



NIR Checkmaster
Near-infrared spectroscopy
On-line analysis
of active ingredients
during tablet production

Slash release times with NIR

Innovative features

- Fully automatic assay of tablet weight, hardness, thickness, diameter and active ingredient content in programmable cycles during ongoing production →
- Continuous analysis and regulation of manufacturing process → → → → → → → → → → → → → → → →
- High analytical speed → → → → → → → → → → → → → → → →
- Transmission analysis of active substance content → → → → → → → → → → → → → → → →
- Qualitative and quantitative on-line analysis → → → →
- Non-destructive analytics → → → → → → → → → → → →
- All parts needing cleaning removable without tools
- Operators can change NIR lamps and laser unit themselves → → → → → → → → → → → → → → → →
- Double lamp module in the NIR Checkmaster → →
- The NIRFlex N-500 polarization interferometer → →
- Long-life, low-intensity quartz halogen lamp → →
- Special coating in sample chamber suppresses light leakage → → → → → → → → → → → → → → → →
- NIR analysis in two format-specific cups with two clamps → → → → → → → → → → → → → → → →
- Compact design → → → → → → → → → → → → → → → →
- NIR Checkmaster complies with IP65 in all respects
- NIR-CM can be used both in the lab and in production → → → → → → → → → → → → → → → →
- Tablet position in integrated sample cassette is documented in protocol → → → → → → → → → → → → → → → →
- Documentation of test results in production protocol → → → → → → → → → → → → → → → →

Your benefits

- High degree of process reliability, variation of test cycles of product properties, production flow and quality specifications possible
- Gain in knowledge and competence, plus enhanced understanding of process
- Shorter release times (real-time release)
- Most consistent repeatability
- Significant cuts in lab and analytical costs
- No need to prepare samples, no waste
- Easy cleaning
- Operator-friendly, cost-optimized maintenance
- No downtime if primary lamp fails
- Less sensitive to mechanical disturbance and vibrations
- No need to expose samples to heat, which could negatively affect active ingredients
- No other light source = optimal spectra
- Extremely accurate positioning yields repeatable results
- Takes up very little space
- Washable and usable in isolator
- Cuts process costs
- Analytical data obtained for each individual tablet can be referred to later
- Records every single quality parameter

FDA's process analytical technology initiative requires pharmaceutical manufacturers to improve the critical quality performance monitoring for ensuring final product quality.

PAT is the whole range of technical procedures used to make processes transparent, visualize procedures and reveal weak points. This initiative launched by the US **Food and Drug Administration** aims to ensure early detection of errors in pharmaceutical manufacturing processes. **Near-infrared spectroscopy** is one of the available early-warning analytical methods, with which it is possible to acquire better understanding of a process and to cut release times, i.e. the delay between production and batch release. It also significantly reduces resource waste in terms of failed production batches.

FETTE Compacting has reacted to the PAT initiative with the launch of its near-infrared spectroscopy systems that are specially designed to meet the needs of the pharmaceutical industry. The NIR Checkmaster, combining online NIR analysis of active ingredients with conventional tablet testing parameters including weight, thickness, hardness and diameter, is the product of a joint development project between FETTE GmbH, the technological leader in the market for tablet presses, Kraemer Elektronik GmbH, the manufacturer of the Checkmaster and Büchi Labortechnik AG, the manufacturer of the Fourier Transform (FT) NIR spectrometer.



Care about health is complex. Tableting technology is our contribution. FETTE COMPACTING.

Genuine customer benefits



The conventional method for analysis of active tablet ingredients used to be HPLC. This is a time-consuming, labor-intensive procedure, in which random samples have to be taken from production, transported to the QC/QA lab and analyzed there. The pharmaceutical industry is keen to introduce new PAT methods that will help to improve product quality and cut manufacturing costs. Near-infrared spectroscopy has proven itself as a quick, cost-cutting, convenient and non-destructive method of analysis.

The NIR Checkmaster is equipped with a system enabling ongoing monitoring of critical qualitative parameters by continuous analysis and control of the tablet manufacturing process. The NIR-CM can be integrated into existing FETTE tablet presses to give them an automatic analytical function. The analytical data can be used to improve product quality by direct regulation of production parameters, either by the NIR Checkmaster itself or by remote transmission from an NIRFlex N-500 FT-NIR spectrometer in the lab.

Shorter process time plus transparency

- NIR analysis of tablets can significantly cut release times.
- NIR ensures better monitoring of the production process.
- Key data on active substance content are determined during production.
- The data are based on a relatively large sample.
- Throughput times are substantially reduced.
- This online measuring procedure enables better analysis of critical parameters in the production process.
- Its regular use obviates the need for separate release analyses, because it is better at understanding and regulating the tableting procedure in the way the FDA wants.
- The process data produced by the system can be used for batch release.
- FETTE will, in the future, offer an additional control system on the tablet press that will regulate content of active ingredient in the tablet.

Comprehensive functionalities of NIR Checkmaster

Designed only for benefits

Fettepharma Vers.: C [L] Standard run Date: 15.04.2008 Time: 17:28
 Batch: NIR 002 Oper: P M-No.: 19401

NIR 002 - NIR-1 - Station 1

Prod.	D-Tab.	D-C	IDM	Potency	Unit	Weight	Thickness	Status	Quant	Method
1	1	2	4,2	mg	115	3,5	Released	P_XYZ	AppRed	
2	2	2	4,2	mg	117	3,5	Released	P_XYZ	AppRed	
3	3	2	4	mg	120	3,6	Released	P_XYZ	AppRed	
4	4	2	4	mg	118	3,5	Released	P_XYZ	AppRed	

Buttons: [Camera] [NIR 1] [NIR 2] [NIR 3] [NIR 4] [NIR 5] [NIR 6] [NIR 7] [NIR 8] [NIR 9] [NIR 10] [NIR 11] [NIR 12] [NIR 13] [NIR 14] [NIR 15] [NIR 16] [NIR 17] [NIR 18] [NIR 19] [NIR 20] [NIR 21] [NIR 22] [NIR 23] [NIR 24] [NIR 25] [NIR 26] [NIR 27] [NIR 28] [NIR 29] [NIR 30] [NIR 31] [NIR 32] [NIR 33] [NIR 34] [NIR 35] [NIR 36] [NIR 37] [NIR 38] [NIR 39] [NIR 40] [NIR 41] [NIR 42] [NIR 43] [NIR 44] [NIR 45] [NIR 46] [NIR 47] [NIR 48] [NIR 49] [NIR 50] [NIR 51] [NIR 52] [NIR 53] [NIR 54] [NIR 55] [NIR 56] [NIR 57] [NIR 58] [NIR 59] [NIR 60] [NIR 61] [NIR 62] [NIR 63] [NIR 64] [NIR 65] [NIR 66] [NIR 67] [NIR 68] [NIR 69] [NIR 70] [NIR 71] [NIR 72] [NIR 73] [NIR 74] [NIR 75] [NIR 76] [NIR 77] [NIR 78] [NIR 79] [NIR 80] [NIR 81] [NIR 82] [NIR 83] [NIR 84] [NIR 85] [NIR 86] [NIR 87] [NIR 88] [NIR 89] [NIR 90] [NIR 91] [NIR 92] [NIR 93] [NIR 94] [NIR 95] [NIR 96] [NIR 97] [NIR 98] [NIR 99] [NIR 100]

Function Keys: F1 Help, F2 Menu, F3 Parameter, F4 Reports, F5 Graphic, F6 Setup, F7 Print

Fettepharma Vers.: C [L] Standard run Date: 15.04.2008 Time: 17:28
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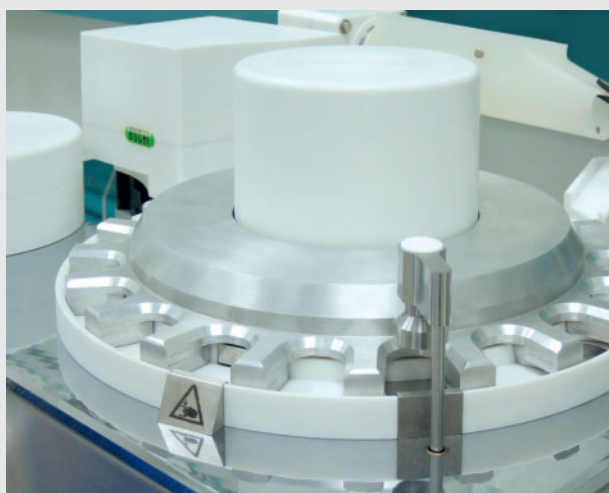
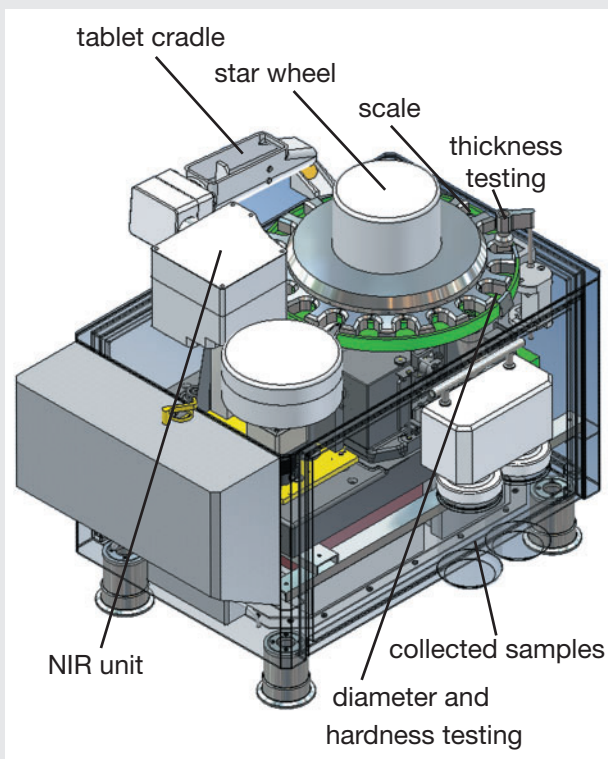
NIR 002 - NIR-2 - Station 1

Prod.	Set	Mean	Srel	Min	Max	Unit	n	>T2	>T1	<T1	<T2	Quant	Method
4	4	4,13	3,64	4,00	4,30	mg	4	0	0	1	0	P_XYZ	AppRed

Buttons: [Camera] [NIR 1] [NIR 2] [NIR 3] [NIR 4] [NIR 5] [NIR 6] [NIR 7] [NIR 8] [NIR 9] [NIR 10] [NIR 11] [NIR 12] [NIR 13] [NIR 14] [NIR 15] [NIR 16] [NIR 17] [NIR 18] [NIR 19] [NIR 20] [NIR 21] [NIR 22] [NIR 23] [NIR 24] [NIR 25] [NIR 26] [NIR 27] [NIR 28] [NIR 29] [NIR 30] [NIR 31] [NIR 32] [NIR 33] [NIR 34] [NIR 35] [NIR 36] [NIR 37] [NIR 38] [NIR 39] [NIR 40] [NIR 41] [NIR 42] [NIR 43] [NIR 44] [NIR 45] [NIR 46] [NIR 47] [NIR 48] [NIR 49] [NIR 50] [NIR 51] [NIR 52] [NIR 53] [NIR 54] [NIR 55] [NIR 56] [NIR 57] [NIR 58] [NIR 59] [NIR 60] [NIR 61] [NIR 62] [NIR 63] [NIR 64] [NIR 65] [NIR 66] [NIR 67] [NIR 68] [NIR 69] [NIR 70] [NIR 71] [NIR 72] [NIR 73] [NIR 74] [NIR 75] [NIR 76] [NIR 77] [NIR 78] [NIR 79] [NIR 80] [NIR 81] [NIR 82] [NIR 83] [NIR 84] [NIR 85] [NIR 86] [NIR 87] [NIR 88] [NIR 89] [NIR 90] [NIR 91] [NIR 92] [NIR 93] [NIR 94] [NIR 95] [NIR 96] [NIR 97] [NIR 98] [NIR 99] [NIR 100]

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- The first step is to enter into the tablet press software the parameters to be assayed, e.g. weight, thickness, diameter, hardness and NIR, and the number of tablets to be tested.
- The tablet press software regulates the function of the NIR Checkmaster, the sampling action and sampling frequency.
- The compressed tablets are transported automatically from the FETTE tablet press to the NIR Checkmaster.
- Depending on the configuration of the analytical sequence, the tablets are first tested for weight and thickness before being transported either to diameter and hardness analysis or to the NIR spectrometer.
- The tablet's physical data and the NIR data obtained by transmission analysis are incorporated automatically into the tableting machine's batch protocol.
- It is impossible to tamper with the data. Measurements start with determination of the data and spectra and finish with entry of the results into the machine's batch protocol.
- On completion of the assays, the tablets are collected on the carousel and their position is recorded.
- The position of each tablet in the collector and its calculated content of active ingredient are entered into the machine's production protocol. This makes it possible to refer to the active ingredients (API) of each analyzed tablet at a later date.
- The NIR unit has an automatic white reference for control purposes and can perform regular auto-validation of the system.
- As NIR analysis causes no rise in tablet temperature, the procedure is ideal for thermo-labile active ingredients.



Details of in-process analytical procedures

Complex functions in minimal space

- In-process control is performed by a sampling procedure in the tablet press.
- The sampled tablets are separated from each other into a tablet cradle and transported by a combination of vibration and centrifugal force onto a conveyor that delivers a single tablet into a tablet holder on the star wheel of the NIR Check-master.
- The star wheel is designed to position a wide range of tablet shapes optimally for analysis.
- The physical tests come first:
 - a Sartorius WZ64 S cell, separately encapsulated to adjust pressure, weighs the tablet to a resolution of ± 0.001 g.
 - a type DM-IP II then measures tablet thickness digitally to an accuracy of ± 0.02 mm.
 - this is followed by measurement of diameter and hardness testing to an accuracy of ± 1 N.
- The tablets for NIR analysis are not tested for hardness.
- The final test is for active ingredients (API) by measurement of transmission. The tablet is positioned to an accuracy of ± 0.1 mm in two cups designed to accept a specific tablet shape and held in position by two clamps. The cups are made of a special, non-reflecting plastic. Extremely precise positioning is essential in order to obtain accurate, repeatable results, because NIR analysis is only possible with a consistent tablet thickness.
- If the NIR result lies outside the tolerances specified for this substance, the machine is stopped immediately and a diagnosis message is displayed.

High-performance FT-NIR module for determination of active substance content

Exact spectra shows precise active ingredient

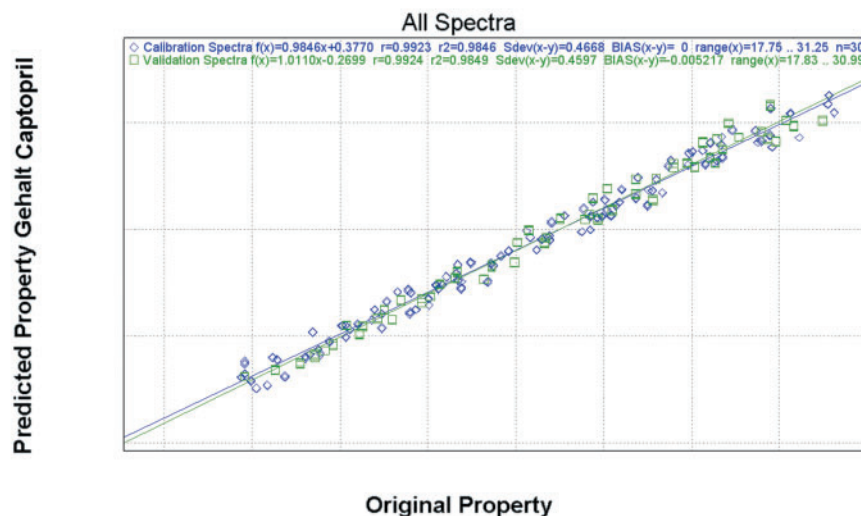
- The diffuse transmission method covering the spectral range between 12,500 and 6,000 cm^{-1} delivers detailed test information on the entire cross-section of the tablet.
- The polarization interferometer, which is designed to be unaffected by mechanical vibrations, operates at a resolution of up to 8 cm^{-1} (optimal for spectroscopy) and a minimum scan duration of 250 ms, obtains the analytical data within a few seconds.
- Transfer of the NIR spectra from the NIRFlex N-500 spectrometer in the lab to the NIR Checkmaster is a simple process and this greatly facilitates calibration.
- Robust and extremely precise calibration down to extremely low dosage levels can be performed with the help of the patented calibration wizard specially developed for the chemometric NIRCal software, and the results are equivalent in accuracy to those obtained by reference analysis.

Calibration procedure

Precisely defined steps for accurate results

- A calibration model must first be prepared with 75-125 % of the reference information from samples with known active ingredient content of the type that would be compressed under normal production conditions, e.g. in a FETTE 102i machine.
- Either the NIRFlex N-500 lab spectrometer or the NIR Checkmaster can be used to plot the calibration curve. Calibration data stored in the lab spectrometer can be transferred directly to the NIR-CM, because its software and the software for the NIR unit are identical.
- In this first step the active ingredient content of each single tablet is determined by NIR analysis for the calibration model, which is then validated by comparing it to the results obtained with high-performance liquid chromatography.
- The calibration model can then be used to determine actual active ingredient content of the tablets by the NIR-CM.

Predicted Property vs. Original Property



High-performance analytical technology with easy-to-maintain design

Intelligent combination of ideal properties

- The NIR Checkmaster contains the conventional Kraemer Checkmaster in-process control system and the Büchi NIRFlex N-500 FT NIR spectrometer.
- The system is controlled by a fast PC and is linked to the FETTE tablet press.
- The NIR Checkmaster's software package complies with FDA Standard 21 CFR Part 11.
- The compact NIR Checkmaster is used for in-process control at the tablet press and has been designed with a height that enables it to fit underneath the tablet discharge of a FETTE press.
- The redesign of the test system for conventional parameters groups the NIR technology in an arrangement that takes up a minimum of space.
- Although the basic principles of the Checkmaster have been retained, the NIR Checkmaster complies in every respect with IP65 and can, after only minor modification, be used in the FETTE isolator.
- All parts needing cleaning are removable without tools.
- Operators can change the lamps and the laser unit of the NIR unit themselves.
- Double lamp module enables continued operation even if one lamp fails.

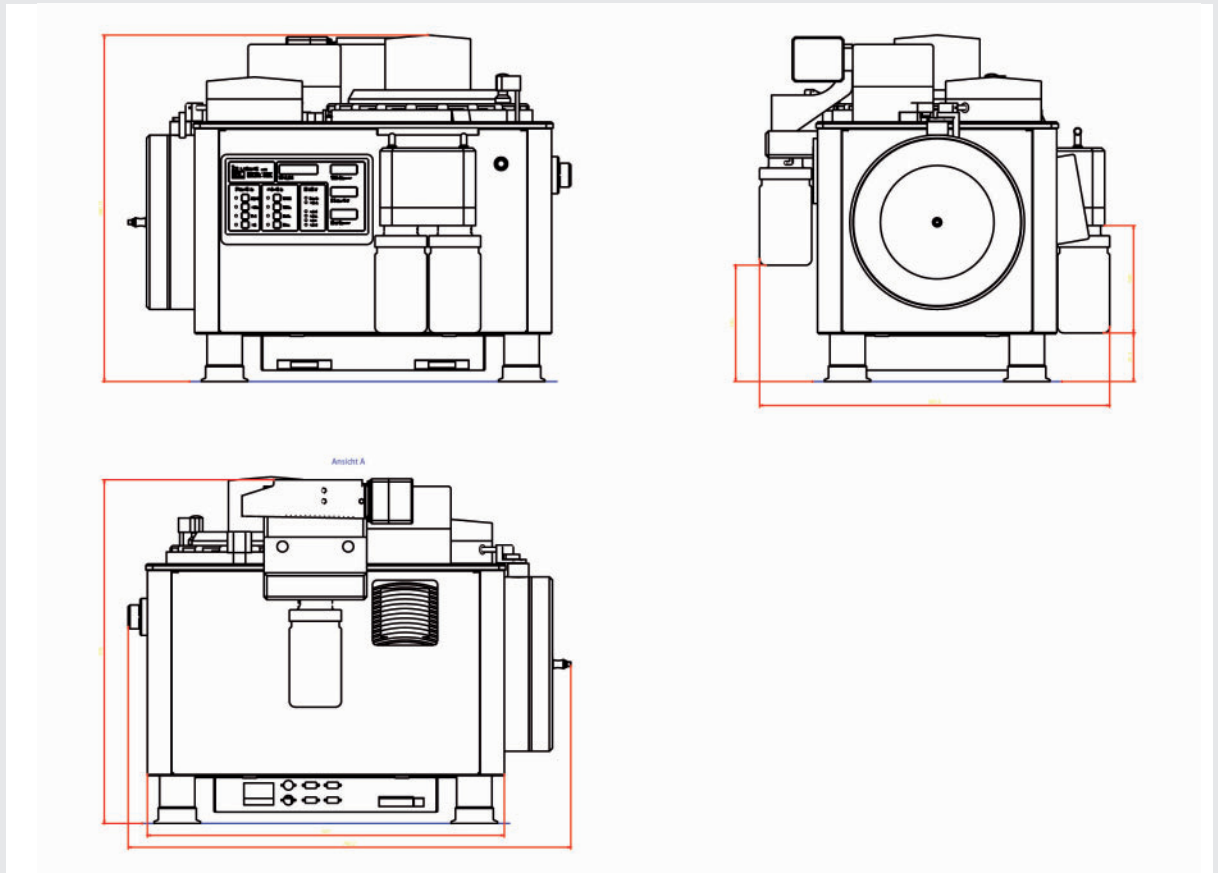
Compatible with a broad spectrum of products

Complete in-process control

- Total integration, high level of automation
 - can be fully integrated into production process
 - complete assay process is automated
 - autosampling of tablets
- Functions irrespective of tablet format
 - assay of all common tablet formats
 - parameters for weight, hardness, thickness, diameter and active ingredient content can be selected by user
 - special star wheel for transport of special formats and format-specific cups fitted with two tablet clamps
- Weighing module
 - integrated weighing module with protective capsule
 - ultra-precise weight determination
 - weight determined to a resolution of ± 0.001 g
- Tablet hardness
 - test by application of pressure to breakage point
 - hardness determined to an accuracy of ± 1 N
- Tablet thickness
 - measurement of tablet in star wheel with probe
 - thickness determined to an accuracy of ± 0.01 mm
- Tablet diameter
 - measured with slide
 - diameter determined to an accuracy of ± 0.01 mm
- Content of active ingredients
 - assay by transmission analysis
 - tablet positioned to an accuracy of ± 0.1 mm

Assembly plan

Technical data



Analytical functions		
Weight		
Range	g	0.01-50
Resolution	g	0.001
Accuracy	g	± 0.0003
Hardness		
Range	N	10-400
Resolution	N	1
Accuracy	N	± 1
Thickness		
Range	mm	1-20
Resolution	mm	0.01
Accuracy	mm	± 0.1
Diameter		
Range	mm	1-30
Resolution	mm	0.01
Accuracy	mm	± 0.1
Dimensions	mm	L 740 x B 586 x H 581
Power supply		110-230 V · 50/60 Hz

In the interests of technical progress we reserve the right to make modifications.

- Interferometer type: polarization interferometer
- Detector type: InGaAs, fitted with thermostat
- Spectral range:
 - 12,500–6,000 cm^{-1}
 - (recommended: 11,520 – 6,000 cm^{-1}),
 - or 800 –1,660 nm
 - (recommended: 870–1,660 nm)
- Resolution: 8 cm^{-1}
- Dynamic photometric range: 0-6 AU
- Wavenumber accuracy: ± 0.2 cm^{-1}
- Typical signal-noise ratio (Rms for spectral segments of 300 cm^{-1} in range between 11,000 and 6,500 cm^{-1}):
 - open beam: mean value: 2x10 (-5) AU
 - measured with 5 mm Spectralon: 10x10 (-5) AU
- Lamp type: tungsten-halogen with 2x6,000 h working life (double lamp module)
- Laser type: HeNe