APPLICATION NOTE

No. AN53344

Ensuring product safety and efficacy of alcohol-based hand sanitizers

Chapter two: In a production environment

The Centers for Disease Control and Prevention (CDC) first revised its hand hygiene guidelines in 2002 to recommend alcohol-based hand sanitizer as a possible alternative to hand cleansing with soap and water for the public and health care personnel.[1] The majority of alcohol-based hand sanitizers contain either isopropanol, ethanol, n-propanol, or a combination of two of these alcohols. The antimicrobial activity of alcohols can be attributed to their ability to denature proteins. The best antimicrobial efficacy can be achieved with ethanol (60 to 85%) and isopropanol (60 to 80%) solutions.[2] Higher concentrations are less potent because proteins are not denatured easily in the absence of water, whereas solutions with lower than 60% alcohol may only reduce the growth of germs but not kill them.

In response to the Coronavirus Disease 2019 (COVID-19) pandemic, the Food and Drug Administration (FDA) has recently issued guidelines[3,4] that temporarily allows compounders and certain entities that are not currently regulated by FDA as drug manufacturers to prepare and distribute hand sanitizer products for the duration of the public health emergency. Despite the relatively simple formulations and preparation protocols, it is critically important that proper quality assurance and control measures be in place to ensure the safety and efficacy of hand sanitizer products. In a previous application note we described the use of our top-of-the-line Thermo Scientific™ Nicolet™ iS50 FTIR Spectrometer to perform several analysis.[5] In this application note we will describe how we transferred the Nicolet iS50 workflow to a routine QA/QC FTIR, the Thermo Scientific™ Nicolet™ Summit PRO FTIR Spectrometer with the Thermo Scientific™ Everest™ ATR accessory running our new Thermo Scientific™ OMNIC™ Paradigm™ Software (Figure 1).

Figure 1: Nicolet Summit PRO FTIR Spectrometer with Everest ATR accessory and on-board touchscreen monitor.

In this application note we will describe how the three applications developed on the Nicolet iS50 were rapidly deployed to the Nicolet Summit. The first was using QC Compare to confirm that incoming material was the alcohol specified. This is particularly important with the recent discovery of methanol[6] in hand sanitizer. The second was using QCheck to verify that the production lot had the same spectral fingerprint as an approved reference sample that meets all specifications. QCheck will also ensure that significant levels of methanol are not present in the final product. The third application determines the percent ethanol in the final product to verify that it meets regulatory requirements.

A workflow was created in the OMNIC Paradigm Software to combine the three applications (Search, QCheck and Quant) into a single application, shown in Figure 2. The operator is asked if this is Incoming Material Identification or Final Product confirmation. A loop has been added for Final Product confirmation to allow multiple samples to be analyzed.

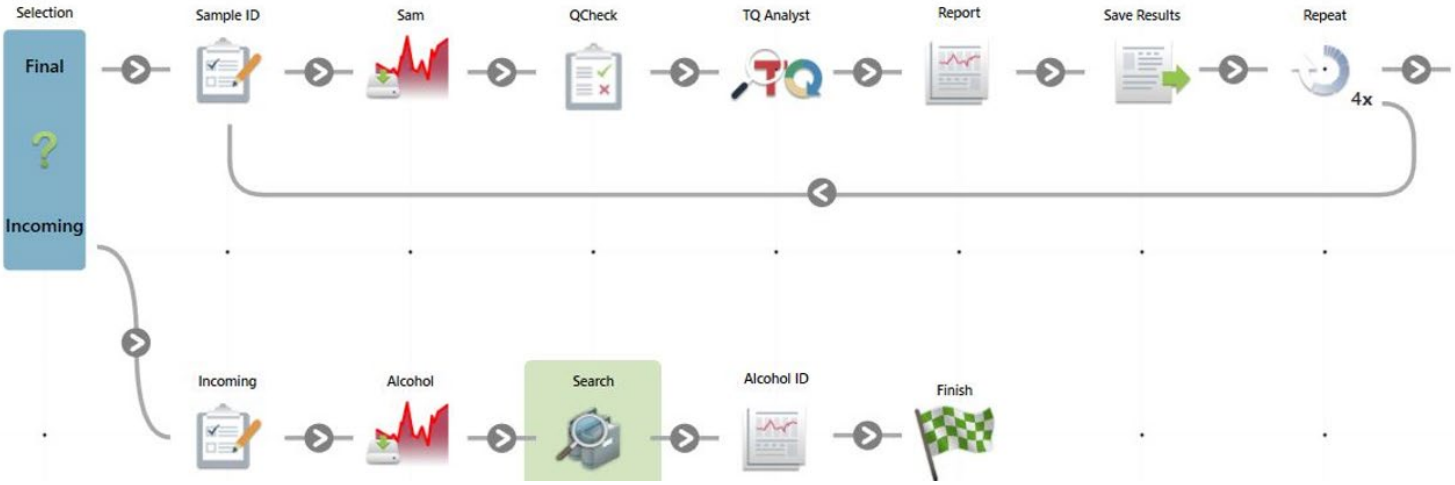

Figure 2: Workflow to verify the final product and to confirm incoming alcohol identification.

The operation in a quality control and assurance laboratory starts with verifying that the incoming material is labeled correctly. Figure 3 shows the results using the QC Compare function to ensure that the incoming material matches an ethanol reference spectrum. The Material Identification Library developed on the Nicolet iS50 with spectra of ethanol, 1-propanol and 2-propanol was directly applied to the spectra measured on the Nicolet Summit utilizing the workflow capabilities of OMNIC Paradigm Software. Methanol was recently added to this application. Note that although n-propanol has been used in alcohol-based hand sanitizers in parts of Europe for many years, it is not an approved active agent for hand sanitizer products in the United States.

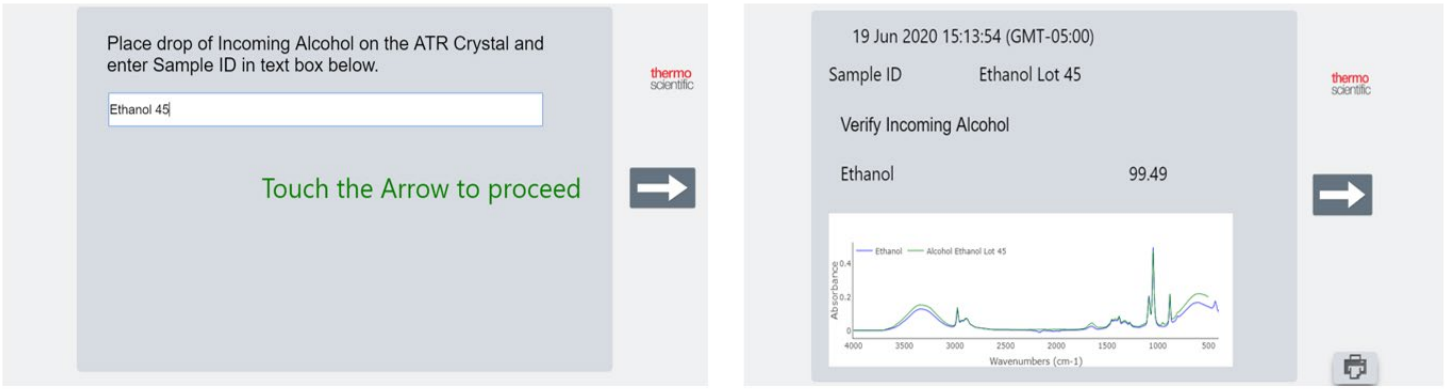

Figure 3: Results of applying the Material Identification Search to a spectrum of ethanol.

Thermo Scientific™ QCheck™ spectral correlation is an ideal tool for the verification of finished products. Again, the parameters and reference spectrum used for the QCheck measurement with the Nicolet iS50 were deployed on the Nicolet Summit. Figure 4 is an example of a QCheck Report saved during the workflow from a sample where several drops of methanol (about 5%) had been added to a commercial hand sanitizer. The presence of the small amount of methanol reduces the correlation below the allowable threshold of 99. This methanol adulterated sample failed the QCheck finished product verification.

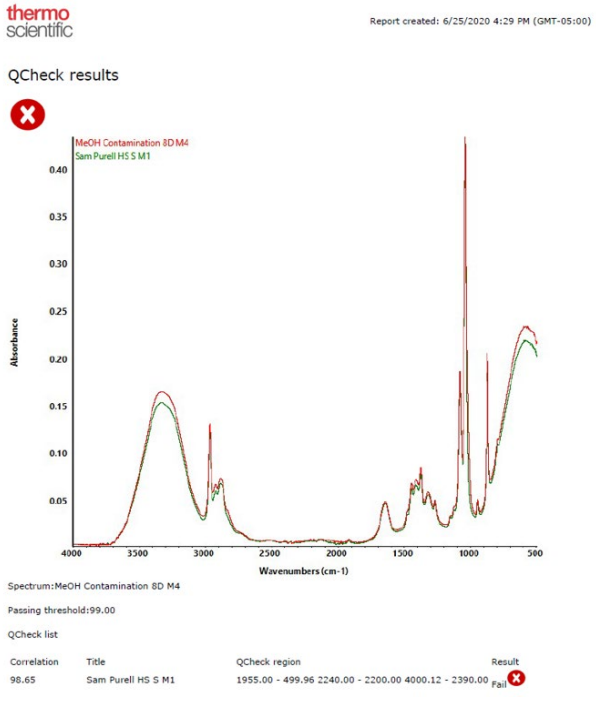

Figure 4: Results of applying QCheck to a methanol adulterated (red trace) hand sanitizer sample.

In addition to incoming material and final product inspection, FTIR can be used for the quantitative determination of alcohol percentage in hand sanitizers. FTIR measurements of a series of ethanol/water standards with ethanol ranging from 25–99% (v/v) were carried out. The area of the peak at 878 cm^{-1} was used to construct a calibration curve using Simple Beer's Law in Thermo Scientific™ TQ Analyst™ Software. The calibration curve exhibits an excellent linearity with a coefficient of 0.9981.

This method was then applied to five repeat samples of a commercially available hand sanitizer to determine the precision for the measurements on the Nicolet Summit instrument. The results were appended to an Excel readable CSV file (Figure 5). Excel was used for statistical analysis and to create a custom control chart.

Repeat Precision			
Sample ID	% ETHANOL	Qcheck	Date and time
HandSanitizer S5 M1	69.24	98.89	18 Jun 2020 09:37:52 (GMT-05:00)
HandSanitizer S5 M2	69.59	98.86	18 Jun 2020 09:37:52 (GMT-05:00)
HandSanitizer S5 M3	69.70	98.93	18 Jun 2020 09:37:52 (GMT-05:00)
HandSanitizer S5 M4	69.74	98.9	18 Jun 2020 09:37:52 (GMT-05:00)
HandSanitizer S5 M5	69.65	98.81	18 Jun 2020 09:37:52 (GMT-05:00)
Average	**69.58**		
Standard Deviation	**0.20**		

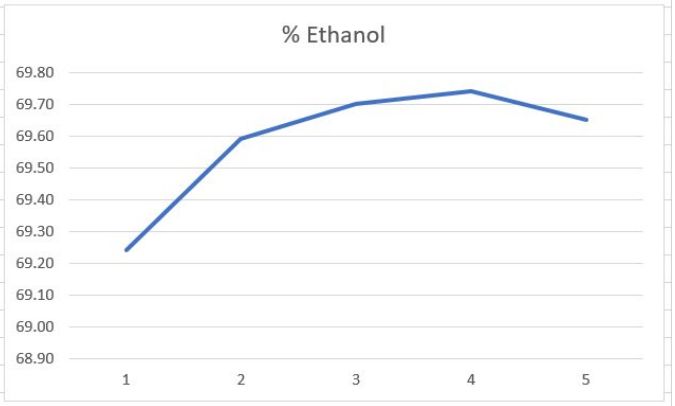

Figure 5: Chart of TQ Analyst Simple Beer's Law quant method results appended to readable CSV file by OMNIC Paradigm workflow.

This TQ Analyst method was recently modified to include calculating the weight percentage (wt%) of methanol and isopropanol in the sample. Here is the analysis of a hand sanitizer sample made with denatured alcohol (isopropanol) and methanol added. The overlay of the sample spectrum with the spectrum of methanol and the analysis results are shown in Figure 6.

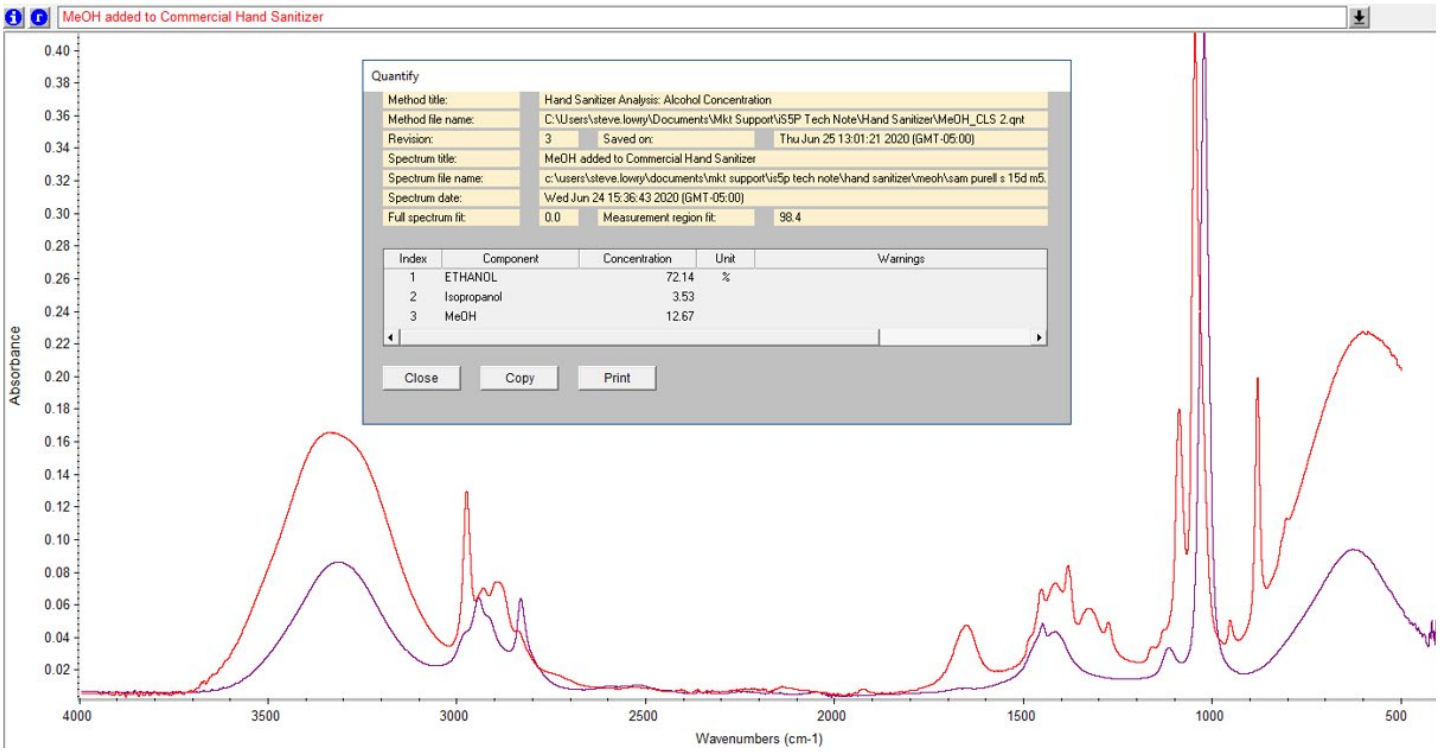

Figure 6: TQ Analyst method calculates weight percentage of methanol and isopropanol in hand sanitizer sample.

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To summarize, ATR FTIR measurements are straightforward and take less than 30 seconds with no need for sample preparation. Methods developed on the Nicolet iS50 FTIR Spectrometer are rapidly deployed to the Nicolet Summit PRO FTIR Spectrometer. QCheck and QC Compare allows for a rapid quality check of materials, enhancing the confidence of materials quality at different stages of the production cycle. The quantitative analysis enabled by TQ Analyst allows for accurate predictions of the alcohol content in final formulations. A single OMNIC Paradigm workflow run on the Nicolet Summit equipped with a diamond Everest ATR is ideally suited for the quality assurance and control of the alcohol-based hand sanitizer products.

References

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3. Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency, Immediately in Effect Guidance for Industry, https://www.fda.gov/media/136118/download
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5. Sukumaran, S., Chen, R. (2020). Ensuring product safety and efficacy of alcohol-based hand sanitizers (Application Note: AN53310). https://assets.thermofisher.com/TFS-Assets/MSD/Application-Notes/AN53310-ensuring-product-safety-efficacy-alcohol-based-hand-sanitizers.pdf
6. FDA Updates on Hand Sanitizers with Methanol, https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitizers-methanol

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