Inspections, Compliance, Enforcement, and Criminal Investigations

Measurement of Relative Humidity in the ETO Process

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DEPT. OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION *ORA/ORO/DEIO/IB*	**Date: 4/30/87 Number: 47 Related Program Areas: Drugs and Medical Devices**

ITG SUBJECT: MEASUREMENT OF RELATIVE HUMIDITY IN THE EO PROCESS

The importance and criticality of the moisture content or relative humidity (RH) of the environment within the enclosed vessel of the Ethylene Oxide (EO) sterilization process has been well established by the drug and device industries. Appropriate instrumentation systems are necessary to sense, control, and record this parameter. Of these, the key element of the system and the most difficult to establish and maintain in terms of accuracy is the moisture sensor. This ITG will briefly describe basic types of sensors together with some limitations.

TYPES OF SENSORS/INSTRUMENTS

The simplest form of RH measurement and one with which most are familiar, is the traditional Mechanical Hygrometer. It is based on the principle that certain materials will expand or contract as a function of the amount of moisture absorbed. Materials such as paper, wood, bone, plant leaves, textiles, animal tissue and plastics have been historically used. The most common materials, however, have been human or horse hair. Direct readout is usually obtained on a dial indicator interconnected to the material via mechanical linkage. It is also obvious that such an instrument would be difficult for remote reading in the enclosed space of a sterilization chamber and for all practically could not be used. It is also obvious that precision would not be a relied-upon quality. Response is slow for both increasing and decreasing humidity and temperature compensation cannot be made (calibration applies only to a specific temperature). Also, the aging process of the material is not uniform, making calibration extremely difficult. It is doubtful that the investigator will ever encounter the use of such an instrument to measure the RH in an EO chamber.

Electric Hygrometer - This type utilizes a sensor that is a hygroscopic film. An instantaneous change of electrical resistance or capacitance can be measured as the result of small changes in absorbed moisture by the film. The hygroscopic film is sometimes replaced by a wire grid wrapped around a substrate. The wire grid is usually coated with a hygroscopic salt solution (lithium chloride is common) which absorbs water vapor. Resistance of the wire grid corresponds to a calibrated RH value. A calibration curve is usually furnished for each unit by the manufacturer. In physical appearance for EO chamber use, the sensor most likely will resemble a metallic or plastic cylinder approximately 3/4 inch diameter by 2 inch long with perforations on the side and electrical contact pins or connector on an end. The response to changing RH is rapid and accuracy tolerances can be as low as ± 1.5% RH. This type of sensor usually is not reliable after multiple exposures to EO. A maintenance program to clean, rejuvenate, and recalibrate periodically is necessary for the user. The investigator should also be alerted to the fact that humidity sensitive materials are also temperature dependent. This means that the sensor must be calibrated over the entire temperature range of operation.

Dew-Point Hygrometer - This is commonly known as the chilled mirror technique wherein the optical qualities of a mirror are measured as it is cooled by the sampled gas to cause condensation. The amount of condensation is related to the dew-point temperature which together with a dry bulb temperature and a standard chart can be interpolated to reveal RH. This method can be quite accurate (± 2% RH). One manufacturer utilizes microprocessor technology to offer simultaneous measurement of not only dew-point but temperature and RH as well, with a digital readout display. Accuracy in determining RH has been claimed as low as ± 0.5%. Maintenance required for this type of sensor would be primarily the cleaning of the mirror and sampled gas line.

Gas Liquid Chromatography (GLC) - This technique utilizes sampling of the gas mixtures in the contained vessel. The area under the curves generated by the GLC are measured manually or automatically with a microprocessor to determine concentrations of sterilant gases, air, and moisture contents (RH). This is probably the most accurate means to measure RH. The critical factor is proper maintenance of the instrument and periodic calibration. The sampling ports must be clear and free of any debris and the sampling lines must be heated and insulated to prevent condensation. Not everyone understands the principles of GC; therefore, a qualified person, usually a chemist should be responsible for adjustments or maintenance of the equipment. This method also lends itself quite well to process control systems.

CONCLUSION

Other forms of sensors and instruments are available for measuring RH. Most are variations of the basic types described but they offer much less in practicality for the EO sterilizer. Some firms choose to use an empirical method for determining RH. Based upon the laws of thermodynamics for an ideal gas, RH, which is a ratio, can be expressed as a percentage of the mole fraction of water vapor in a space (chamber) to the mole fraction of water vapor in the space at saturation at a particular temperature. In the case of the EO chamber, this could be expressed in pressures for practical engineering applications by the equation:

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% RH =/_\ P (Change in absolute pressure) psia x 100

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       P sv (Saturation vapor pressure) psia
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Where,/_\ P is the change in absolute pressure of the chamber resulting from steam injection after the pre-evacuation portion of the cycle and P sv is the saturation vapor pressure taken from published tables of saturated steam and temperature. (See the attached excerpt of such a table). As an example, steam is injected into the EO chamber to increase the pressure by 3.0 in. Hg. (1.47 psia). Sterilization temperature is 130 F and from the attached table of saturation vapor pressure at a temperature, P sv = 2.2230 psia. The equation then becomes:

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RH = 1.47

     -------- x 100 = 66%

     2.2230
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The use of the empirical method is adequate providing that all instrumentation to measure both pressures and temperature are adequately calibrated and maintained. Validation/qualification of the process should verify the accuracy of the calculations. Some firms utilize this method as a means for back-up or for cross-checking to determine faulty sensors. The investigator is invited to also utilize this method for a rapid check of the RH parameter of the EO process during the Establishment Inspection.

References

1. The American Society of Mechanical Engineers; ASME Steam Tables; 1967.
2. Robertson, J.H., Townsend, M.W., Allen, P.M., Devisser, A., and Enzinger, R.M.; Validation of Ethylene Oxide Sterilization Cycles; PDA Spring Meeting; Chicago, IL; March 25, 1977.
3. Quin, F.C.; Humidity/Moisture Considerations; American Instrument Co., Silver Spring, MD; Reprint No. 490.


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                              i  Attachment to ITG #47
                                 ______________________
                          Saturated Steam: Temperature Table
                                      Chamber
                                     Temp. Psv
______________________________________________________________________

       Abs Press.       Specific Volume      Enthalpy              Entropy
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Temp	Lb per	Sat.	Sat.	Sat.	Sat.		Sat.	Sat.		Sat	Temp
Fahr	Sq In.	Liquid	Evap	Vapor	Liquid	Evap	Vapor	Liquid	Evap	Vapor	Fahr
t	p	v f	v fg	v g	h f	h fg	h g	S f	S fg	S g	t
32.0*	0.08859	0.016022	3304.7	3304.7	-0.0179	1075.5	1075.5	0.0000	2.1873	2.1873	32.0*
34.0	0.09600	0.016021	3061.9	3061.9	1.996	1074.4	1076.4	0.0041	2.1762	2.1802	34.0
36.0	0.10395	0.016020	2839.0	2839.0	4.008	1073.2	1077.2	0.0081	2.1651	2.1732	36.0
38.0	0.11249	0.016019	2634.1	2634.2	6.018	1072.1	1078.1	0.0122	2.1541	2.1663	38.0
40.0	0.12163	0.016019	2445.8	2445.8	8.027	1071.0	1079.0	0.0162	2.1432	2.1594	40.0
42.0	0.13143	0.016019	2272.4	2272.4	10.035	1069.8	1079.9	0.0202	2.1325	2.1527	42.0
44.0	0.14192	0.016019	2112.8	2112.8	12.041	1068.7	1080.7	0.0242	2.1217	2.1459	44.0
46.0	0.15314	0.016020	1965.7	1965.7	14.047	1067.6	1081.6	0.0282	2.1111	2.1393	46.0
48.0	0.16514	0.016021	1830.0	1830.0	16.051	1066.4	1082.5	0.0321	2.1006	2.1327	48.0
50.0	0.17796	0.016023	1704.8	1704.8	18.054	1065.3	1083.4	0.0361	2.0901	2.1262	50.0
52.0	0.19165	0.016024	1589.2	1589.2	20.057	1064.2	1084.2	0.0400	2.0798	2.1197	52.0
54.0	0.20625	0.016026	1482.4	1482.4	22.058	1063.1	1085.1	0.0439	2.0695	2.1134	54.0
56.0	0.22183	0.016028	1383.6	1383.6	24.059	1061.9	1086.0	0.0478	2.0593	2.1070	56.0
58.0	0.23843	0.016031	1292.2	1292.2	26.060	1060.8	1086.9	0.0516	2.0491	2.1008	58.0
60.0	0.25611	0.016033	1207.6	1207.6	28.060	1059.7	1087.7	0.0555	2.0391	2.0946	60.0
62.0	0.27494	0.016036	1129.2	1129.2	30.059	1058.5	1088.6	0.0593	2.0291	2.0885	62.0
64.0	0.29497	0.016039	1056.5	1056.5	32.058	1057.4	1089.5	0.0632	2.0192	2.0824	64.0
66.0	0.31626	0.016043	989.0	989.1	34.056	1056.3	1090.4	0.0670	2.0094	2.0764	66.0
68.0	0.33889	0.016046	926.5	926.5	36.054	1055.2	1091.2	0.0708	1.9996	2.0704	68.0
70.0	0.36292	0.016050	868.3	868.4	38.052	1054.0	1092.1	0.0745	1.9900	2.0645	70.0
72.0	0.38844	0.016054	814.3	814.3	40.049	1052.9	1093.0	0.0783	1.9804	2.0587	72.0
74.0	0.41550	0.016058	764.1	764.1	42.046	1051.8	1093.8	0.0821	1.9708	2.0529	74.0
76.0	0.44420	0.016063	717.4	717.4	44.043	1050.7	1094.7	0.0858	1.9614	2.0472	76.0
78.0	0.47461	0.016067	673.8	673.9	46.040	1049.5	1095.6	0.0895	1.9520	2.0415	78.0

80.0 0.50683 0.016072 633.3 633.3 48.037 1048.4 1096.4 0.0932 1.9426 2.0959 80.0

82.0 0.54093 0.016077 595.5 595.5 50.033 1047.3 1097.3 0.0969 1.9334 2.0303 82.0

84.0 0.57702 0.016082 560.3 560.3 52.029 1046.1 1098.2 0.1006 1.9242 2.0248 84.0

86.0 0.61518 0.016087 227.5 527.5 54.026 1045.0 1099.0 0.1043 1.9151 2.0193 86.0

88.0 0.65551 0.016093 496.8 496.8 56.022 1043.9 1099.9 0.1079 1.9060 2.0139 88.0

90.0 0.69813 0.016099 468.1 468.1 58.018 1042.7 1100.8 0.1115 1.8970 2.0086 90.0

92.0 0.74313 0.016105 441.3 441.3 60.014 1041.6 1101.6 0.1152 1.8881 2.0033 92.0

94.0 0.79062 0.016111 416.3 416.3 62.010 1040.5 1102.5 0.1188 1.8792 1.9980 94.0

96.0 0.84072 0.016117 392.8 392.9 64.006 1039.3 1103.3 0.1224 1.8704 1.9928 96.0

98.0 0.89356 0.016123 370.9 370.9 66.003 1038.2 1104.2 0.1260 1.8617 1.9876 98.0

100.0 0.94924 0.016130 350.4 350.4 67.999 1037.1 1105.1 0.1295 1.8530 1.9825 100.0

102.0 1.00789 0.016137 331.1 331.1 69.995 1035.9 1105.9 0.1331 1.8444 1.9775 102.0

104.0 1.06965 0.016144 313.1 313.1 71.992 1034.8 1106.8 0.1366 1.8358 1.9725 104.0

106.0 1.1347 0.016151 296.16 296.18 73.99 1033.6 1107.6 0.1402 1.8273 1.9675 106.0

108.0 1.2030 0.016158 280.28 280.30 75.98 1032.5 1108.5 0.1437 1.8188 1.9626 108.0

110.0 1.2750 0.016165 265.37 265.39 77.98 1031.4 1109.3 0.1472 1.8105 1.9577 110.0

112.0 1.3505 0.016173 251.37 251.38 79.98 1030.2 1110.2 0.1507 1.8021 1.9528 112.0

114.0 1.4299 0.016180 238.21 238.22 81.97 1029.1 1111.0 0.1542 1.7938 1.9480 114.0

116.0 1.5133 0.016188 225.84 225.85 83.97 1027.9 1111.9 0.1577 1.7856 1.9433 116.0

118.0 1.6009 0.016196 214.20 214.21 85.97 1026.8 1112.7 0.1611 1.7774 1.9386 118.0

120.0 1.6927 0.016204 203.25 203.26 87.97 1025.6 1113.6 0.1646 1.7693 1.9339 120.0

122.0 1.7891 0.016213 192.94 192.95 89.96 1024.5 1114.4 0.1680 1.7613 1.9293 122.0

124.0 1.8901 0.016221 183.23 183.24 91.96 1023.3 1115.3 0.1715 1.7533 1.9247 124.0

126.0 1.9959 0.016229 174.08 174.09 93.96 1022.2 1116.1 0.1749 1.7453 1.9202 126.0

128.0 2.1068 0.016238 165.45 165.47 95.96 1021.0 1117.0 0.1783 1.7374 1.9157 128.0

130.0 2.2230 0.016247 157.32 157.33 97.96 1019.8 1117.8 0.1817 1.7295 1.9112 130.0

132.0 2.3445 0.016256 149.64 149.66 99.95 1018.7 1118.6 0.1851 1.7217 1.9068 132.0

134.0 2.4717 0.016265 142.40 142.41 101.95 1017.5 1119.5 0.1884 1.7140 1.9024 134.0

136.0 2.6047 0.016274 135.55 135.57 103.95 1016.4 1120.3 0.1918 1.7063 1.8980 136.0

138.0	2.7438	0.016284	129.09	129.11	105.95	1015.2	1121.1	0.1951	1.6986	1.8937	138.0
140.0	2.8892	0.016293	122.98	123.00	107.95	1014.0	1122.0	0.1985	1.6910	1.8895	140.0
142.0	3.0411	0.016303	117.21	117.22	109.95	1012.9	1122.8	0.2018	1.6534	1.8852	142.0
144.0	3.1997	0.016312	111.74	111.76	111.95	1011.7	1123.6	0.2051	1.6759	1.8810	144.0
146.0	3.3653	0.016322	106.58	106.59	113.95	1010.5	1124.5	0.2084	1.6684	1.8769	146.0
148.0	3.5381	0.016332	101.68	101.70	115.95	1009.3	1125.3	0.2117	1.6610	1.8727	148.0
150.0	3.7184	0.016343	97.05	97.07	117.95	1008.2	1126.1	0.2150	1.6536	1.8686	150.0
152.0	3.9065	0.016353	92.66	92.68	119.95	1007.0	1126.9	0.2183	1.6463	1.8646	152.0
154.0	4.1025	0.016363	88.50	88.52	121.95	1005.8	1127.7	0.2216	1.6390	1.8606	154.0
156.0	4.3068	0.016374	84.56	84.57	123.95	1004.6	1128.6	0.2248	1.6318	1.8566	156.0
158.0	4.5197	0.016384	80.82	80.83	125.96	1003.4	1129.4	0.2281	1.6245	1.8526	158.0
160.0	4.7414	0.016395	77.27	77.29	127.96	1002.2	1130.2	0.2313	1.6174	1.8487	160.0
162.0	4.9722	0.016406	73.90	73.92	129.96	1001.0	1131.0	0.2345	1.6103	1.8448	162.0
164.0	5.2124	0.016417	70.70	70.72	131.96	999.8	1131.8	0.2377	1.6032	1.8409	164.0
166.0	5.4623	0.016428	67.67	67.68	133.97	998.6	1132.6	0.2409	1.5961	1.8371	166.0
168.0	5.7223	0.016440	64.78	64.80	135.97	997.4	1133.4	0.2441	1.5892	1.8333	168.0
170.0	5.9926	0.016451	62.04	62.06	137.97	996.2	1134.2	0.2473	1.5822	1.8295	170.0
172.0	6.2736	0.016463	59.43	59.45	139.98	995.0	1135.0	0.2505	1.5753	1.8258	172.0
174.0	6.5656	0.016474	56.95	56.97	141.98	993.8	1135.8	0.2537	1.5684	1.8221	174.0
176.0	6.8690	0.016486	54.59	54.61	143.99	992.6	1136.6	0.2568	1.5616	1.8184	176.0
178.0	7.1840	0.016498	52.35	52.36	145.99	991.4	1137.4	0.2600	1.5548	1.8147	178.0

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Page Last Updated: 02/17/2009

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