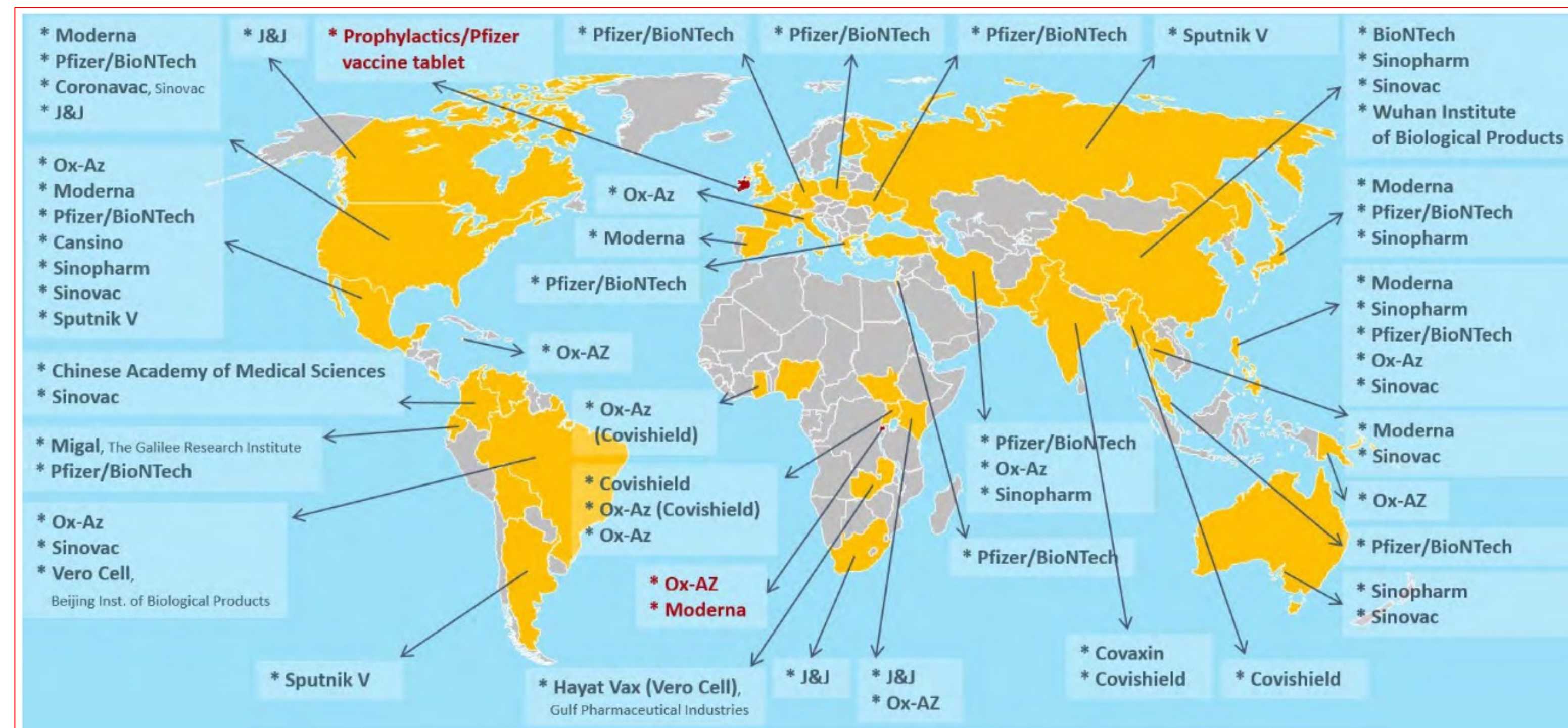


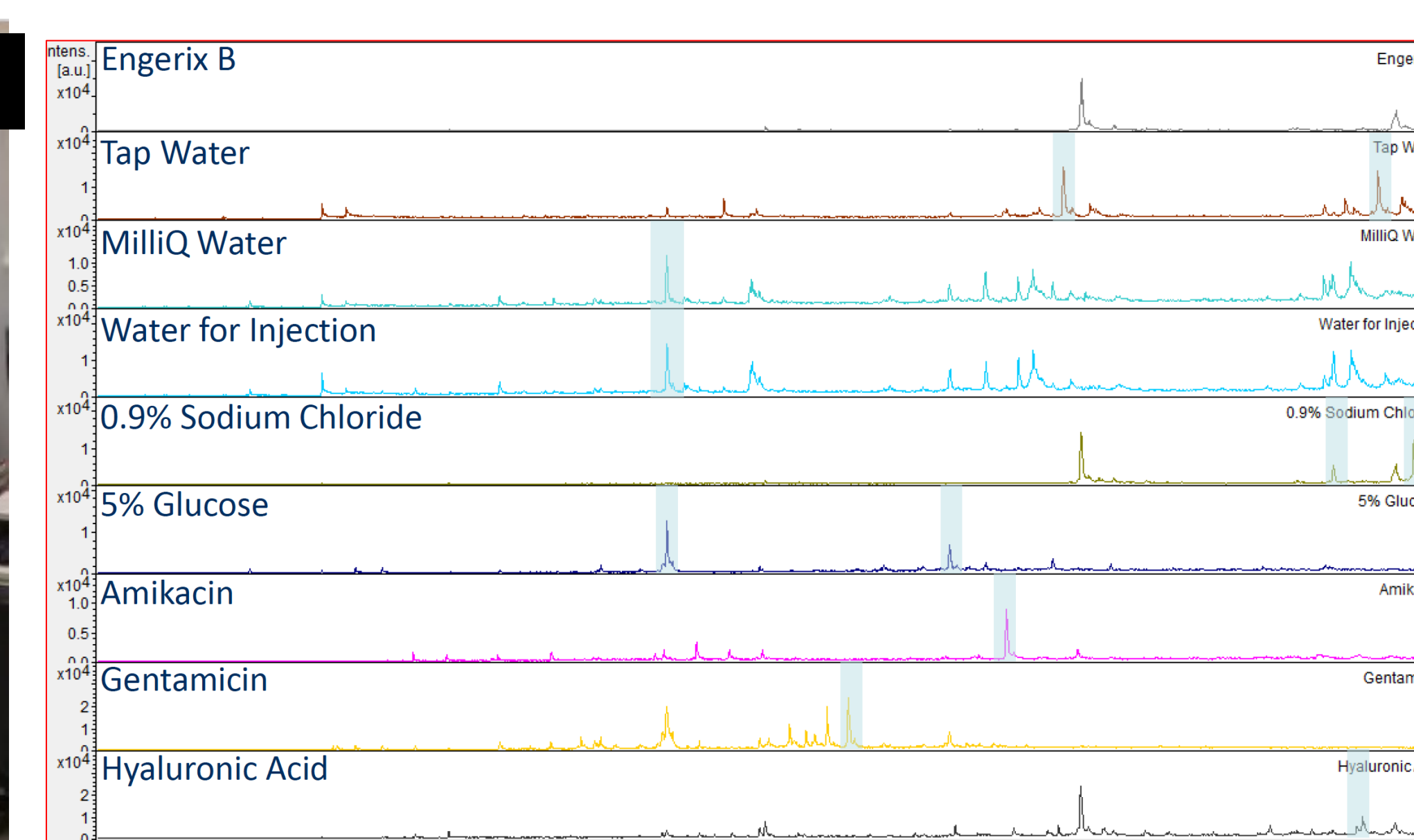
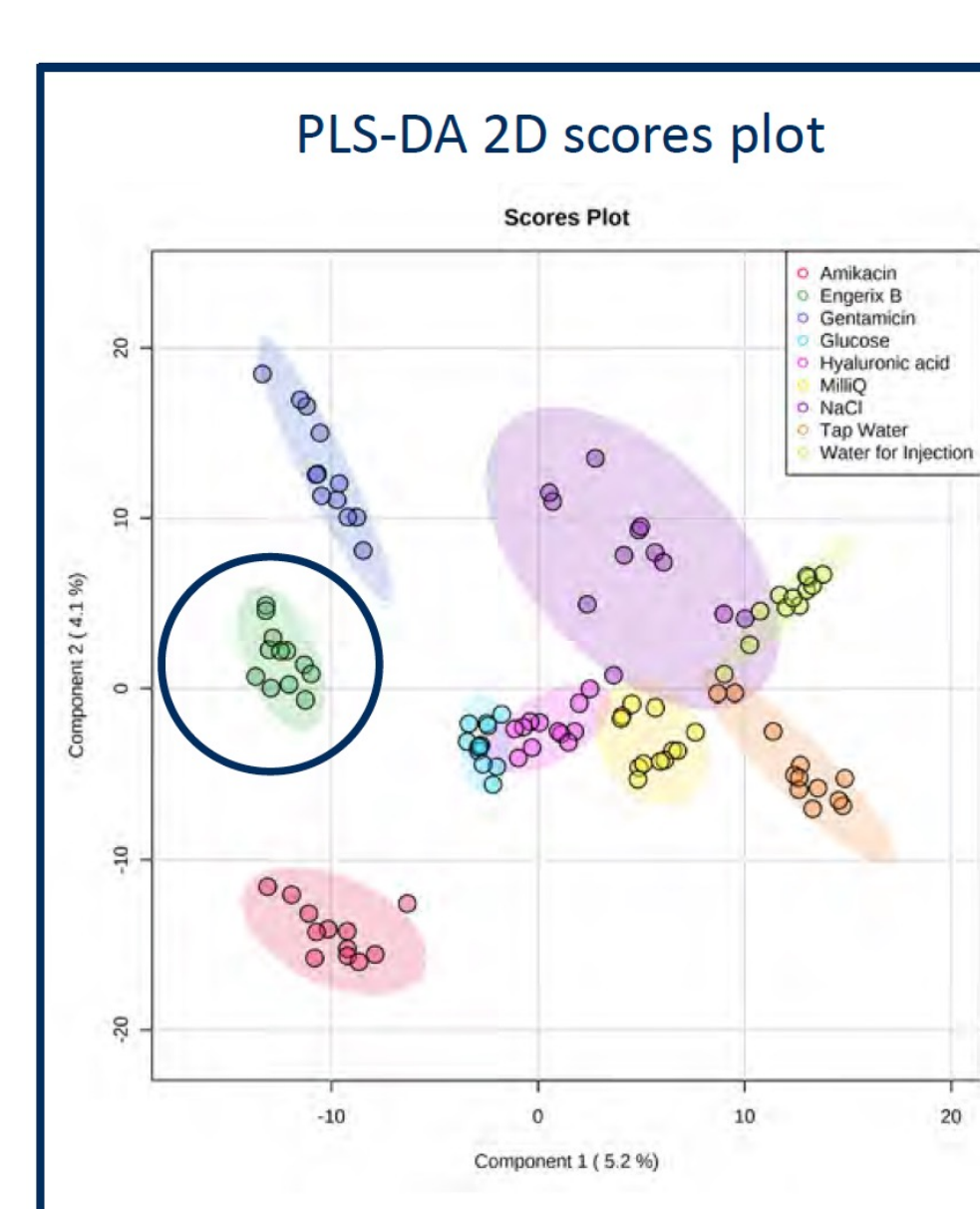
Fig. 1. Countries with public reports on COVID-19 vaccine quality issues on the Medicine Quality Monitoring Globe. Ox-Az: Oxford-AstraZeneca, and J&J: Johnson & Johnson. See: https://www.iddo.org/sites/default/files/publication/2022-09/Medical%20Product%20Quality%20Report_Covid-19_Issue15_January-March2022_V1.1.pdf

Screening devices

We have explored repurposing diverse devices for detecting SF vaccines:

1. Matrix-assisted laser desorption/ionization-time-of-flight mass spectrometry (MALDI-TOF) – e.g. Vitek MS
2. Spatially-offset Raman spectroscopy (SORS) – e.g. Resolve device
3. Rapid diagnostic tests (RDTs) – e.g. Hepatitis B RDT
4. Multiple lower cost devices

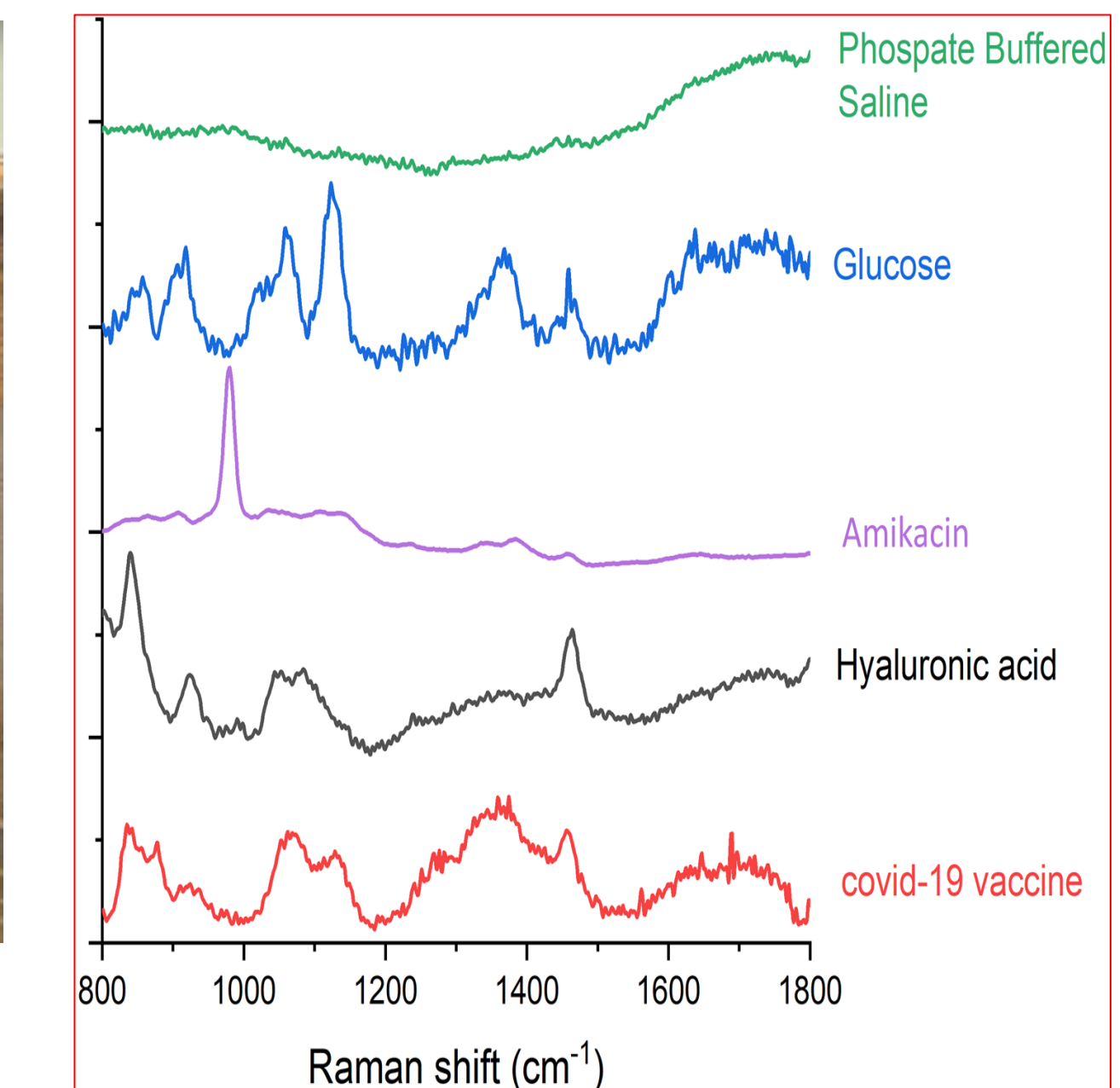
With very promising results. Requires further evaluation and implementation research to answer key questions, such as the diagnostic accuracy in real life and where in different supply chains levels devices are best used. We are also evaluating these technologies for detecting diethylene glycol & ethylene glycol.



2. Resolve SORS



The first SORS experiments during the pandemic in Oxford rain



SORS spectra of a COVID-19 vaccine versus liquids used in falsified vaccines

3. Hepatitis B RDT

Hepatitis B Surface Antigen (HBsAg) detecting lateral flow tests, developed for patient hepatitis B diagnosis, can be repurposed for detecting HBsAg in hepatitis B vaccines – a tool for detecting their falsification.

Similar repurposing of rapid diagnostic tests works for multiple other pathogen-vaccine pair.

Collaboration

We would be delighted to discuss collaborating with other vaccine manufacturers and organisations. The techniques may also be valuable for in-line QC. In addition, in a separate project (FORESFA) we are evaluating environmental DNA and stable isotope analysis for estimating falsified vaccine origin.

Balancing acts

Discussion of SF vaccines needs to be approached with caution, to ensure that the correct balance between creating awareness and driving vaccine hesitancy is achieved. Publishing data on the results of device evaluations should not unnecessarily include results that will help criminals evade these new detection techniques.

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