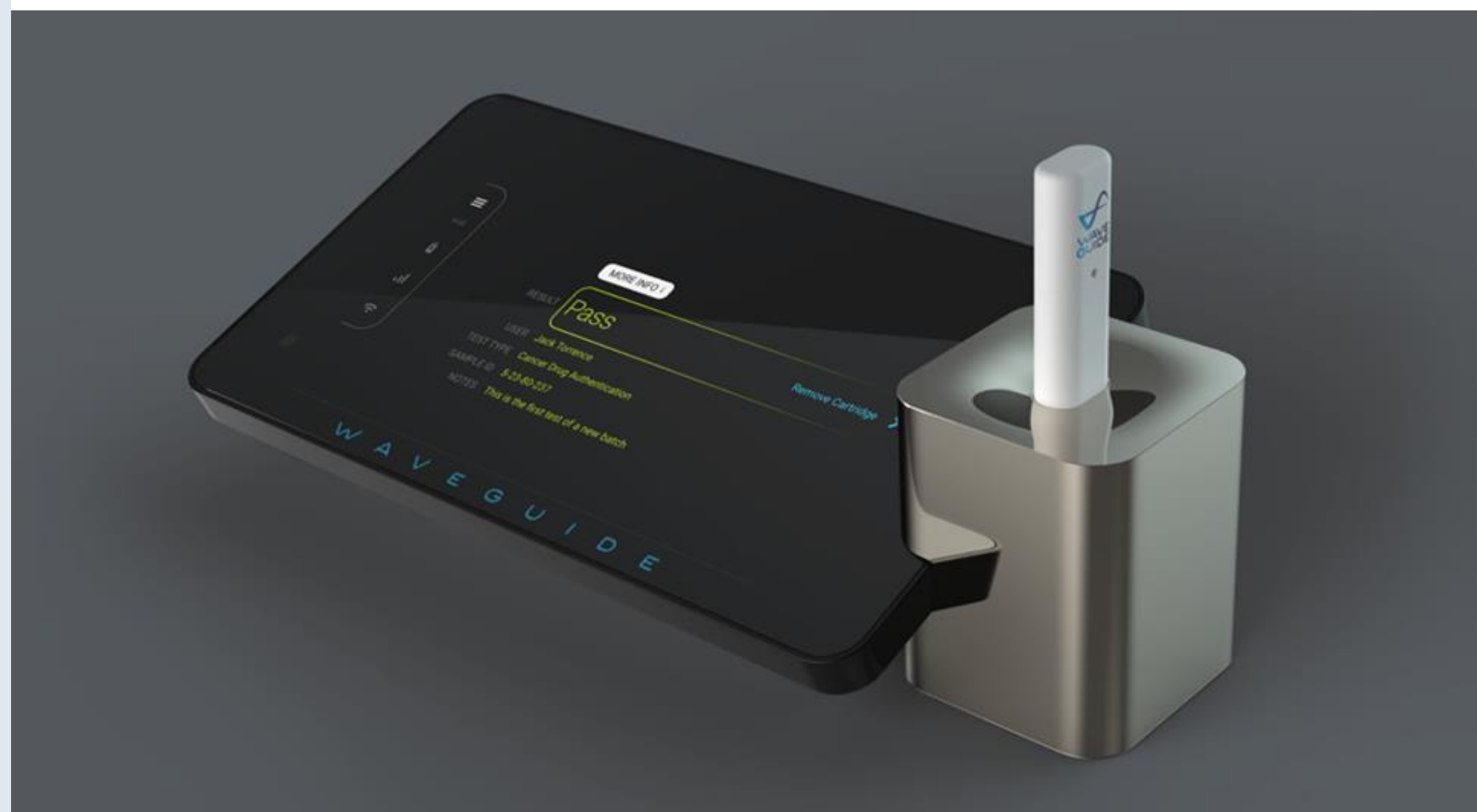


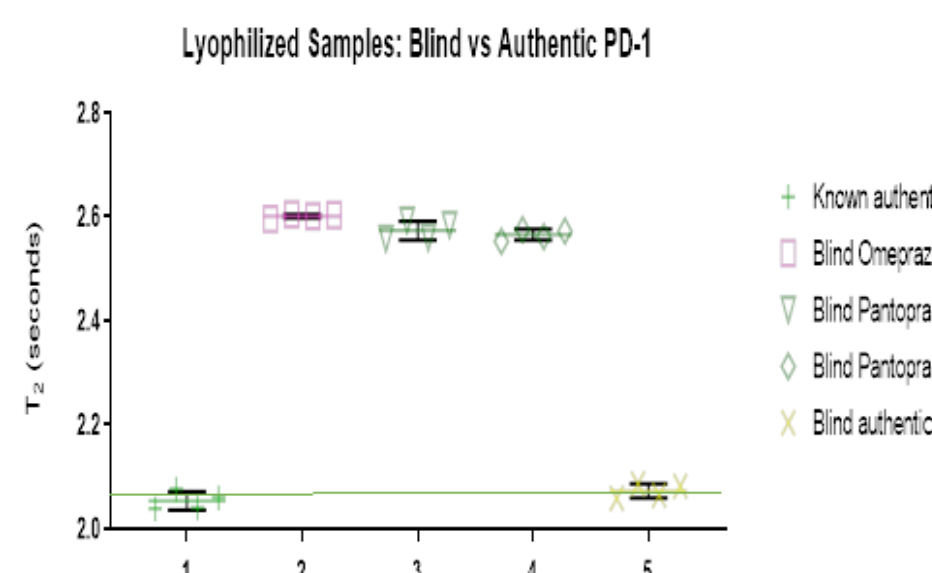
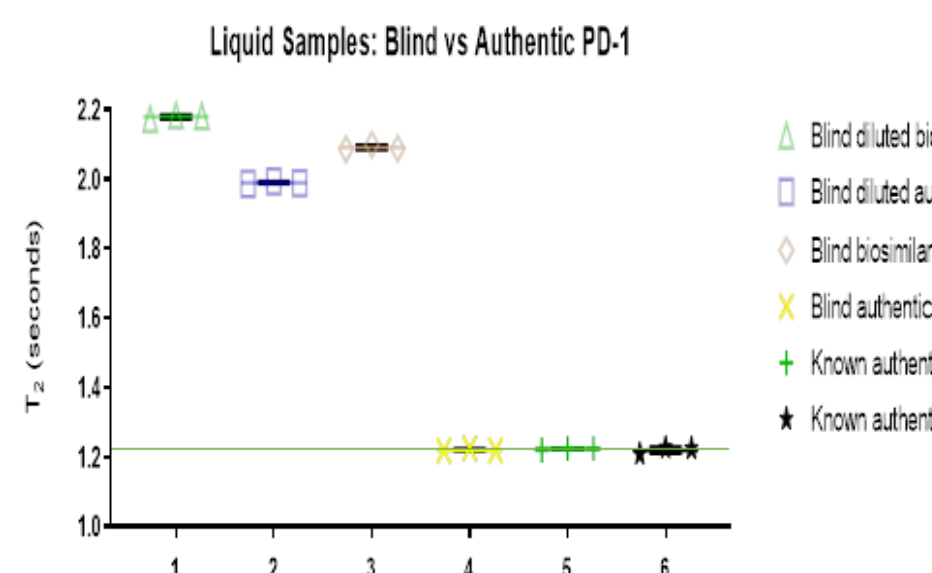
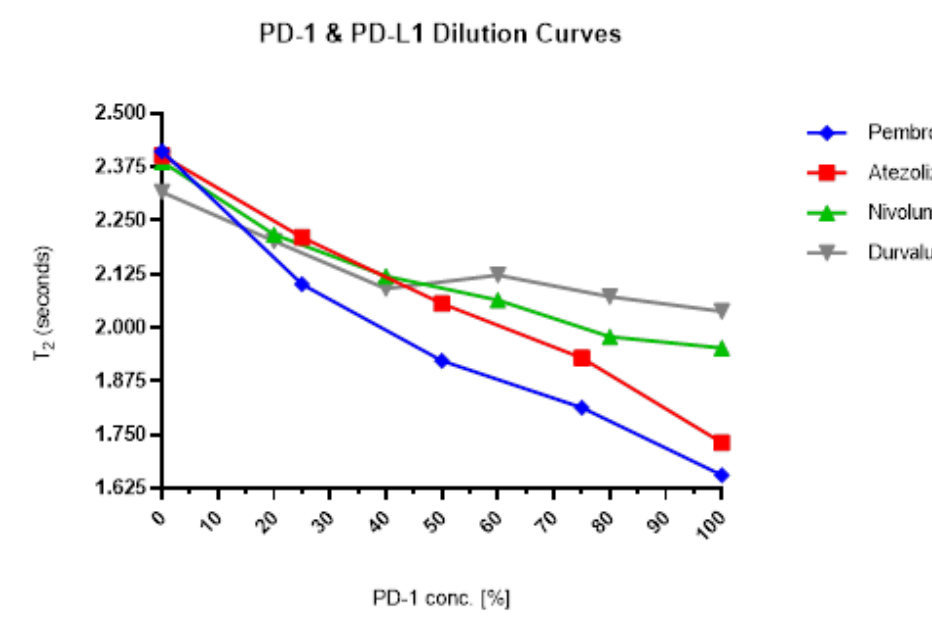
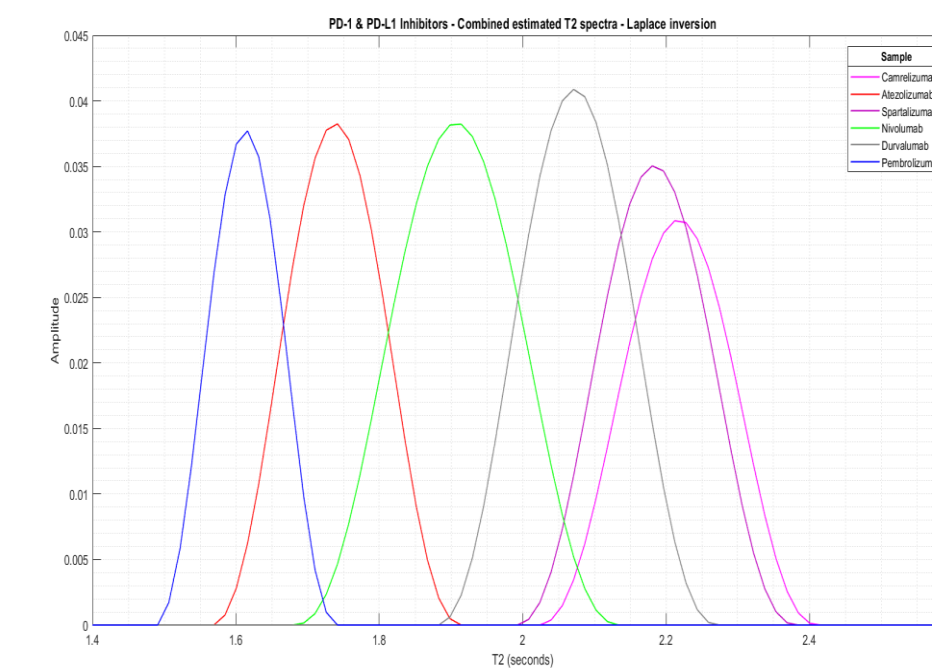
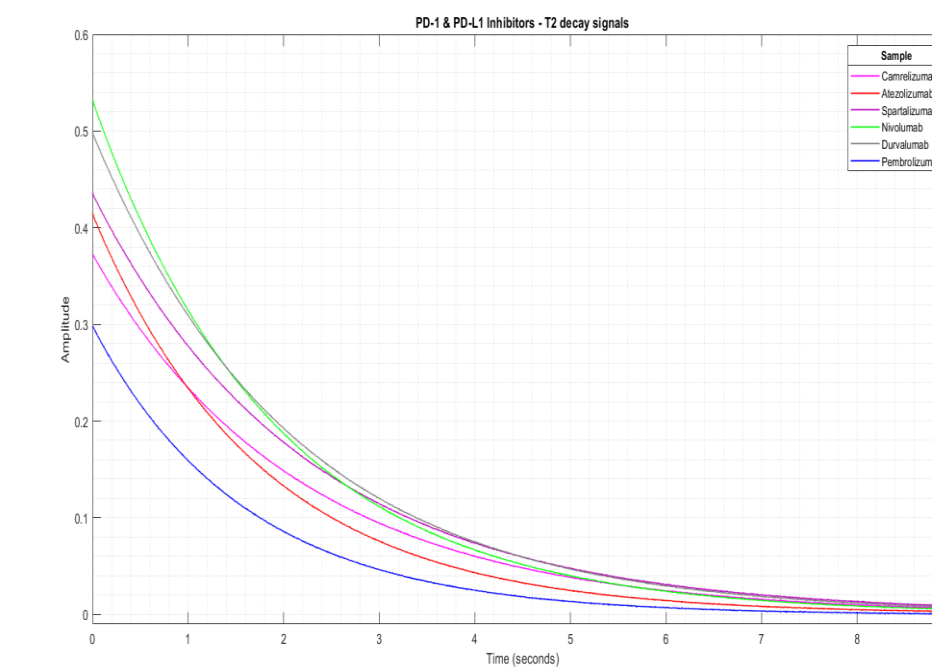
Abstract

Worldwide, an estimated 10% of all medicines are counterfeit, resulting in approximately 300,000 deaths and costing over \$200 billion in US dollars annually.¹ WaveGuide's portable μ NMR has shown the ability to distinguish biosimilars when analyzing immuno-oncology agents PD-1 and PD-L1 inhibitors as well as the differentiation of Hyaluronic Acid (HA) concentrations from Silicone oil in dermal fillers. Currently, there are no reliable field methods for the detection and monitoring of these types of biologics and consumer products. WaveGuide utilizes time-domain NMR to measure the relaxation time characteristics (T_2) of the native biological sample. The measured T_2 relaxation decays are fitted with both single- and bi-exponential decay models, and the corresponding decay-times and component amplitudes are determined and analyzed. This novel time-domain NMR technique can distinguish biosimilars in the PD-1 and PD-L1 inhibitor family. The technique analyzes fast chemical exchange between water and exposed NH and OH protons of amino acid side chains in the folded protein structure unique to each PD-1 and PD-L1 inhibitor. Analysis of dominant features in folded proteins in solution can be exploited for other types of biopharma assets as well as consumer products for authentication, forensics, and supply chain integrity. WaveGuide's portable μ NMR is the first battery-powered instrument that is robust enough to operate in the field without the need for a trained NMR technician. The device is 22x smaller, ~80x lighter, and 30x lower cost than contemporary commercial analytical systems.



The WaveGuide Formula™ portable μ NMR
Little to no sample preparation required
Sample analysis take only minutes
Less than 30 μ L of sample typically used per test

Results: Biological Agents



Analysis of research grade products (API): Nivolumab, Atezolizumab, Pembrolizumab, Durvalumab, Camrelizumab, and Spartalizumab. All dissolved in PBS buffer, pH 7.2, at the concentration of 5 mg/mL

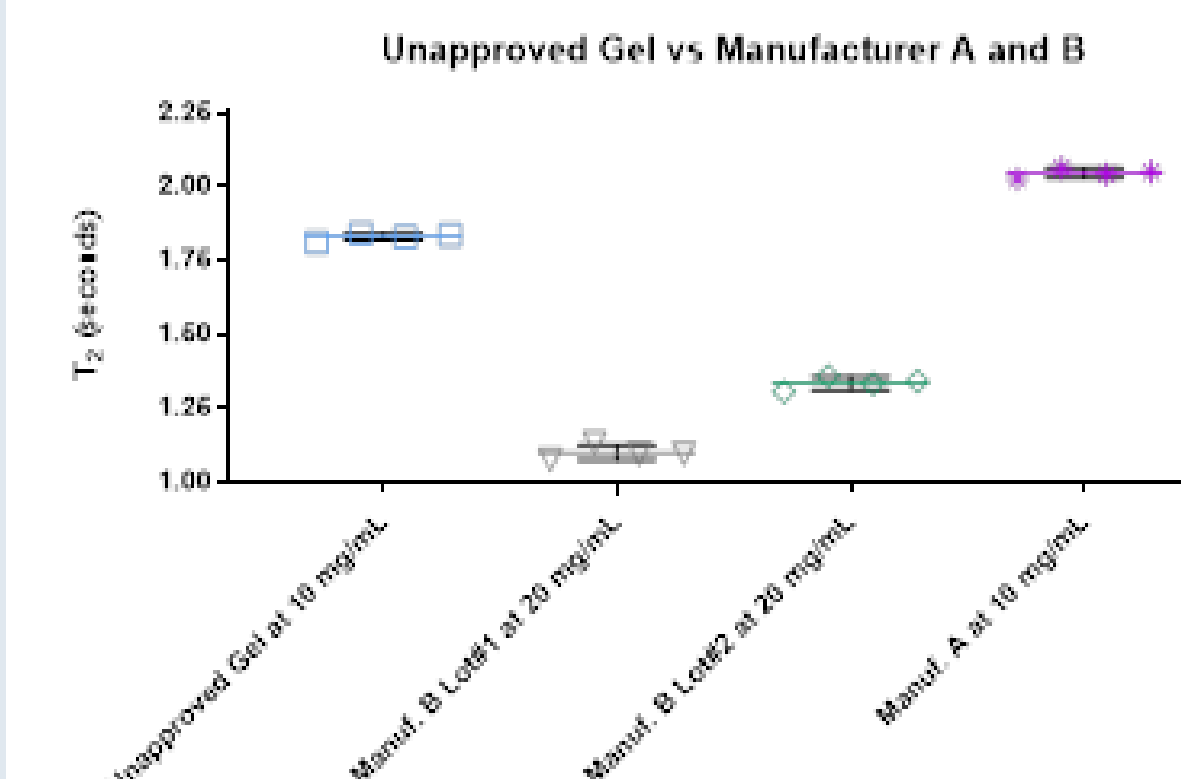
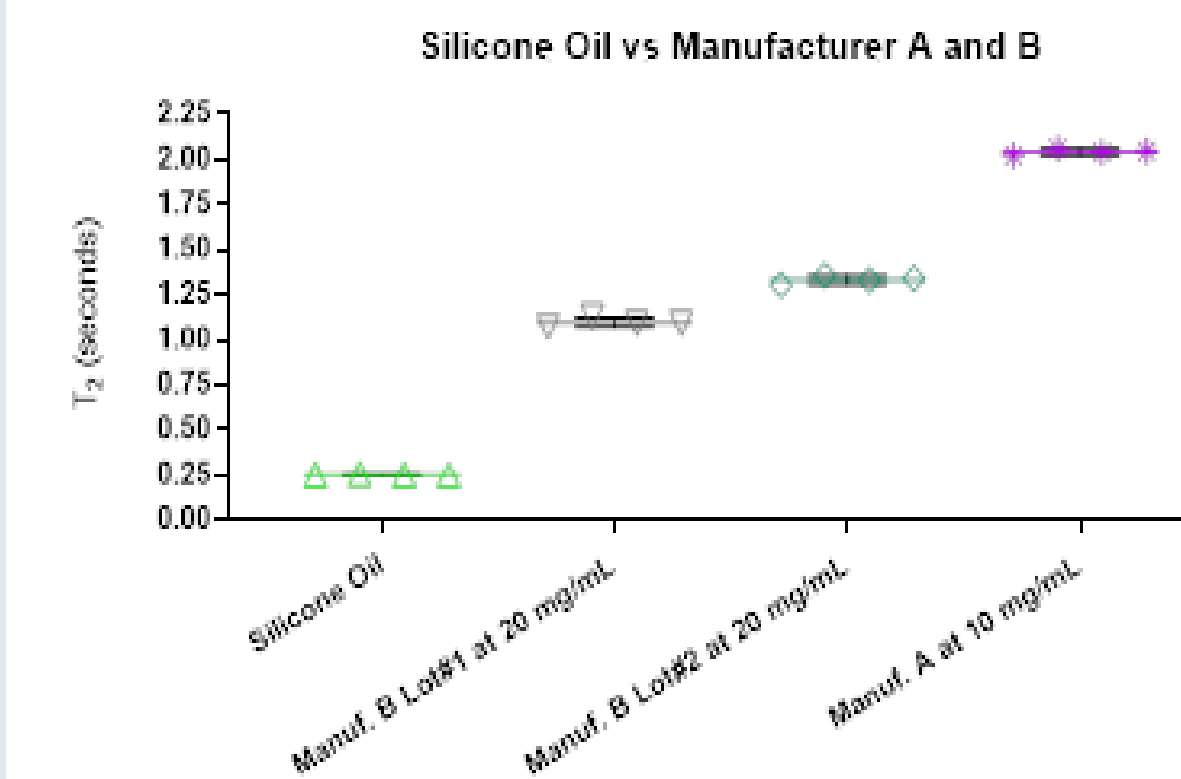
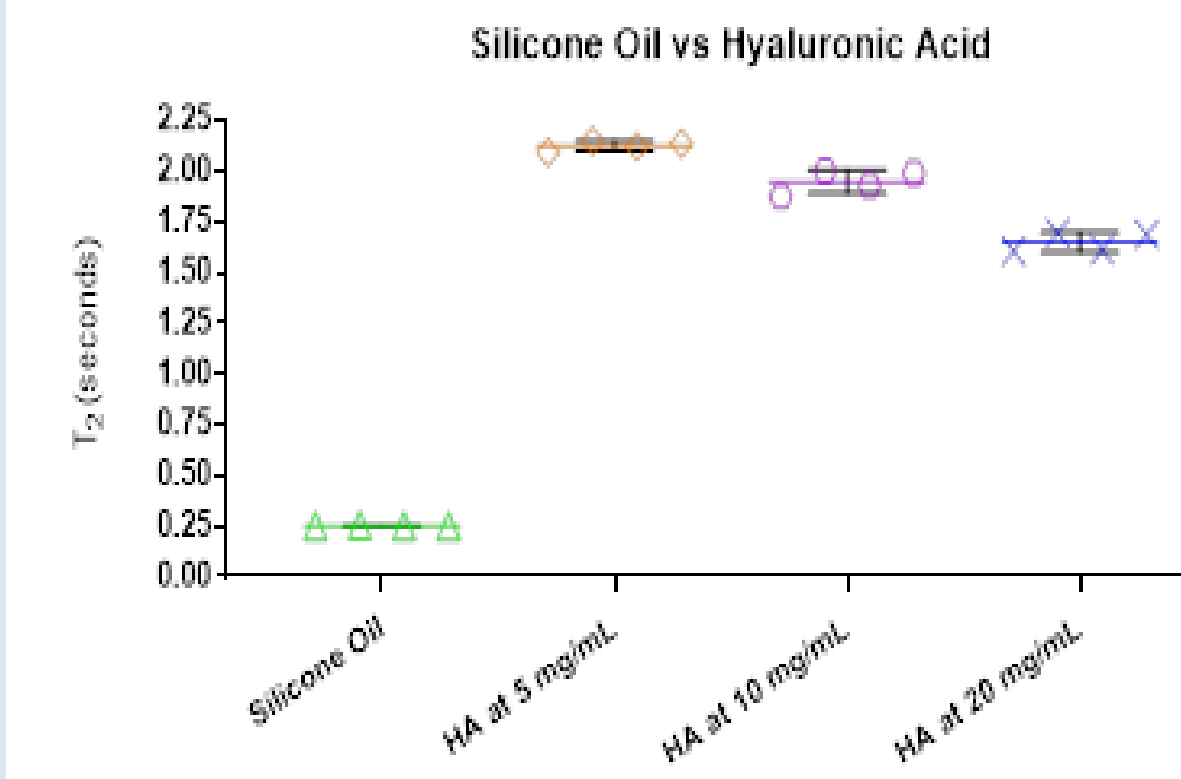
Unique Transverse Proton Relaxation (T_2) dispersion (top left) and Laplace Inversion spectra (left) for each of the six PD-1/PD-L1 inhibitors analyzed

T_2 of diluted APIs: Nivolumab, Atezolizumab, Pembrolizumab and Durvalumab. Each API was diluted from original concentration in either 25% or 20% decrements

Blind study with authentic and final formulation of PD-1 inhibitor. Sample #1, 2, 3, and 4 were blind samples; sample #5 and 6 were known authentic PD-1 from two different lots

Blind study with lyophilized authentic PD-1 inhibitor. Sample #2, 3, 4 and 5 were blind samples. Sample #1 was a known authentic PD-1

Results: Consumer Product (HA)



Silicone is the most common unapproved substitute filler for HA.

When tested, the WaveGuide's Formula™ was able to differentiate the Silicone oil sample from authentic HA samples at different concentrations

In addition, the Silicone oil sample was differentiated from two independent FDA approved authentic HA manufactures (A & B).

Moreover, manufacturer B Lot #1 and Lot #2 had two different formulations and were discreetly distinguishable even at the same concentration of HA (20 mg/mL)

Lastly, WaveGuide's Formula™ was able to differentiate two independent FDA approved authentic manufacturers (A & B) of HA, from an Unapproved Gel from a Foreign Market even at the same concentrations (10 mg/mL)

Background

- Immuno-Oncology agents PD-1/PD-L1 inhibitors showed multi billion-dollar Q4 2018 market results^{2,3,4,5,6}
- There have been several global 2019 reports in the news of counterfeit PD-1/PD-L1 inhibitors that have reached the clinic as well as increased counterfeit non-surgical injectables⁷
- According to The America Society for Aesthetic Plastic Surgery, >\$1 billion was spent on injectables in 2018⁸
- HA is currently the most widely used soft-tissue filler with 810,240 legal non-surgical procedures in 2018 which is up 58% since 2014^{8,9}
- HA longevity of ~ 6 months makes it the most common soft-tissue injectable and second most common injectable^{8,9}
- 2017 FDA official warning urging consumers to "never buy dermal fillers on the internet: they may be fake, contaminated, or harmful"¹⁰

Conclusions

- Time Domain proton NMR, a nondestructive technique, can be conducted using an inexpensive handheld time-domain μ NMR spectrometer
- Measurements are very simple and fast making it possible to collect quantitative data on every vial of a biologic or consumer product throughout its entire lifecycle, from point-of-release to point-of-treatment
- WaveGuide's Formula™ was able to differentiate between six different PD-1/PD-L1 APIs, as well as detect their dilutions
- WaveGuide's Formula™ was able to differentiate finished authentic PD-1 inhibitor from counterfeit or diluted products (blind study)
- WaveGuide's Formula™ was able to differentiate authentic HA samples from Silicone oil, Unapproved Gel from foreign market and different concentrations and formulations of authentic HA

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