

AMITemp[®]

Personal Thermometer

I. Standards, Technical, and Safety Information

The technology embodied in the AMITemp[®] Personal Thermometer offers a unique combination of accuracy, speed, safety, convenience and economy in the measurement of temperature. This technology is highly competitive with both electronic and traditional mercury-glass thermometers. Its potential for consumer appeal is especially promising in view of the rapid growth and change in the thermometer market and the erosion of mercury-glass sales in recent years.

A. **Standards: Meets American Society for Testing and Materials Standard # E1299-89 for thermometer accuracy, stability, and safety. FDA Regulatory Class I, 510K# 863181, Germany PTBA#15.19/94.06 certificate # 9.13-80/94. CE Marque is likely to be obtained by June 1998.**

B. **Structure and Function:** The new AMITemp[®] clinical thermometer is a thin, flexible, padded plastic strip containing 45 cavities in the Fahrenheit version and 50 cavities in the Celsius version. The cavities are arranged in a double matrix at the functioning end of the unit. The rows of the matrix are numbered in one-degree units for degrees F° and 0.5 degree units for degrees C°, covering the ranges 96.0 to 104.8 and 35.5 to 40.4, respectively. The columns of the Fahrenheit version carry printed indicia representing 0.2 degrees F° (i.e., .0, .2, .4, .6, .8).

Each cavity contains a fixed chemical composition comprising three liquid crystal compounds and a varying concentration of a soluble additive. These chemical compositions have discrete and repeatable change-of-state properties, the temperatures of which are determined by the concentrations of additive. Additive concentrations are varied in accordance with an empirically established formula to produce a series of change-of-state temperatures consistent with the indicia on the device. The chemicals are fully encapsulated by a clear film which allows observation of the chemical change but prevents any user contact with the chemicals.

When the thermometer is placed in an environment within its range, such as 98.2 degrees F°, the chemicals in all of the cavities up to and including 98.2 change within a few seconds from a liquid crystal to an isotropic liquid state. This change of state is accompanied by an optical change that is easily observed by the user. The resplendent green light reflected from the liquid crystal state is transmitted through the isotropic state. As a result, those cavities containing composition with transition temperatures up to and including 98.2 degrees F° change to black, whereas those with transition temperatures of 98.4F° and higher continue to appear green. After the thermometer is removed from the 98.2 degree F° environment and returned to room temperatures, the black dots begin to diminish and return to their original state in about 45 seconds, thereby providing the user with more than ample time to make a reading.

C. **Reversibility:** The AMITemp[®] thermometer is designed to return automatically to a reusable state after a few minutes, as the perturbed compositions gradually revert to their liquid crystal structure and again reflect green light. Complete reversibility has been established in both in-vitro and in-vivo studies. The in-vitro studies were conducted in 20 water baths, each set at a specific temperature rising sequentially in increments of 0.4 degrees F° AMITemp[®] thermometers placed in these water baths and repetitively immersed after five-minute intervals gave consistent and accurate readings over both increasing and decreasing temperature sequences. This reversibility and repeatability of readings has been established for 100 temperature cycles in such controlled water baths.

One important attribute of the automatic and complete reversibility of the AMITemp[®]

thermometer is that the product can be shipped and stored under conditions requiring no special measures to control temperature exposure of the devices. Tests indicate that the product can experience sustained environmental temperatures as high as 140 degrees F° without compromising its accuracy and readability.

- D. **Accuracy and Response Time:** The in-vitro accuracy of the AMITemp® liquid crystal thermometer equals or exceeds that of glass-mercury and electronic thermometers. Thousands of units produced in pilot production runs show agreement with calibrated water baths to within 0.2 degrees F° across the entire range.

Preliminary in-vivo tests on a small test population of healthy individuals resulted in close agreement with measurements using specially-calibrated glassmercury thermometers after three-minute duration. The mean difference between the AMITemp® thermometers and the calibrated glass-mercury devices was only 0.12 degrees F°. The AMITemp® thermometer also achieves equilibrium very rapidly, due to its small "drawdown" (the cooling effect on tissue of introduction of a room-temperature device) and the small energy attending the chemical phase transition.

- E. **Safety:** The total mass of thermally responsive chemicals in a AMITemp® thermometer is only 2 milligrams. It is nonetheless desirable to assure the safety of these chemicals, and for this reason the liquid crystal compounds have been the subject of detailed toxicity, irritation and sensitization analyses. Parallel tests were applied to control substances formulated for daily oral use, consisting of a popular toothpaste and a mouthwash. In all of these tests the liquid crystal compounds proved non-hazardous, with fewer reactions than either the toothpaste or the mouthwash.

The innocuous nature of these liquid crystal compounds is also an important consideration with regard to the safety of production employees. There is increasing concern regarding occupational exposure to toxic mercury in the production of glass-mercury thermometers. All recently-built production facilities have been located in developing countries such as India and Pakistan. In contrast, because there is no measurable vapor pressure in the atmosphere of the AMITemp® liquid crystal materials, and because there are no adverse effects on contact with the skin, these materials present no discernable risk to the employee.

Insofar as it is desirable to clean and disinfect thermometers after each use, such sanitizing measures can be applied more efficaciously to the AMITemp® instrument than to glass-mercury or electronic devices. Unlike these latter types, the AMITemp® thermometer can be washed in very hot water or cleaned in other disinfecting solutions.

- F. **Stability:** The combination of chemical formulation and encapsulating materials was selected so as to maximize shelf life under both normal and abusive storage and distribution conditions. Prototype units manufactured in 1978 were still accurate when tested six years later. Product based upon similar materials and manufactured during short production runs in 1982 and 1983 have not drifted out of their original specifications.

An accelerated life study was conducted in 1986, following the specifications of the American Society of Testing Materials (ASTM) draft standard for such devices, Section 6.4, Storage Environment Test. This study indicates that the AMITemp® thermometer fully meets the draft ASTM standard.

- G. **Technical Advantages:** Several technical advantages of the AMITemp® technology contribute to making temperature-taking less onerous and less costly to consumers and professionals than with any existing alternatives:

Cost - The AMITemp® technology of temperature measurement provides distinctly lower costs when compared to all other temperature devices.

Safety - The safety advantages of AMITemp® technology are substantial. There is no danger, as with a conventional thermometer, of glass ingestion or mercury poisoning if a child bites the active part of the unit.

Speed and ease-of-use - The AMITemp® thermometer is quick, portable, non-breakable and easy to use (e.g. no shake-down or re-setting).

II. Quality Control Procedures

A. Chemical Transition Temperatures

1. Liquid Crystal Base - each batch of approximately 4 kg (sufficient to produce 5 million thermometers) is checked for purity, melting point (54.5°C), color and stability (no change in melting point after storage at 70°C for 7 days).
2. The transition temperatures of the five Primaries prepared from the Liquid Crystal Base are determined in duplicate to $\pm 0.02^\circ$ and plotted against weight percent mineral oil. The average deviation of the observed values from the linear regression fit cannot exceed 0.02° .
3. The transition temperatures of the fifty Mixtures prepared from five Primaries are determined in duplicate. No transition temperature can deviate from the target by more than 0.03° .

B. In-Process Control

1. The first section of web produced from each new lot of Liquid Crystal Mixtures is tested at each of the fifty points for accuracy and sequence of firing order.
2. The first half meter of each roll of thermometers (25,000 units) is cut into sections of four units and tested at six temperatures (96.6°, 97.8°, 98.6°, 100.6°, 102.2°, 104.2°) for accuracy and fill levels.
3. Every thermometer in each roll is inspected for fill, bridging and figure printing quality. Any thermometer with a critical, major or minor defect is marked by the inspector and is automatically rejected in the final cut-out process. (This visual inspection will be converted to a machine vision system over the next six months.)
4. During final cut-out thermometers are continuously sampled and visually checked for cleanliness (free of adhesive and foreign matter) placement of the dots and figures relative to edge, and absence of filaments.

C. Final Product Accuracy and Appearance Tests

1. 480 samples are selected from each lot of 50,000 units and tested in the six water baths specified above. One measurement which differs from the water bath temperature by more than 0.1° is classified as a critical defect. One dot in a sequence of dots which fails to change color in any of the 480 units is classified as a critical defect. One critical defect is cause for rejection of the entire lot.
2. Another 500 samples from each lot are visually examined for major and minor cosmetic defects. If the sum of defects exceeds 5 (1%), the entire lot is reinspected, the units with defects are withdrawn, the lot is resampled and the visual test is repeated.

D. Calibration

1. The individual high resolution mercury-in-glass thermometers used to measure the temperatures in each of the six temperature controlled water baths are calibrated against a United States Government National Bureau of Standards (NBS) thermometer every three months. All water bath temperatures are set and regulated to 0.01° accuracy. The NBS thermometer is returned to the Bureau for recalibration every two years.

E. Administrative Control

1. The company is inspected by an investigator from the United States Food and Drug Administration (FDA) once each year. This inspection measures the company's manufacturing and quality assurance practices against the FDA published GMP standards and cites all adverse findings. A written response to such findings is required in which the company presents its plan for correcting any deficiencies. This plan must be implemented within the period allowed. In its last inspection of the manufacturing facility the FDA reported no adverse findings.
2. A Certificate of Compliance signed by an officer of the company for each lot of thermometers is issued at the time of shipment.