Innovative Microwave Resonance Technology

Process and Laboratory Moisture and Density Measuring In the Pharmaceutical Industry
Research and Development, Production and Sales
44 years of TEWS Elektronik

TEWS ELEKTRONIK GMBH & CO. KG

44 years of industrial experience
24 years of experience in microwave resonance technology for moisture and density measurement
4000 systems employed for 600 customers
Approximately 50% of the equipment are installed and maintained overseas
50 employees in research, development and production
Sales and service throughout the world
Made in Germany
Moisture Measuring for Quality Assurance and Process Control

Why Measure Moisture in the Pharmaceutical Process?

- Water content as cost factor (valuable product, cheap water)
- Processability (e.g. stability, proportioning avoiding of dust)
- Optimization of process steps (e.g. time and energy during drying)
- Legal and contract conditions (e.g. avoiding chemical hydrolyse-reactions)

Require reliable, accurate and fast moisture measuring!
Direct and Indirect Methods

Industrial Moisture Measuring Procedures

Accuracy

- Karl Fischer titration
- Drying kiln, LOD balance

Capacity, conductivity

Near infrared (NIR)

Microwave resonance

Hours Minutes Seconds Milliseconds
Construction and Components

Microwave Resonance Measuring System

Display

LAN, bus, etc.

SPS

Microwave measuring equipment

Interface

Microcontroller, Software

Microwave generator

Microwave detector

Microwave sensor
Electromagnetic Field Measurement

Interactions Between Water and Microwaves

- Low-powered microwave field
- Selective interactions between field and polar water molecules
- Resonance is sensor-specific
- Water molecules in the product change the resonance frequency and amplitude
- Measurements for moisture and density or mass
For High-quality Industrial Application

Characteristics of the Microwave Resonance Procedure

- **High accuracy**
  - Surface and core moisture
  - Independent of density, color, surface structure

- **High speed**
  - Direct measurement during product flow
  - Online capacity

- **Simple service**
  - Free of wear and tear, low-maintenance
  - No sample preparation
  - No regulations like for Nucleonic Systems
Exposition on Microwave Resonance Procedures

Summary: Advantages and Benefits

Advantages

• **ACCURATE** – due to high water selectivity
• **FAST** – the results are available within milliseconds
• **INDEPENDENT** – the moisture determination is independent of density, surface structure and color of the sample
• **FREE OF MAINTENANCE** – no consumables, no aging, no wear

Benefits for the user

• Fast amortization
• Energy-saving
• Optimization of production process
• Increase in product quality
TEWS Elektronik Blue Line ®

Measuring Units to Meet Your Demands
**TEWS Elektronik Blue Line®**

**The Unit Program**

- **Special solutions**
- **Process facilities**
- **Laboratory atline units**
- **Hand-held units**

**Measuring rate**
- 10/sec
- 100/sec
- 20,000/sec
Adjusted to Product and Application

Forms of Microwave Resonators

Planar sensors
- Powder
- Granules
- Fibers

Tubular sensors
- Powder
- Granules
- Fibers (atline)

Fork sensors
- Strips
- Sheets
- Fleece
Measuring the moisture in the Pharmaceuticals
Meeting the Demand for 100% Verification

<table>
<thead>
<tr>
<th>Product</th>
<th>Moisture Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelatine capsules</td>
<td>5 – 15 %</td>
</tr>
<tr>
<td>Granules</td>
<td>2 – 5 %</td>
</tr>
<tr>
<td>Vitamin powder</td>
<td>3 – 8 %</td>
</tr>
<tr>
<td>Silicic acid</td>
<td>2 – 5 %</td>
</tr>
</tbody>
</table>
Microwave Measurement of Moisture, Mass, Density
Application in the Pharmaceutical Industry

- Moisture of tablets & granules (samples)
- Moisture of gelatine capsules
- Mass of tablets (fast 100% control)
- Filling mass of capsules (fast 100% control)
- Moisture of powder and granules in fluid bed dryer
- Inline-control of dosing-process

Moisture Measurement | Fluid Bed Dryer
Mass Measurement | 3D Mass Measurement
Software TEWS Moisture View TMV ®
Display, Analysis, Documentation

- Simple service, configuration and calibration of the measuring units
- Statistics and graphics functions for the measured data analysis
- Integrated software for all applications
Our Service

Around-the-Clock Qualified Service
Our Service

Qualified Service

- Project support from initial consultation via maintenance to project success completion / after sales service.
- Support for customers throughout the world in many languages.

OVERVIEW OF SERVICE

Application laboratory for test measurements
Customer-specific solutions
Qualified maintenance and instructions to users
Application-specific calibration
Free support provided by engineers via telephone and modem
Upgrading service
Service and Sales
Representing TEWS Elektronik international
TEWS Elektronik – Industrial Moisture and Density Measuring Technology
Thank You Very Much for Your Interest!

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EXCURSION
Moisture Measurement
Examples for the Application - Pharmaceutical Industry

Online and Atline - Moisture measurement of empty capsules

- Automatical sampling from Bypass
- Samples each of 9 Gelatine capsules
- Calibration based on 90 samples
- Mean deviation of moisture +/-0.03%
Examples for the Application - Pharmaceutical Industry

Atline - Automatical periodical check of empty gelatine capsules after the dryer

![Graph showing moisture content (%) vs measure value]
Examples for the Application - Pharmaceutical Industry

Atline - laboratory measurement of empty gelatine capsules
Examples for the Application - Pharmaceutical Industry

Moisture calibrations of hard gelatine capsules

<table>
<thead>
<tr>
<th>Device</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device 1</td>
<td>2007-07-02</td>
</tr>
<tr>
<td>Device 2</td>
<td>2003-04-10</td>
</tr>
<tr>
<td>Device 3</td>
<td>2002-11-14</td>
</tr>
<tr>
<td>Device 4</td>
<td>2003-12-10</td>
</tr>
<tr>
<td>Device 5</td>
<td>2004-08-05</td>
</tr>
<tr>
<td>Device 6</td>
<td>2009-08-05</td>
</tr>
</tbody>
</table>

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Examples for the Application - Pharmaceutical Industry

Sealing inspection of liquid filled hard gelatine capsules

EXCURSION

Mass Measurement
Examples for the Application - Pharmaceutical Industry

Mass Measurement of gelatine capsules at the filling machine

- Measurement of filling of capsules
- Measurement of content of capsules
Examples for the Application - Pharmaceutical Industry

Mass measurement of capsules at the filling machine, Example 1

Filled capsules

Filling machine

Empty capsules

Patent EP 1 467 191 B1, TEWS Elektronik
Examples for the Application - Pharmaceutical Industry

Mass measurement of capsules at the filling machine, Example 2

Patent EP 1 467 191 B1, TEWS Elektronik
Examples for the Application - Pharmaceutical Industry

Mass measurement of capsules at the filling machine, Example 3
EXCURSION
Fluid Bed Dryer
Examples for the Application - Pharmaceutical Industry

Moisture measurement in fluid bed dryers
Moisture Sensor for Fluid Beds (1)

Microwave Resonance Sensor

Sensor generates low energy microwave field on front face

Front face in contact with product

Microwave field penetrates powder resp. Granules, interacts with water molecules

Applicable moisture range 0.2 % – 5 %

Accuracy typically 0.1% - 0.2%
Moisture Sensor for Fluid Beds (2)

Sensor Installation at Processor

Sensor is mounted at the side of the fluid bed processor

Measurement in lower part of fluid bed

No opening of processor, no sampling
Moisture Sensor for Fluid Beds (3)

Microwave Measurement in Circulating Granules

Granules run over the sensor’s front face

Measurement independent of varying particle size, bulk density, colour of granules

Continuous monitoring of granulation and drying
Optimizing Process Time

Genuine Monitoring of a Drying Process

1. Frequent automatic cleaning of filters causes moisture peaks
2. Increase of temperature at end of drying process
3. Target moisture reached, process can be terminated
PAT in Fluid Bed Processors

Convenience of Inline Moisture Measurement

- Real-time monitoring of moisture
- Measurement directly in the granules
- High accuracy, independent of varying particle size, density, color
- No manual sampling
- No interruption of process
- Better processability and shelf live
- Saving energy and processing time
Configuration, Calibration, Operation

Integration in Process Control

Calibration

Product – specific Calibration → Storage of Calibration Data

Operation

Moisture Readings ← Calibration Data → Displaying, Processing, Storage

Moisture Sensor

Process Control PLC (1)

(1) with certified data base, complying with CFR part 11
Practical Application

Moisture Sensor Specification

Process Analytical Technology

Microwave Resonance Measurement

Furnishing of new and operating fluid bed processors

Standard flange allows for easy sensor installation

Data output to PLC

Easy calibration, easy operation
Regulations & Compliance

Meeting the Requirements of Pharmaceutical Industry

- Stainless steel cabinet, protection class IP 54
- Sensor front face materials complying with foodstuff regulations (1)
- Microwave field not harmful to product (2)
- Cleaning In Place (CIP) suitable, 10 bar pressure shock proof
- ATEX zone 20 (sensor face), ATEX zone 21 (instrument)
- GMP compliant

(1) European Regulation No.1935/2004EC
(2) European Regulation No. 2123/2006 (GMP)
Combining Know-How

A Cooperation of Specialists

1992: TEWS patent for Microwave Resonance (MWR) Moisture Measurement

1997: first tests of MWR moisture sensor in fluid bed processor

1998: GLATT files patent for microwave moisture measurement in fluid bed processors

2010: TEWS Elektronik develops improved Inline sensor for fluid bed processors

2011: new cooperation agreement
EXCURSION 4

3D Mass Measurement
Examples for the Application - Pharmaceutical Industry

3D mass measurement of capsules and tablets
Examples for the Application - Pharmaceutical Industry

3D mass measurement of capsules and tablets

Standard deviation SD = 0,40 mg
Examples for the Application - Pharmaceutical Industry

3D mass measurement of capsules and tablets

1700 tablets

Check weigher:
average mass: 351,78 mg
sd: 2,75 mg

3-D microwave:
average mass: 351,92 mg
sd: 2,79 mg

- Measurement with check weigher
- 3-D microwave measurement
EXCURSION

Microwave Resonance Procedures
Exposition on Microwave Resonance Procedures

Dual-Parameter Measurement

**Processor**
- Generator control
- Detector read-out
- Moisture calculation
- Peripheral connection (e.g. PC)

**Generator/Detector**
- Microwave generation in the gigahertz range
- Sensor input
- Microwaves changed by the product are received
- Transmission of the measuring signal to the CPU

**Product/Sensor**
- Build-up of a resonating microwave field
- Product changes the field in the sensor
- Measuring the signal by antenna at the detector
Exposition on Microwave Resonance Procedures

Dual-Parameter Measurement

Frequency

Transmission

Filled sensor

Empty sensor
Exposition on Microwave Resonance Procedures

Dual-Parameter Measurement

Two resonance parameters are dependent on moisture and density.
Exposition on Microwave Resonance Procedures

Dual-Parameter Measurement

Product in resonator.
More water or higher density
Exposition on Microwave Resonance Procedures

Separation of Moisture and Density

Diagram
• x-axis: Frequency shift
• y-axis: Change of amplitude

Different lines
• Line 1: dried product
• Line 2: moist product
• Linear values: different densities but same moisture

Angle
• The "α" angle is only dependent on moisture
• The angle determines the MW value
• The density only determines the line position
Exposition on Microwave Resonance Procedures

Calibration

- **Diagram**
  - x-axis: Moisture reference (e.g. oven)
  - y-axis: MW value

- **Regression**
  - Calculation of a calibration line
  - Measuring in the moisture range of interest
  - Correlation and mean deviation are provided

- **Number of calibrations**
  - Several calibrations can be stored.
  - 20, 40 or 200 (optional) depending on unit

---

<table>
<thead>
<tr>
<th>Moisture (%)</th>
<th>MW value</th>
</tr>
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<tbody>
<tr>
<td>2.0</td>
<td>0.020</td>
</tr>
<tr>
<td>3.0</td>
<td>0.025</td>
</tr>
<tr>
<td>4.0</td>
<td>0.030</td>
</tr>
<tr>
<td>5.0</td>
<td>0.035</td>
</tr>
<tr>
<td>6.0</td>
<td>0.040</td>
</tr>
<tr>
<td>7.0</td>
<td>0.045</td>
</tr>
<tr>
<td>8.0</td>
<td>0.050</td>
</tr>
</tbody>
</table>
Exposition on Microwave Resonance Procedures

Temperature Compensation

Water molecules
- Vary freely at high temperatures
- MW values increase for the same moisture

Special calibration lines
- For cold samples (blue)
- For hot samples (red)

Calculation
- Automatic for all temperatures lying in the range
- Sensible for temperature variations > 10° C
- Can be activated by server software
**Exposition on Microwave Resonance Procedures**

**Display and Storage of Measurements (1)**

<table>
<thead>
<tr>
<th>Number</th>
<th>Date</th>
<th>Hour</th>
<th>Moisture</th>
<th>Density</th>
<th>Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>01.09.2008</td>
<td>23:45</td>
<td>7,8</td>
<td>4,9</td>
<td>22°</td>
</tr>
<tr>
<td>2</td>
<td>01.09.2008</td>
<td>23:50</td>
<td>8,1</td>
<td>4,9</td>
<td>23°</td>
</tr>
<tr>
<td>3</td>
<td>01.09.2008</td>
<td>23:55</td>
<td>7,9</td>
<td>5,0</td>
<td>22°</td>
</tr>
<tr>
<td>4</td>
<td>02.09.2008</td>
<td>0:00</td>
<td>8,0</td>
<td>5,1</td>
<td>23°</td>
</tr>
<tr>
<td>5</td>
<td>02.09.2008</td>
<td>0:05</td>
<td>7,9</td>
<td>5,1</td>
<td>24°</td>
</tr>
</tbody>
</table>

**Moisture: 8.0   Density: 5.0   Temperature: 23°**
Exposition on Microwave Resonance Procedures

Display and Storage of Measurements (2)

Moisture: 8.15%  Density: 4.28 mg/cm³  2008-09-02 00:05:00
Exposition on Microwave Resonance Procedures

Summary: Advantages and Benefits

Advantages

- **ACCURATE** – due to high water selectivity
- **FAST** – the measurements are available within milliseconds
- **INDEPENDENT** – the moisture determination is independent of density, surface structure and color of the sample.
- **FREE OF MAINTENANCE** – no consumable, no aging, no wear

BENEFITS FOR THE USER

- Fast amortization
- Energy saving
- Optimization of production process
- Increase in production quality
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