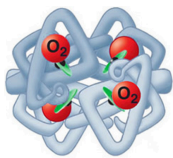
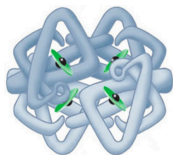


To understand the advantages and principles behind CueSee® CO-OX, for the validation of CO-oximeters, we need to start with the basics of hemoglobin. Hemoglobin in red blood cells is the primary vehicle for transporting oxygen in the body. Each hemoglobin molecule contains 4 heme groups with iron cores which binds oxygen. Hemoglobin exists as four main hemoglobin derivatives as listed in table 1.

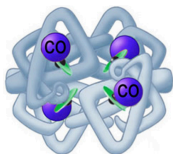
Table 1. Main Hemoglobin derivatives



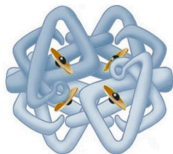
Oxyhemoglobin (O_2Hb) is Hemoglobin with bound oxygen.



Deoxygenated Hemoglobin (HHb) is hemoglobin without the bound oxygen.



Carboxyhemoglobin (COHb) is a stable complex of carbon monoxide and hemoglobin that forms in red blood cells upon contact with carbon monoxide and has lost the ability to bind oxygen.



Methemoglobin (MetHb) is the form of hemoglobin in which the iron in the heme group is oxidized from the normal ferrous state (Fe^{+2}) to the ferric state (Fe^{+3}) and therefore has also lost the ability to bind oxygen.

Co-oximeters are used to determine the concentration of hemoglobin derivatives in patient blood. These analyzers are multi-wave hemoglobin photometers and therefore if we plot on the x-axis the wavelength of visible light and on the y-axis the absorbance, we can clearly see the peaks of the derivatives. Figure 1 shows that O_2Hb has

two distinct separate peaks. This is like the spectrum of normal fresh blood in which hemoglobin is mostly in the O₂Hb form.

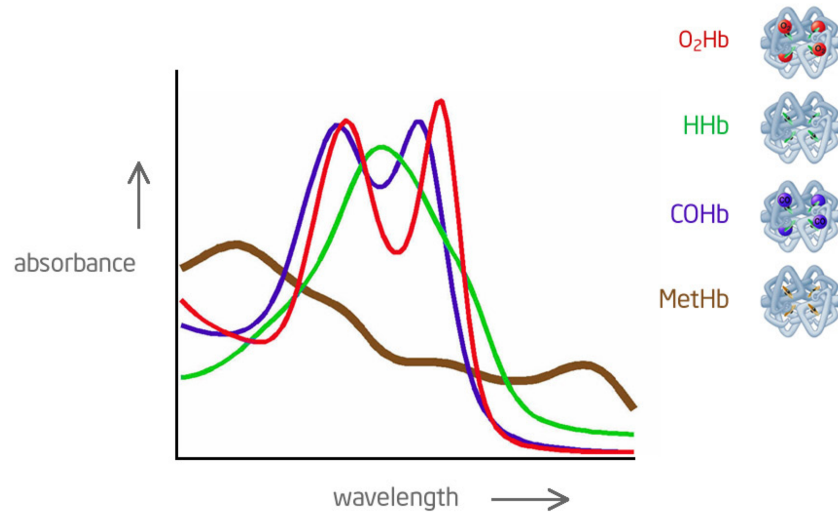


Figure 1. Absorbance spectra of hemoglobin derivatives

Deoxygenated hemoglobin has a single peak that is in between the peaks of oxyhemoglobin. Carboxyhemoglobin has two separate peaks very close to the peaks of oxyhemoglobin which makes it harder to separate between them. Methemoglobin has a much flatter spectrum with some waves across the other spectra.

Looking at Figure 2 we see a comparison of CueSee CO-OX to currently quality controls for CO-oximetry which are solutions containing dyes and therefore have major disadvantages.

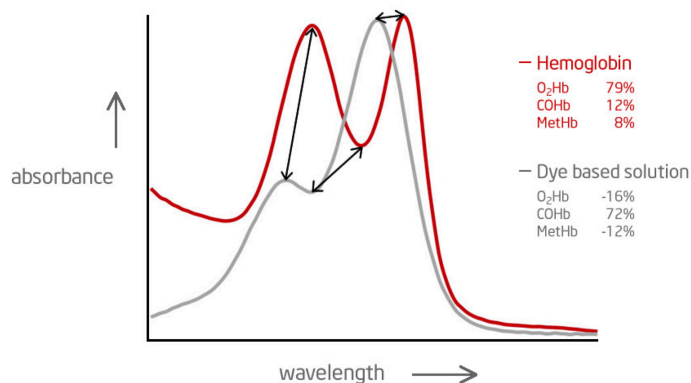


Figure 2. Hemoglobin versus dye spectrum



In red you see a spectrum of real hemoglobin and in grey the spectrum of a typical dye-based quality control liquid. It is obvious that the dye shows a very different spectrum. Peaks are at different wavelengths and have different heights. Also, slopes are very different. In some areas the hemoglobin spectrum is flat where the dye spectrum has the steepest slope and vice versa. Consequently, the major disadvantages of dye-based controls:

- Results are reported outside of the clinically relevant range; often even negative values are observed.
- Results reported for various models of CO-oximeters show huge differences, and often different dyes are required for different instruments.
- Most importantly, dyes do not show proper sensitivity to detect problems with CO-oximeters.

As an example, a change to a measuring wavelength shown on the x-axis produces minimal change in the absorbance of the dye-based solution (Figure 3a). But, that same change in wavelength has a major consequence for the absorbance of real hemoglobin (figure 3b).

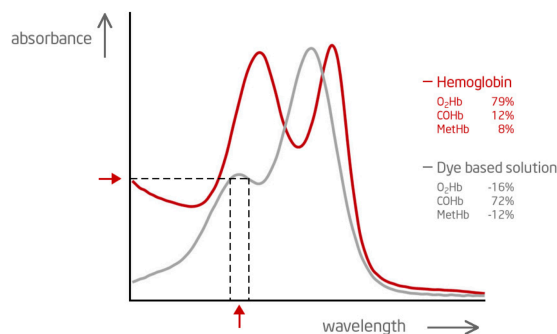


Figure 3a.

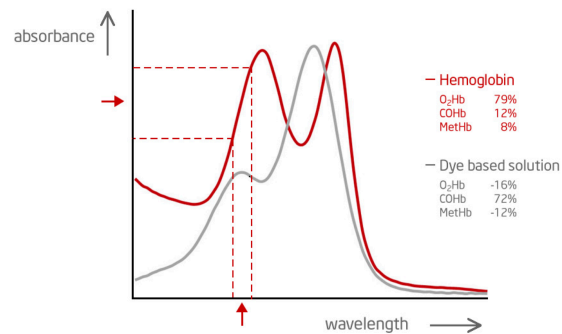
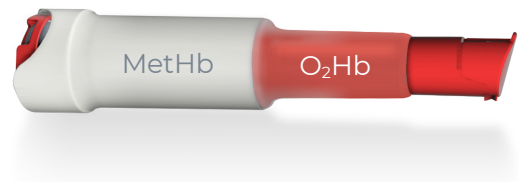


Figure 3b.

The ideal test material is a solution with real hemoglobin derivatives, which has the sensitivity and interferences these instruments are presented with by patient samples. Making a test material containing all hemoglobin derivatives that has sufficient time stability is extremely difficult. Oxyhemoglobin is by nature converted into methemoglobin. There are ways to prevent this from happening, but the consequence is that you will not have a sample with measurable and clinically relevant levels for both oxyhemoglobin and methemoglobin in one sample.

CueSee CO-OX is a unique quality control with real hemoglobin derivatives in one sample. Packaged in the ACU-Drop II, a dual-chambered device, the oxyhemoglobin is separated from the methemoglobin to provide a long shelf-life. Just before use, the user simply pushes a button to allow the liquids to combine. Then mix, and a sample with clinically relevant levels of all hemoglobin derivatives is ready to use, either from the built-in dropper bottle or by attaching a syringe.



As described on the [CueSee® CO-OX Performance](#) sheet such reliable and reproducible overall results on various types of instruments have never been shown before for CO-oximetry quality control materials.

In summary, CueSee® CO-OX is a unique and superior product to validate CO-oximeters. It offers the following benefits:

- Safe and easy to use with long open vial stability.
- The bloodlike matrix is commutable with all instruments providing identical results.
- It provides hemoglobin derivatives for all clinically relevant ranges.
- It is ideal for quality control, method comparisons, calibration verification, linearity studies, competency testing, AMR validation and proficiency testing.

As with all our quality control products, Eurotrol provides CueSee® Online, a free online service for comparing your quality control data with peers. With a simple import tool, enter your results and then generate statistics, reports and graphs that will satisfy any regulatory inspector. CueSee® Online is a true enhancement to any quality control program.