K-PATENTS
PROCESS INSTRUMENTS

Certified by EHEDG

K-PATENTS PHARMA PROCESS REFRACTOMETER PR-43-P

FOR IN-LINE CONCENTRATION MEASUREMENT

SB: PR-43-P-1
January 2016

TYPICAL APPLICATIONS

PHARMACEUTICAL CHEMICALS
Acetylsalicylic acid, Calcium gluconate, Glycerophosphates, Chloral hydrate, Saccharin, Antihistamines, Tranquilizers, Antifilarials, Diethyl carbamazine citrate, Antidiabetics and more.

ACTIVE PHARMACEUTICAL INGREDIENTS
Actives, Excipients, Intermediates, Raw material, Fine chemicals, and Bulk chemicals.

ANTIBIOTICS
Penicillin, Streptomycin, Tetracyclines, Chloramphenicol, and Antifungals.

BLOOD PRODUCTS
Blood, Plasma, Serum, Infusion liquids, Sodium chloride, and Glucose.

PROTEINS
Proteins and Protein buffer solutions

VITAMINS
Ascorbid acid, Ca-arabonate, Riboflavin, Vitamin-B, Vitamin-C Sodium Pantonate. and more.

SYNTHETIC HORMONES

SYRUPS
Concentrated aqueous solutions of sucrose.

DRUGS OF VEGETABLE ORIGIN
Quinine, Strychnine and Brucine, Emetine, and Digitalis Glycosides, and Herbal extracts.

VACCINES AND SERA
Sucrose gradient purification by zonal ultracentrifugation: rotor unloading and fractionation, sucrose solution.

ACIDS, BASES AND SOLVENTS

QUALITY CONTROL AND TESTING

PRODUCT AND CIP INTERFACES
Product to product interfaces, product to CIP interfaces, CIP fluids.

CHROMATOGRAPHIC SEPARATION
Fractionation.

PERFORMANCE OVERVIEW

IN-LINE MEASUREMENT TECHNOLOGY FOR THE PHARMACEUTICAL INDUSTRY

K-Patents has applied its expertise to developing the unique and innovative Pharma process refractometer PR-43-P to measure, refine, manage and indicate liquid concentration or density and diagnostic information. The Pharma refractometer PR-43-P is designed to meet pharmaceutical industry standards and guidelines including PAT, GMP, CIP/SIP, 21 CFR Part 11 and validation.

The Pharma PR-43-P system consists of a compact process refractometer and a graphical user interface. The PR-43-P has a measurement range of 0 to 100 Brix and provides an Ethernet or 4–20 mA output signal proportional to the temperature-compensated concentration value for real-time process control. The user can choose between a rugged, multichannel, industrial computer or a compact light-weight user interface.

The PR-43-P Refractometer has a built-in web server with an instrument homepage. The homepage enables the configuration, monitoring, verification and diagnosis of the refractometer via an Ethernet connection. Every PR-43-A Refractometer also generates an mA output signal for control purposes.

The PR-43-P refractometer needs no recalibration or regular maintenance. Furthermore, the calibration of each refractometer can be verified using standard refractive index liquids and a built-in verification procedure.

PHARMA COMPLIANCE

The K-Patents Pharma PR-43-P is an ideal in-line process instrument for pharmaceutical processing and for the Process analytical technology (PAT) framework, because:

- It provides a modern process and endpoint tool for the real-time monitoring and control of liquid concentration or density.
- It has FDA 21 CFR Part 11 compliant electronic data capture and storage technology.
- Full IQ/OQ documentation is available for the fulfillment of the equipment qualification.
- The K-Patents PR-43-P is a scalable solution, from the early lab scale testing stages to full-scale process production.
- The K-Patents PR-43-P comes with pharma grade materials, material traceability documentation and controls:
  - Steel parts are made of 316L stainless steel
  - Product contact surface finishes are electropolished and the surface roughness is Ra 0.4µm (15µ inch)
  - USP Class VI Elastomers are tested for materials' biocompability and toxigology safety
  - No animal derived ingredients (ADI) are used in processing or machining
- The K-Patents PR-43-P is Sanitary 3-A approved and EHEDG (European Hygienic Equipment Design Group) Type EL Class I certified.

EQUIPMENT SCALABILITY, QUALIFICATION AND INSTALLATION

The Pharma refractometer PR-43-P is installed in the main processing line or vessel and no by-pass arrangements are required. The user interface of the refractometer can be installed locally in the field, remotely in the control room or in both locations by connecting several user interfaces to a network.

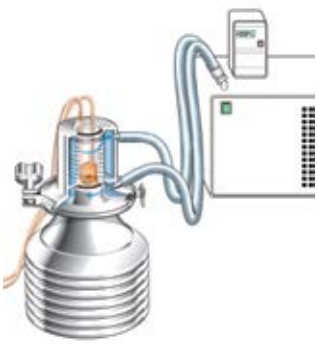
The following steps are common to a K-Patents Pharma Refractometer PR-43-AP qualification process:

1A. LAB TEST WITH STATIC SAMPLE

Laboratory test for manual sampling in a laboratory cuvette consisting of an agitator with a stirrer and connections for thermostat-controlled water.

1B. LAB TEST WITH CONTINUOUS SAMPLE

Laboratory test for continuous sampling in a laboratory cuvette, consisting of connections for a sample inlet and an outlet and for thermostat-controlled water.



2. TEST AT PILOT SCALE

Installation in a pilot process using a pharma mini flow cell.

3. INSTALLATION AT FULL PRODUCTION SCALE

STANDARD PACKAGES

REFRACTOMETER PR-43-P

MULTICHANNEL USER INTERFACE MI

PHARMA REFRACTOMETER PR-43-P AND MULTICHANNEL USER INTERFACE MI

A fully equipped K-Patents system with a refractometer, interconnecting cable and multichannel user interface with high performance industrial computing, wash control and high expandability capabilities and connectivity.

This multichannel user interface provides the highest level of industrial computing, intelligence and sophisticated features, as well as environmental protection.

REFRACTOMETER PR-43-P

COMPACT USER INTERFACE CI

PHARMA REFRACTOMETER PR-43-P AND COMPACT USER INTERFACE CI

A K-Patents compact, single device connectivity system with a refractometer, interconnecting cable and compact user interface for applications where a local or remote display and access is preferred and no wash is required.

REFRACTOMETER PR-43-P AND LABORATORY TEST CUVETTE LTC

PHARMA REFRACTOMETER PR-43-P AND LABORATORY TEST CUVETTE LTC

Refractometer, laboratory test cuvette LTC, computer, multichannel or compact user interface and microprocessor controlled thermostat.

The laboratory test cuvette can be used for the further study of sample characteristics e.g. concentrations at varied temperatures. Repeat preparations of the laboratory pilot batch are required as an intermediate step in a scale-up process. The laboratory test cuvette with its continuous sampling feature is designed for testing small volumes of samples in a laboratory pilot batch.

USER INTERFACES

The K-Patents Pharma refractometer PR-43-P can be equipped with two user interface options for the user and refractometer, as well as refractometer and control system interaction.

MULTICHANNEL USER INTERFACE MI

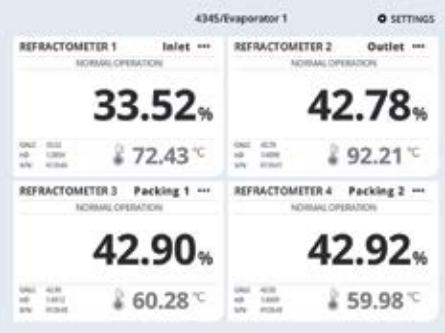
- High-performance, industrial computing system
- Expandable system and connectivity for up to four (4) PR-43-A refractometers and eight (8) I/O modules
- Environmentally sealed IP67, NEMA 6, rugged 316 stainless steel enclosure that withstands corrosive cleaning agents and frequent washes in food and beverage processing plants. In addition, the stainless steel enclosure has superior hygiene qualities and inhibits the growth of bacteria and germs. Also suitable for demanding field and outdoor conditions (-40−50°C, -40−122°F).
- Prism wash diagnostics and control
- Trend display that displays one or two graphs over a selected period of time.
- Embedded measurement apps: these apps are small programs that provide different types of measurement data and functionality.
- Modules, e.g. mA-output and mA-input module
- 10” graphical touchscreen color display
- User authentication, electronic data records and data-logging and event log. Together with the user’s own procedural and administrative user controls, these facilitate FDA 21 CFR Part 11 adherence. The user interface uses a UDP/IP protocol to communicate over the Ethernet with any type of computer. This eliminates human error and enables refractometer-generated measurement and diagnostic data capture for storage, analysis and reporting.
- Access to the refractometer and to the refractometer generated data is restricted to authorized personnel only, by a password and padlock protection.

COMPACT USER INTERFACE CI

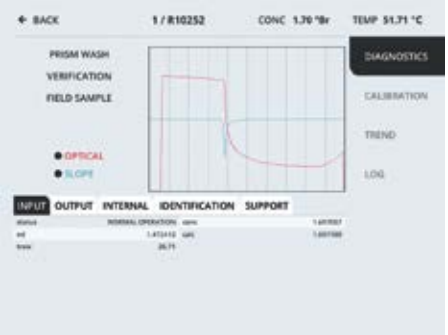
- Single device connectivity
- Local and/or remote display and access
- IP65, NEMA 4, light-weight, aluminum enclosure for control room conditions and epoxy coated enclosure with polycarbonate display shield for field conditions
- Trend display
- 10” graphical touchscreen color display.
- User authentication, electronic data records and data-logging and event log.

DISPLAYS

MI Main output display for four (4) measurement apps



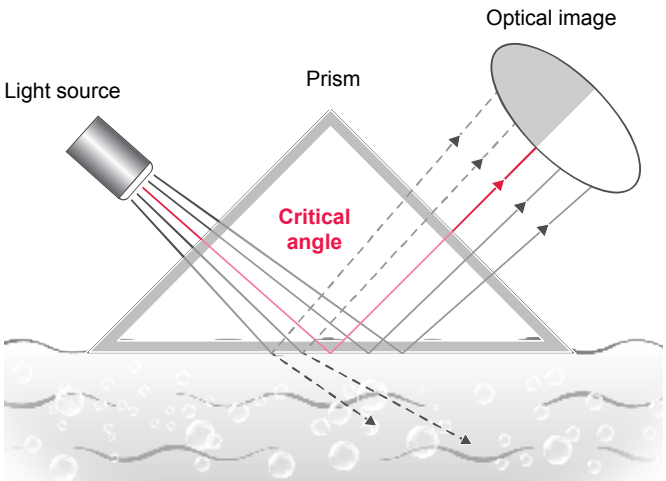
Diagnostics display



Trend display

User authentication with user ID and password

PRINCIPLE



DIGITAL MEASUREMENT PRINCIPLE

The light source sends light to the interface between a prism and the process solution, where the rays meet the surface at different angles. Depending on the angle, some rays undergo a total internal reflection, while the rest of the light is refracted into the process solution.

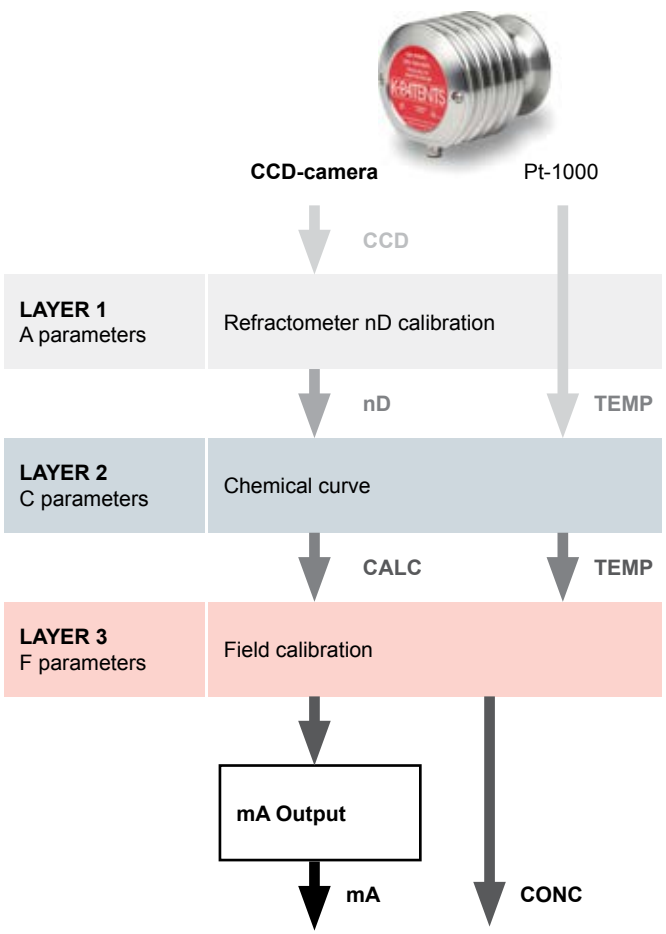
Thus, an optical image with a dark sector and a light sector is created. The angle corresponding to the shadow line is called the critical angle of total internal reflection.

This angle is a function of the refractive index and therefore the concentration of the solution. A CCD-camera detects the optical image. The image is transformed point-by-point into a digital signal. Digital signal processing is used to locate the exact shadow line position and to determine the refractive index nD.

A built-in temperature sensor measures the temperature T on the interface of the process liquid. The sensor converts the refractive index nD and temperature T into Brix units.

The diagnostics program ensures that the measurement is reliable.

CALIBRATION



UNIQUE 3-LAYER CALIBRATION

The concentration calibration of the K-Patents PR-43-P refractometer is organized into three (3) layers: the Refractometer nD calibration, chemical curve and field calibration. The advantages of the layer feature are free interchangeability between refractometers, applications and recipes, with no need for mechanical calibration adjustment in the field.

The optical image information is detected by the CCD-element and transformed into a number (CCD). The process temperature T is measured in terms of Pt-1000 resistance.

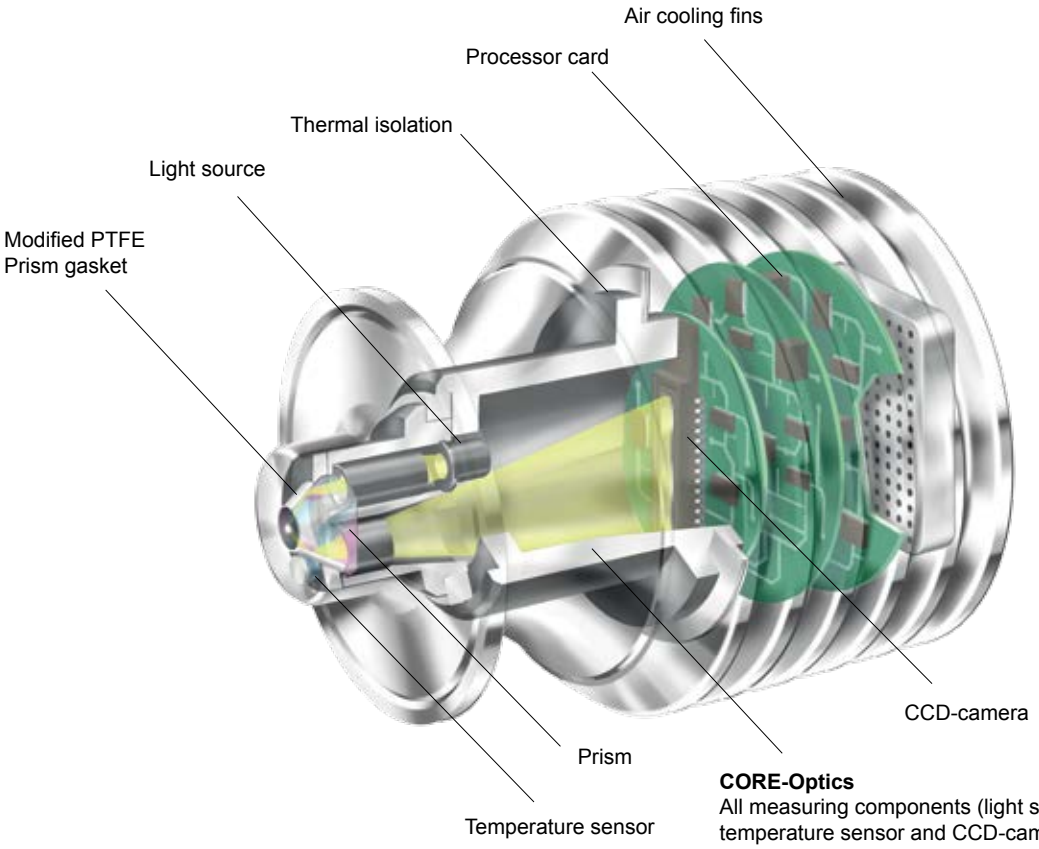
LAYER 1:
The refractometer calibration: The actual refractive index nD is calculated from the CCD.

LAYER 2:
The chemical curve: The refractometer calculates the Brix or concentration value based on nD and TEMP. The result is a temperature-compensated calculated concentration value, CALC.

LAYER 3:
Field calibration: Adjustment of the calculated concentration value CALC may be required in order to compensate for some process conditions or to fit the measurement to the laboratory results. The Field calibration procedure determines the appropriate adjustment of CALC. The adjusted concentration is called CONC.

Output signal: The output signal is transmitted over the 4–20 mA current output or through the Ethernet connection.

DESIGN



CORE-Optics
All measuring components (light source, prism, temperature sensor and CCD-camera) are contained in one solid CORE-optics module.

The patented CORE-optics is mechanically isolated from the influence of external forces and vibrations. The CORE-optics contains no mechanical adjustments.

(US Patent No. 6067151)

SPECIFICATIONS

REFRACTOMETER PR-43-P	Standard	Optional
Refractive Index range	Full range, nD = 1.3200...1.5300 corresponds to hot water...100 Brix or % by weight.	nD = 1.2600…1.4700.
Accuracy	Across the full range of 0−100 Brix: Refractive index nD ±0.0002 typically corresponds to ±0.1 Brix or % by weight.	High accuracy version -HAC in the range of 0−30 Brix and 4−30°C: ±0.05 Brix or % by weight. ±0.02 Brix or % by weight (in set-point applications).
Repeatability	Across the full range of 0−100 Brix: nD ±0.00004 (typically corresponds to ± 0.02 Brix or % by weight).	
Speed of response	1 s undamped, damping time selectable up to 5 min.	
Calibration	With NIST traceable Cargille standard R.I. liquids over full range.	
Patented CORE-Optics	No mechanical adjustments and digital measurement with 3648 pixel CCD element, sodium D-line light emitting diode (LED), built-in Pt-1000 temperature sensor (linearization according to IEC 751).	
Temperature compensation	Automatic, digital compensation.	
Instrument verification	With NIST traceable Cargille standard R.I. liquids and guided procedure, including a printable verification report.	
Process connection	PR-43-P: Sanitary 3A-clamp 2.5”; Varivent in-line access unit clamp DN65 or via elbow flowcell (for line sizes of 2.5” and smaller); 2.5” I-clamp.	
Pharma grade materials and material traceability documentation	Product contact surface finishes are electropolished with a surface roughness of Ra 0.4µm (15µ inch); USP Class VI Elastomers are tested for the materials’ biocompability and toxigology safety; No animal derived ingredients (ADI) are used in processing or machining parts.	
Hygienic design certification	3-A Sanitary Standard 46-03 certified and EHEDG (European Hygienic Equipment Design Group) Type EL Class I certified.	
Process pressure	Sanitary 3A and I-clamp max. 15 bar (200 psi) at 20°C (70°F)/9 bar (125 psi) at 120°C (250°F). High pressure Sanitary 3A clamp HP 40 bar at 20°C (70°F).	
Process temperature	PR-43-P: -40°C...130°C (-40°F...266°F)	
Ambient temperature	Refractometer: min. -40°C (-40°F), max. 45°C (113°F); Multichannel user interface MI: min. -40°C (-40°F), max. 50°C (122°F); Compact user interface CI: min. 0°C (32°F), max. 50°C (122°F).	
Process wetted parts	AISI 316L stainless steel, prism sapphire, prism gasket modified PTFE (Teflon), sanitary process connection gasket EPDM for Sanitary 3A-clamp; EHEDG certified process connection gasket for EHEDG compliant installation.	Hastelloy C ASTM C276
Refractometer protection class	IP67, NEMA 6P (for outdoor use).	
Refractometer weight	PR-43-P: 1.6 kg (3.5 lbs)	
Current output	Isolated 4-20 mA, max. load 1000 Ohm, galvanic isolation 1000 VDC or AC (peak), hold function during prism wash.	
Remote and Ethernet connections	10/100BaseT Ethernet, web server for configuration and diagnostics, UDP/IP Protocol connection for data acquisition.	
Power supply	+24 VDC +/-10%, Max. 2 VA.	
INTERCONNECTING CABLES	Standard length 10 m. Interconnecting cable length is field-adjustable with a Platform 4 Cable extender for up to 100 m.	
USER INTERFACE **Models**	Multichannel user interface MI, Compact user interface CI	
Multichannel user interface MI	Environmentally sealed 316 stainless steel IP67, NEMA 6 enclosure for demanding field, outdoor and laboratory or control room conditions (-40-50°C, -40-122°F). Prism wash diagnostics and control. Trends, Apps. Eight (8) module slots. 10” graphical touchscreen color display with door. 21 CFR 11 compliant user authentication with user ID and password, electronic records and data-logging, event log/audit trail. Expandable system and I/O options: connect up to four (4) PR-43-P refractometers and up to eight (8) I/O modules. Wall and table-top mount.	
Compact user interface CI	IP65, NEMA 4, Light-weight aluminum enclosure for laboratory and control room conditions; Epoxy coated enclosure with polycarbonate display shield for field conditions. Trends. 10” graphical touchscreen color display. Wall, table-top and panel mount.	
User interface weight	Multichannel user interface MI: 13.6 kg (29 lbs), Compact user interface CI: 5.4 kg (11 lbs)	
POWER SUPPLY	Refractometer: +24 VDC +/-10%, Max 2 VA; Multichannel user interface MI: AC input 100-240 VAC/50-60HZ or 24 VDC, 60W; Compact user interface CI: +24 VDC +/-10%, Max. 8.5W.	
OPTIONS	Laboratory test cuvette LTC for off-line laboratory testing: AISI 316 L stainless steel laboratory test cuvette contains an agitator with PTFE (teflon) stirrer, and connections for sample inlet and outlet, and 1/4” tube connections for thermostat controlled water; Pharma mini flow cell PMFC: process connection Sanitary 3A-clamp 1,5”; Prism wash; Hazardous and intrinsic safety approvals for hazardous area installations.	
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We reserve right to technical alterations.

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