EVATHERM

WORLD SALT SYMPOSIUM

June 19-21, 2018 Park City UT, USA

Technologies for the Production of Pharmaceutical Grade NaCl

Opportunities for a fast growing market

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Main Applications for Pharmaceutical Grade NaCl

Dialysis Solutions

- **Dominates with 50% share the global market !**
- Hemodialysis
- Peritoneal Dialysis
- Hemofiltration

Main Applications for Pharmaceutical Grade NaCl

Intravenous Injections (IV)

- Oral Rehydration Salts
- Channeling Agents
- Osmotic Agents
- Cleansing Solutions

Main Applications for Pharmaceutical Grade NaCl

Non-Medical Applications

- Nutrition
- Corrosion testing
- Cosmetics

Brief Market Survey

Main market driver

- World-wide increasing population and wealth
- Generally increased life expectancy

Major consumers

- North America
- Asia Pacific region as the fastest growing market
- Europe

Market volume

- estimated to reach **690’000 t/h** in 2019
- expected volume in 2025 of **1’000’000 t/h** (5% growth rate)

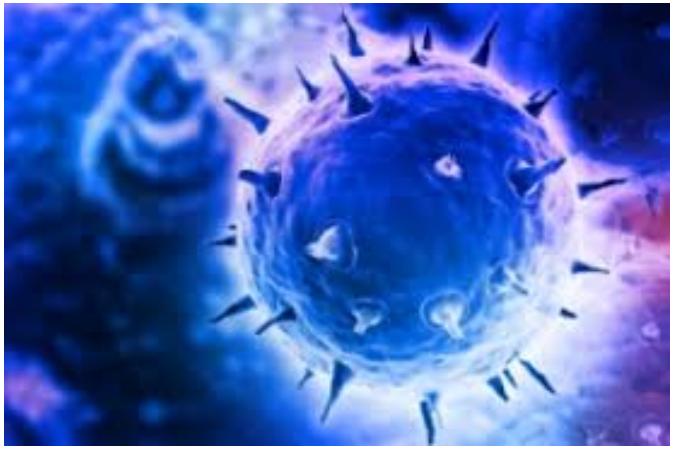
Market players

- only around 30 companies out of hundreds of salt producers!
- Pharmaceutical salt’s market share much less than 1% of the global vacuum production

General Quality Requirements

Basic requirements

- Differentiation between **Excipient** and **Active Pharmaceutical Ingredient (API)** salts
- Qualities according to the monographs in the pharmacopoeias such as
- Ph.Eur., USP, BP, JP, Ch.P., Ph.Rus., KP. etc.
- Limits for **Bacterial Endotoxins** for parenteral preparations



Additional requirements

- Certified QM system ISO 9001
- HACCP
- Traceability system with product labelling
- Regular audits by customers and experts
- API quality produced under GMP conditions (ICH Q7, EU GMP)

Requirements for the crystallization plant

- Only minor deviations to a “normal” vacuum salt plant

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Chemical Requirements for Pharmaceutical Grade Salt (extract)

Pharmacopoeia		USP	JP	Ph.Eur.	BP	Ch.P
NaCl	%	99.0-100.5	99.0-100.5	99.0-100.5	99.0-100.5	99.5-100.5
Arsenic	ppm	≤ 1	≤ 2	≤ 1	≤ 1	≤ 0.4
Iron	ppm	≤ 2	≤ 2	≤ 2	≤ 2	≤ 3
Bromide	ppm	≤ 100	≤ 100	≤ 100	≤ 100	≤ 100
Phosphate	ppm	≤ 25	≤ 25	≤ 25	≤ 25	≤ 25
Potassium	ppm	≤ 500		≤ 500	≤ 500	≤ 200
Magnesium+Alkaline-Earth Metals	ppm	≤ 100 (as Ca)	≤ 100 (as Ca)	≤ 100 (as Ca)	≤ 100 (as Ca)	
Magnesium	ppm					10
Aluminium	ppm	≤ 0.2	≤ 200 ppb	≤ 0.2	≤ 0.2	≤ 0.2
Sulfate	ppm	≤ 200	≤ 200	≤ 200	≤ 200	≤ 20
Heavy Metals	ppm	≤ 5	≤ 3	≤ 5	≤ 5	≤ 2
Loss on Drying	%	≤ 0.5	≤ 0.5	≤ 0.5	≤ 0.5	≤ 0.5

Chemical Requirements for Pharmaceutical Grade Brine

- Additional Sulfate precipitation required

Parameter	Unit	Content	Parameter	Unit	Content
Identification		It responds to the tests for sodium and chloride	Phosphates	mg/l	≤5
Appearance		The solution is clear and colorless	Mg+Alkaline Earth Metals	mg/l	≤25
pH		4.5-7.0	Iron	mg/l	≤0.5
Particulate matter		Meets the requirements	Sulfate	mg/l	≤65
Arsenic	mg/l	≤0.2	Ferrocyanides		Free (passes test)
Barium	mg/l	≤0.5	Assay	%	Not less than 95.0% of the labeled content
Heavy Metals (as Pb)	mg/l	≤1	Potassium	mg/l	≤125
Bromides	mg/l	≤25	Aluminium	mg/l	≤0.2
Iodides		Free (passes test)	Bioburden	CFU/ml	≤10
Nitrites		Free (passes test)	Endotoxins	I.U./ml	≤3

Aspects of the Production Technologies

Vacuum salt technologies

- Single effect evaporation
- Multiple effect evaporation (MEE)
- Mechanical Vapor Recompression (MVR)
- Recrystallization (rock- or solar salt as feed)

“Normal” Sulfate contents in salt

- Chemical brine treatment **ca. 200-250 ppm**
- Recrystallization process **< 100 ppm**

Preventing of caking

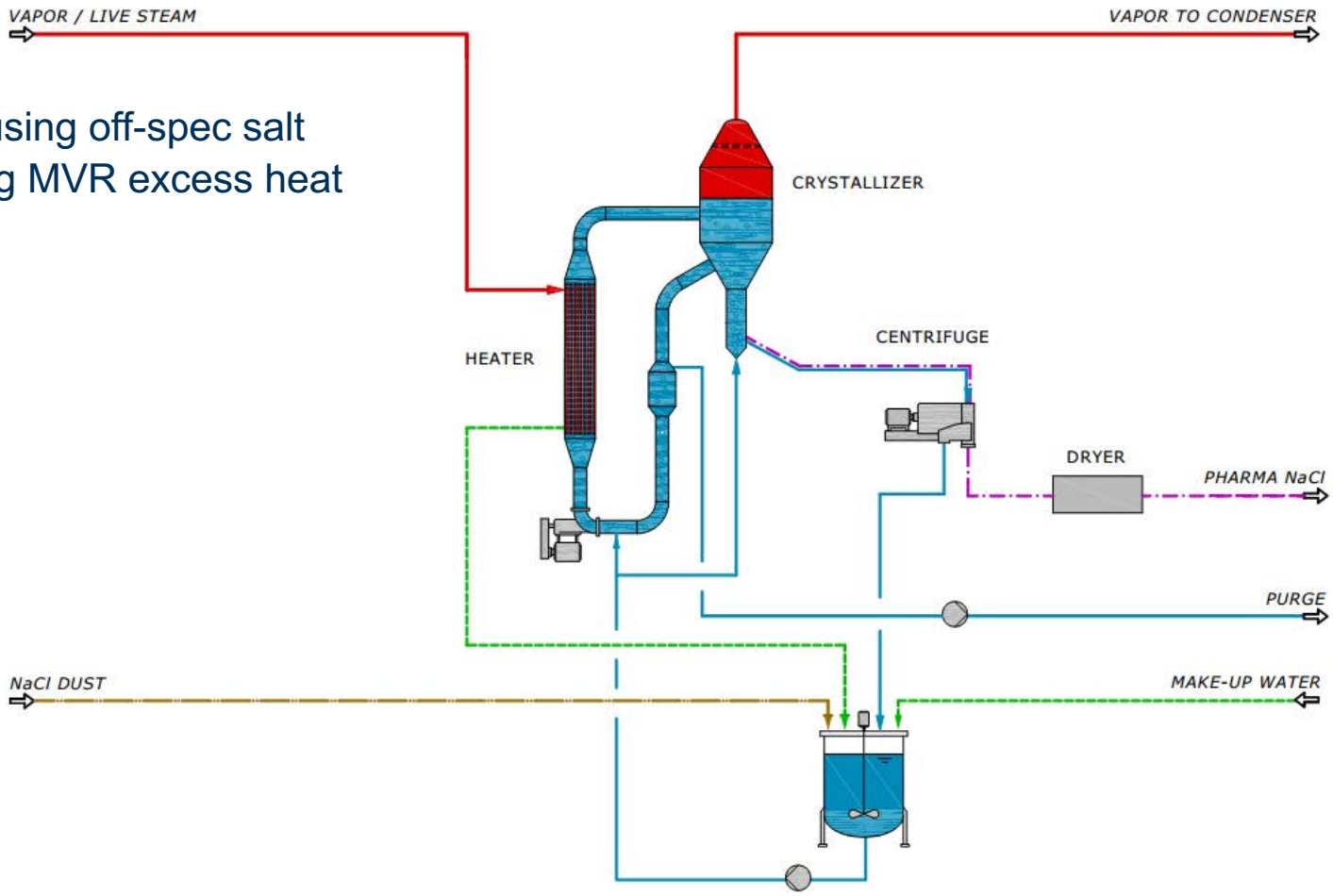
- very low residual moisture required << 0.10%wt
- low salt temperature before storing < 40°C

Granulation

- Product remains sustainably free-flowing
- Advantages in the dissolving process

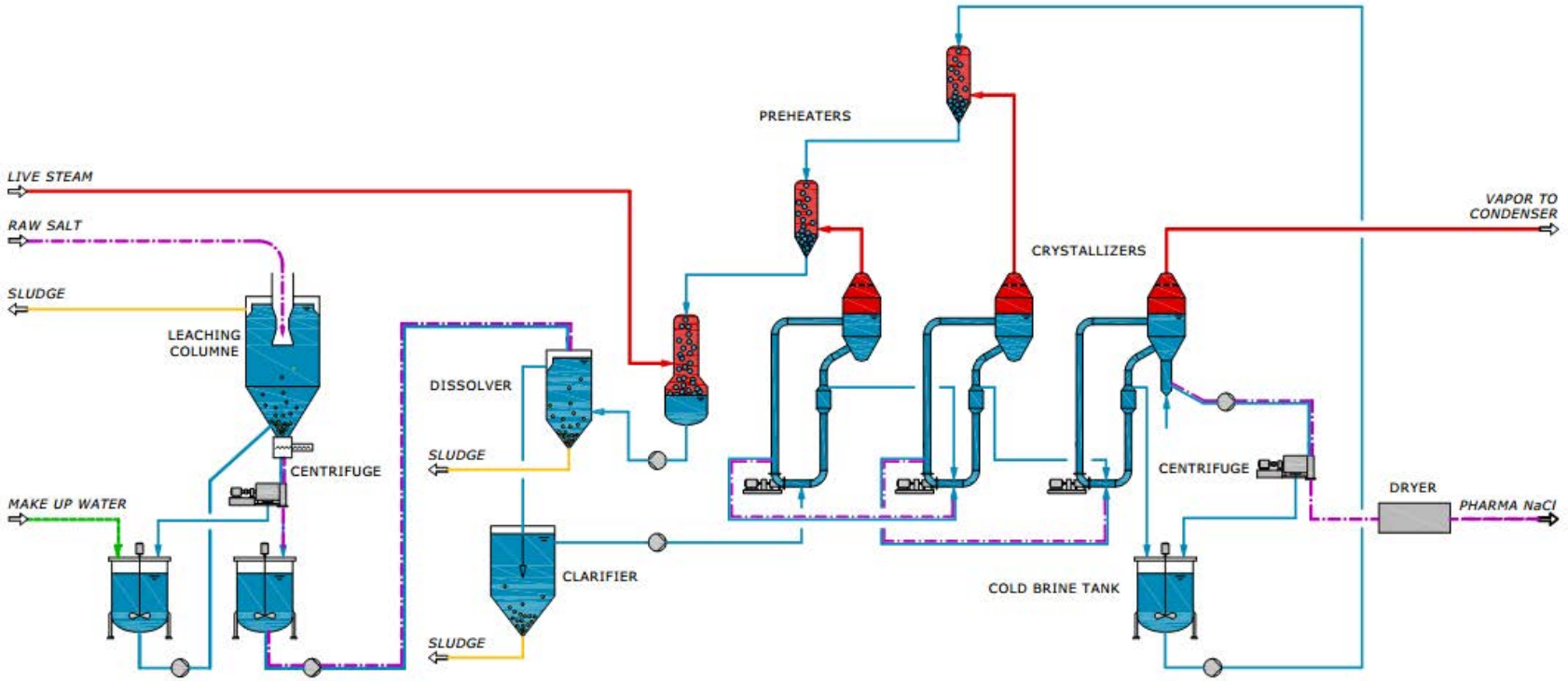
Case study #1: Pharma salt production from salt dust

- Re-using off-spec salt
- Using MVR excess heat



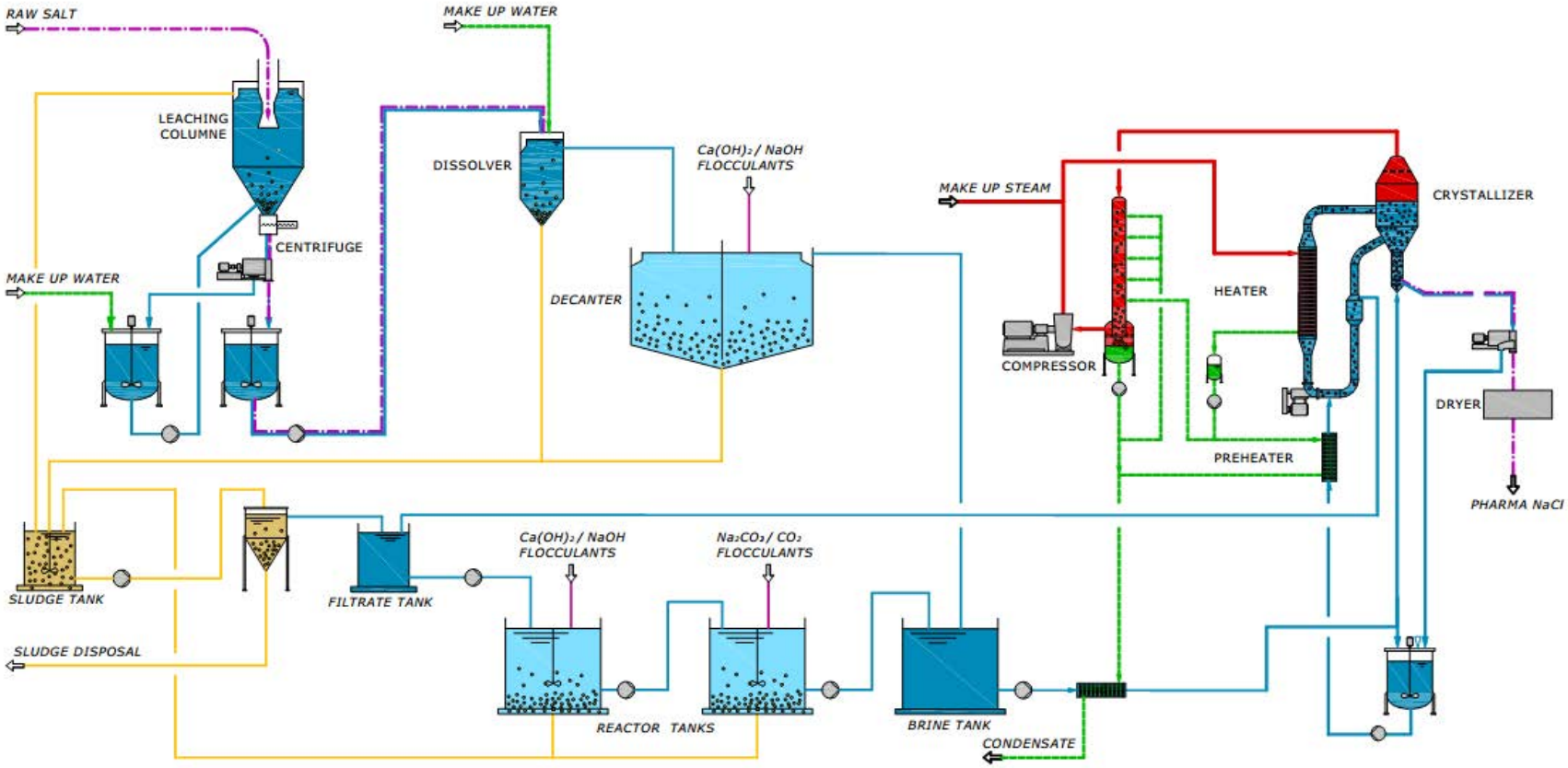
Case study #2: Pharma salt production from low quality solar salt

- Recrystallization technology
- Cold leaching for Mg removal



Case study #3: Pharma salt production from rock salt

- MVR technology with $CaSO_4$ seeding process
- Cold leaching for Mg removal
- partial full chemical brine treatment



Conclusions

- fast growing market with relative few players
- high “certification” requirements for API product
- only minor deviations to a modern vacuum salt plant
- almost all kind of raw salt upgradable

Thank you very much for your kind attention