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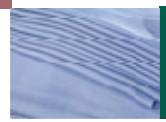


CHED

A New Fungicide for the Leather Industry

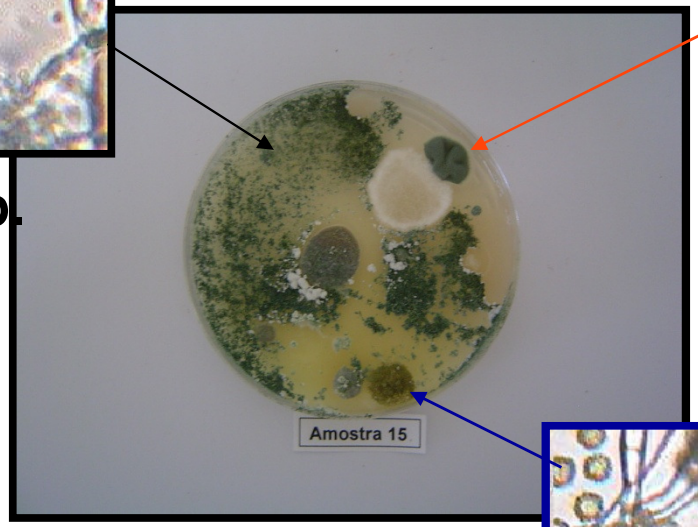
Elton Hurlow

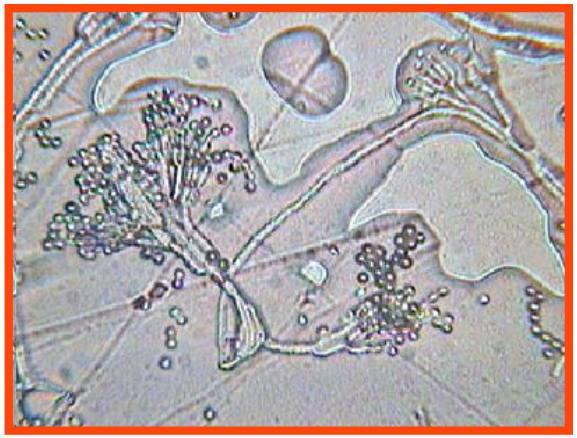
Global Market Development Manager - Leather

October, 2012

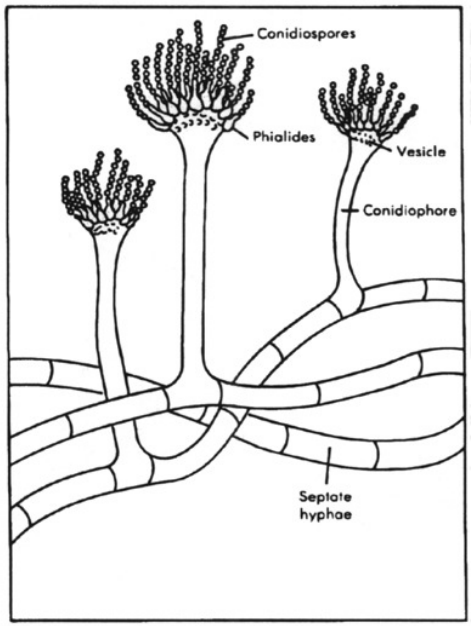
Typical Leather molds

Trichoderma sp.





Penicillium sp.



Aspergillus sp.

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Mould Growth on Leather

- When environmental conditions are right, wetblue, wet white, crust and even finished leather will sustain attack from fungi.
- Growth can be very rapid.
- Uncontrolled mould growth will result in:
  - Physico-chemical changes to the leather surface
  - Degradation of fats
  - Discoloration / staining of crust and finished stock
  - Downgrading of material
  - Other direct costs – rework (labor & chemicals)
  - Indirect costs (delayed deliveries, managers time)
  - Potential health hazard (mycotoxins)

$

This is why we use a fungicide in leather processing

Factors Affecting Growth

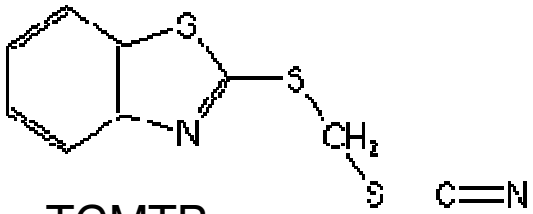
Fungal growth is initiated by airborne spores.

Fungal growth is influenced by:

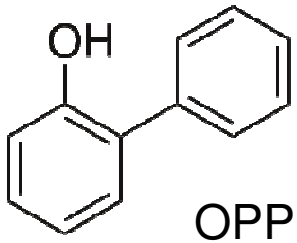
1. **pH** - prefer acid range
2. **Time** – need a few days to grow
3. **Temperature** – prefer a range between 25 - 35 ^{o}C
4. **Moisture** - can grow in a fairly dry environment
5. **Nutrients** and **growth factors** – food / fats

6. **Chemical control agents**

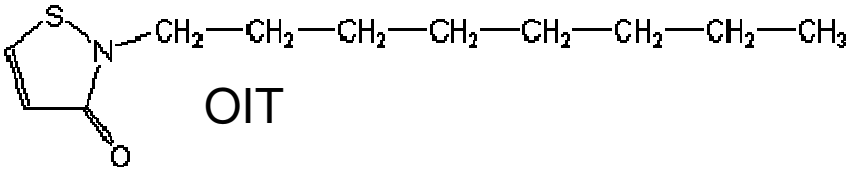
Common Actives in Leather



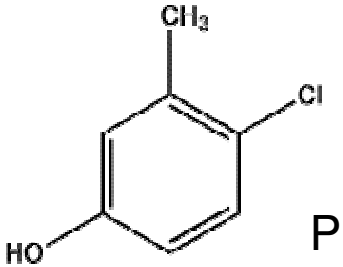
TCMTB



OPP



OIT



PCMC

These four active substances account for more than 95% of fungicides used commercially.

These have all been around for a long time

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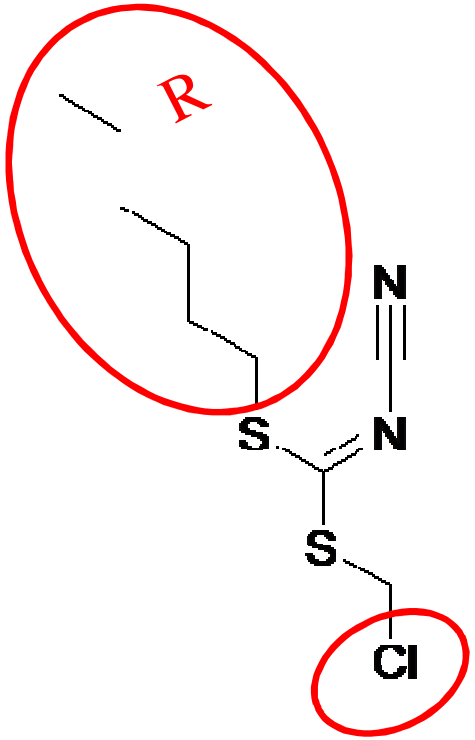
Development of CHED

- CHED was developed as a result of optimization studies looking at the asymmetric sidechains of dithiocarbimates.
- Results were confirmed in scale-up testing
- An efficient synthesis route was devised
- Manufacturing process was optimized
- Formulations were developed:
  - Stable on storage
  - Distribute uniformly in tanning bath
  - Uniformly taken up on leather surface.
- CHED products & applications were patented
- Field Trials and Test marketing was conducted



X

S-chloromethyl-S'-hexylcyanodithiocarbimate

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Optimization Studies

Halogen	Alkyl / Aryl group	Antifungal MIC
Cl	$-CH_2CHC{=}CH_2$	1.0
	$-(CH_2)_7CH_3$	2.0
	$-CH_3$	1.0
	$-(CH_2)_{11}CH_3$	6.0
	$-(CH_2)_5CH_3$ (CHED)	0.2
	$-(CH_2)_3CH_3$	0.4
	$-(CH_2)_2CH_3$	0.5
	$-CH_2C_6H_5$	1.0
	$-CH_2(CH_3)_2$	0.5
	$-(CH_2)_3OH$	6.0
	$-(CH_2CH_2O)_2CH_2CH_2OH$	6.0
	$-(CH_2)_2OH$	6.0
	$-(CH_2)_2CO_2H$	> 100
Br	$-(CH_2)_3CH_3$	1.4
	$-CH_2C_6H_5$	2.0
I	$-(CH_2)_3CH_3$	2.0
	$-CH_2C_6H_5$	5.0

Very Low MIC

Fungicide Evaluation

How do we go about evaluating a new fungicide formulation in the leather industry:

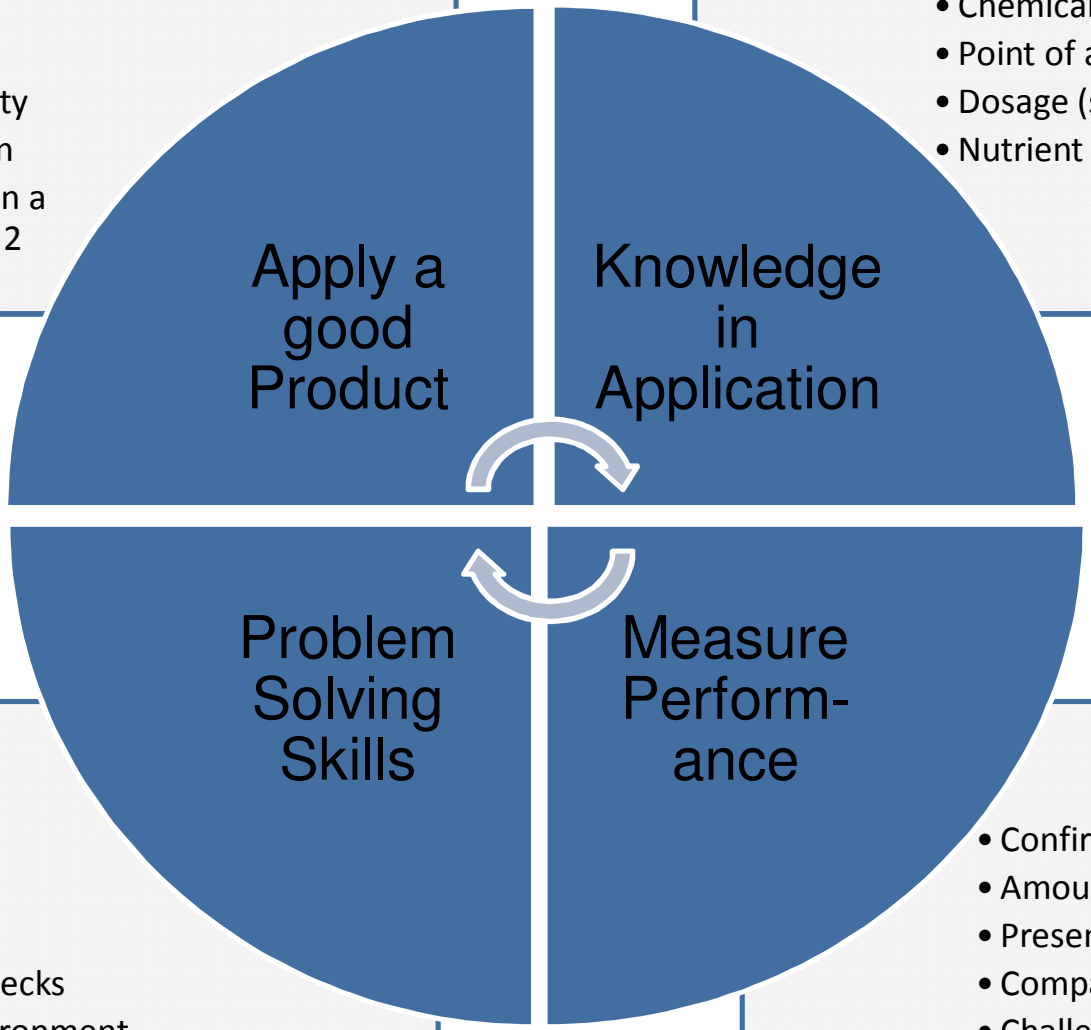
- What are the critical success factors?
- What are the performance metrics?

NOTE: There is a big difference between the lab and long-term performance in the real-world.

Critical Success Factors

- Active Substance
- Concentration
- Blends & Synergy
- Formulation stability
- Aqueous dispersion
- Emulsion stability in a 6% salt sol'n at pH 2

- Review of process / recipe
- Chemical Compatibility
- Point of application
- Dosage (s)
- Nutrient levels / fats



- Troubleshooting
- Storage, Handling
- Spectrum, MIC
- Environmental checks
- In a dynamic environment problems can and will arise

- Confirmed uptake
- Amount and uniformity
- Present in active form
- Compatible process
- Challenge test - Tropical chamber, Petri dish

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Performance Metrics

Yes, you added the microbicide… but how do you know it is working?

If you can't measure, how can you manage?

"What's measured improves!"

Initial Evaluation of Process & Requirements

1. Best application point / check for process incompatibilities.
2. Establish requirements based on raw material, process time, conditions of storage, handling, and the prevailing environment.
3. Product approvals and safe use

Ongoing Monitoring Metrics:

1. Regular monitoring for presence or uptake of active substance(s)
2. Regularly confirm performance by challenge testing
3. Regularly evaluate and document any process changes

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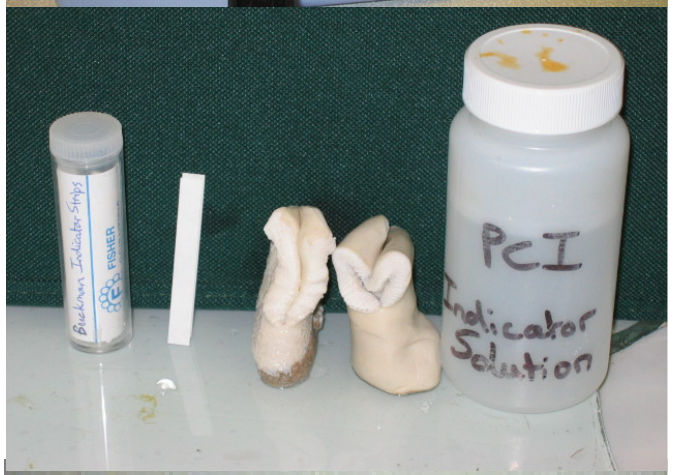
Process Compatibility

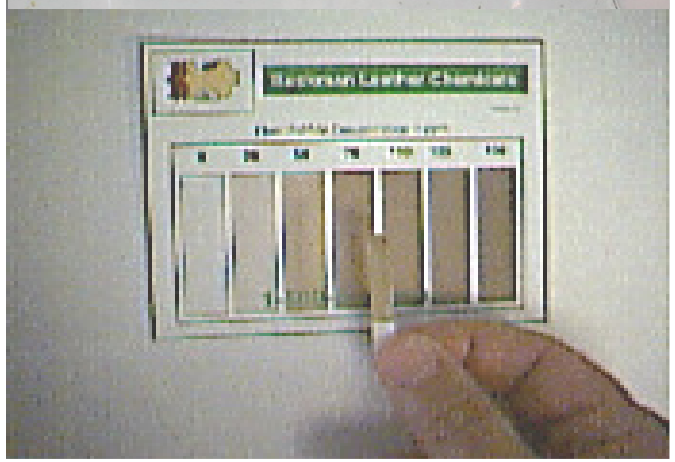
Check for incompatible chemistries or process conditions:

- Strong oxidizing agents - e.g. bleaches, chlorite, peroxide
- Reducing agents - e.g. sulfite, sulfide
- Other potential interferences - e.g. pH, basifying agents, fats

Monitoring Checks:

- Review chemical additives in recipe
- Direct check of actual pickle & tan liquors
- Check pelt cross-cut



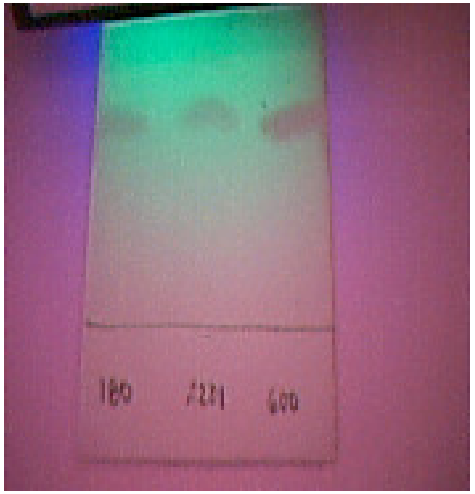


Uptake of Fungicide

Analytical Measurement of Active Substance:

- Solvent extraction → detection using HPLC or TLC
  PCI = Process Compatibility Index (TCMTB)
- **Quantity**: Critical minimum amount is required for performance
- **Uniformity:** Uptake and distribution

Reference: IUC 29 / EN ISO 13365



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Challenge Testing

Environmental Chamber Test: (ASTM D7584-10)

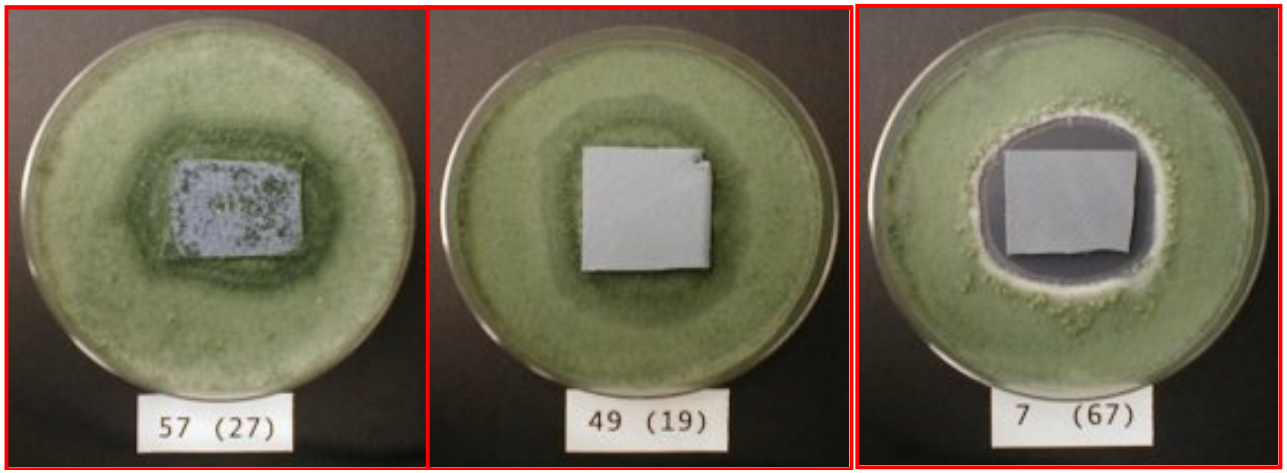
- Controlled temperature and humidity
- Populated with various fungal species
- Exposure period – e.g. 4 to 8 weeks
- Monitor regularly for mould growth

Good correlation with real world

Not always representative of real world

Agar Plate Challenge Test:

- Controlled temperature and humidity
- Inoculated with various fungal species
- Monitor for growth



CHED Commercial Formulations

- Focus on two commercial product formulations:
  - CHED as only active substance
  - CHED in synergistic combination with two other active substances.

Performance: CHED 20%

Development and production trials were run with CHED formulations on fresh and salted hides of Brazil, Australia, German, France, and India origin

Trial	Sample Size	Dosage	Normalized Extraction Values	EC @ 4 weeks	EC @ 8 weeks
1	n = 6	0.04%	Avg = 48	10 / 10	10 / 10
2	n = 6	0.04%	N/A	9.5 / 9.5	N/A
3	n = 6	0.05%	Avg = 42	9.9 / 9.9	8.9 / 9.0
4	n = 80	0.05%	N/A	9.8 / 9.5	9.1 / 9.1
5	n = 6	0.05%	N/A	9.7 / 9.8	N/A
6	n = 6	0.08%	N/A	10 / 10	10 / 10
8	n = 4	0.08%	Avg = 74	10 / 10	10 / 10
9	n = 4	0.10%	Avg = 82	10 / 10	10 / 10
7	n = 6	0.10%	Avg = 82	10 / 10	10 / 10

			WEEK 1		WEEK 2		WEEK 3		WEEK 4	
No.	SAMPLE	TREATMENT	Grain	Flesh	Grain	Flesh	Grain	Flesh	Grain	Flesh
1	XMN	0.03% BLX 13645	10	10	10	10	10	10	9.9	10
2	XMB		10	10	10	10	10	10	10	10
3	XMBT		10	10	10	10	10	10	10	10
4	XXMN	0.03% BLX 13645	10	10	10	10	10	10	10	10
5	XXMB		10	10	10	10	10	10	10	10
6	XXMBT		10	10	10	10	9.9*	10	9.5	10
7	XXXMN	0.05% BLX 13645	10	10	10	10	10	10	10	10
8	XXXMB		10	10	10	10	10	10	10	10
9	XXXMBT		10	10	10	10	10	10	10	10
10	IVMN	0.05% BLX 13645	10	10	10	10	10	10	10	10
11	IVMB		10	10	10	10	10	10	10	10
12	IVMBT		10	10	10	10	10	10	10	10
13	VIIMN	0.10% BLX 13645	10	10	10	10	10	10	10	10
14	VIIMB		10	10	10	10	10	10	10	10
15	VIIMBT		10	10	10	10	10	10	10	10
16	VIIIMN	0.10% BLX 13645	10	10	10	10	10	10	10	10
17	VIIIMB		10	10	10	10	10	10	10	10
18	VIIIMBT		10	10	10	10	10	10	10	10

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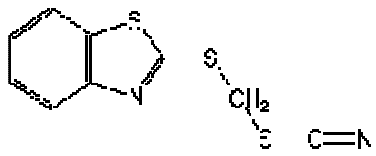
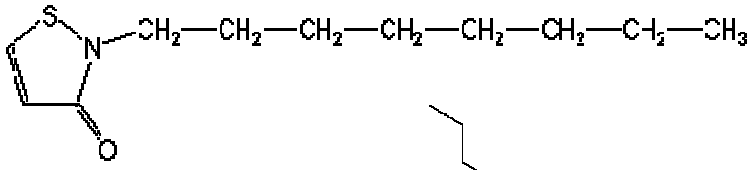
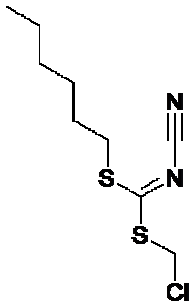
Synergistic Combinations

Formulation with 3 active substances:

- TCMTB: the most widely used active substance for long-term preservation
- OIT: highly effective, but typically found in combination programs
- CHED: newly patented active substance







Benefits of combining three highly effective fungicides in one single, potent formulation:

1. Wide spectrum control of all leather molds
2. Lower residuals on leather surface for optimized ecology
3. Cost effective long-term preservation for all types of leathers

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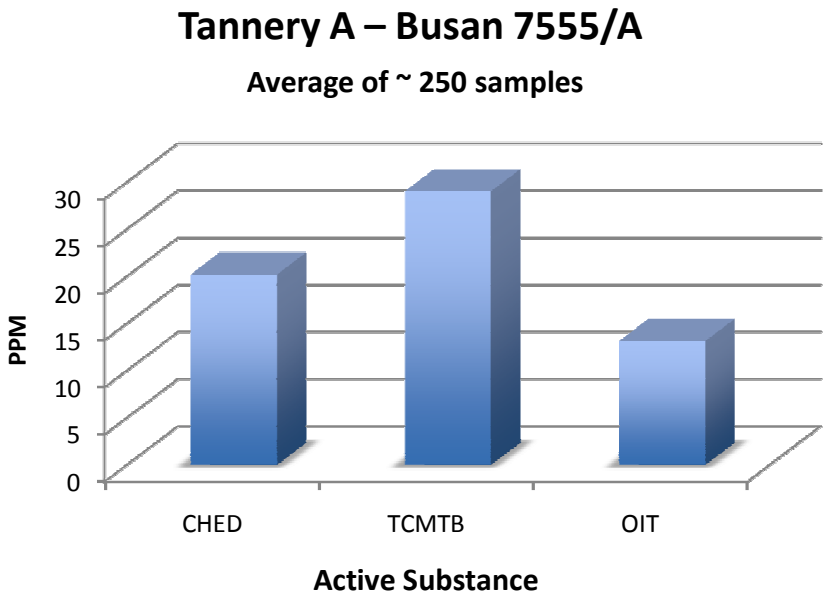
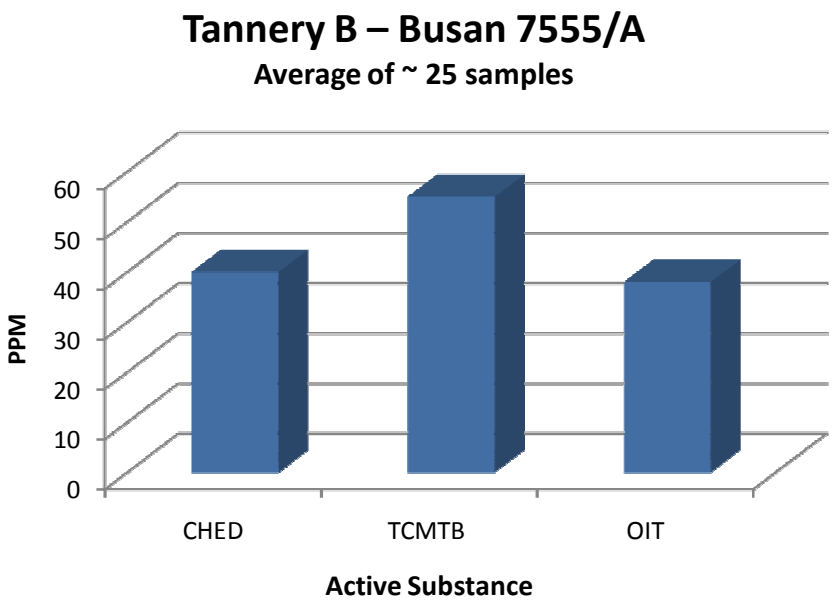
Synergistic Combinations

- Typical dosage of commercial product ranges from 0.1% to 0.2%
- Product contains ~ 15% total active substance
- Results from long term performance trials show good consistency of active substance uptake and performance





Every tannery is different – process / requirements → dosage needs to be adjusted

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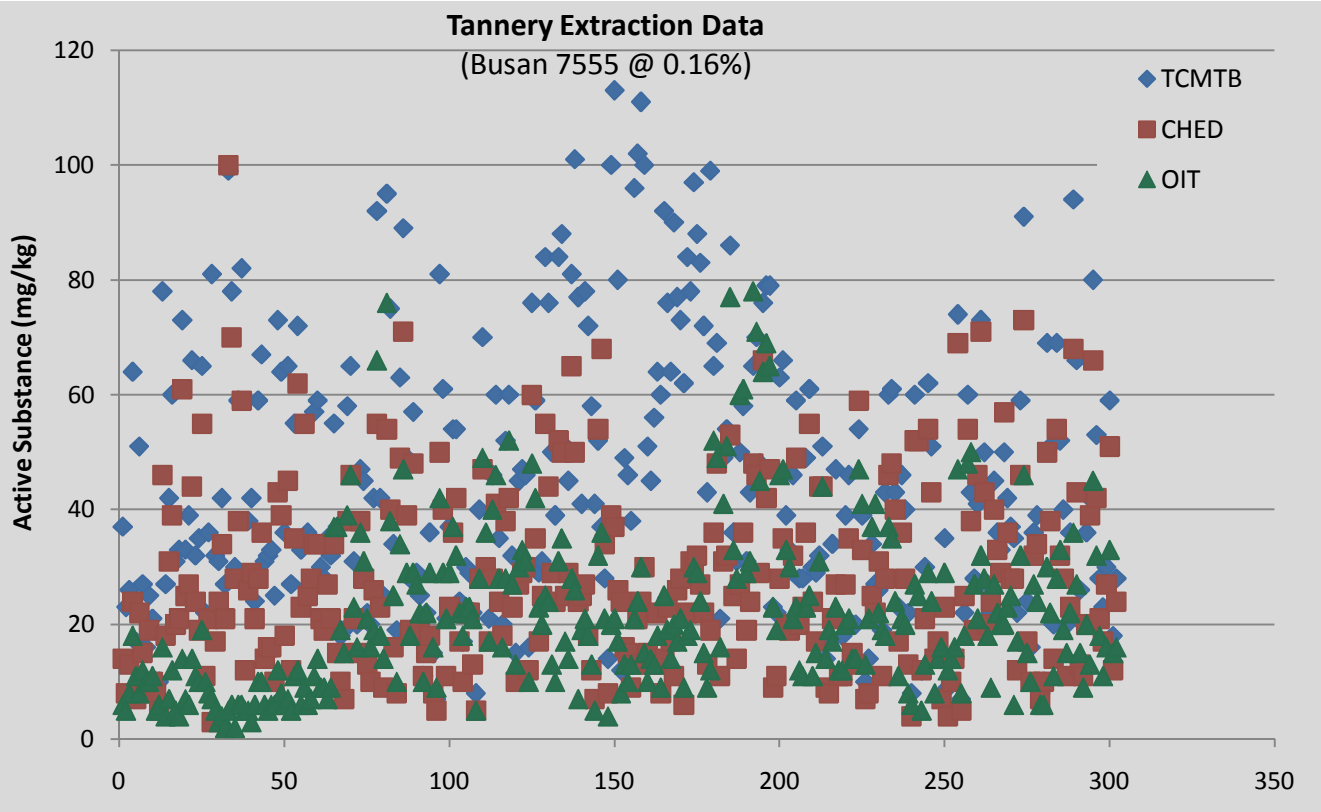
Case Study: Brazil

Sample Size	Dosage %	Normalized Extraction Values			EC @ 4 weeks	EC @ 8 weeks
		TCMTB	CHED	OIT		
301	0.16	45.3 STD = 23.6	28.0 STD = 16.3	21.6 STD = 14.7	10 / 10	9.9 / 9.9



- Full thickness wetblue
- Fresh hides for domestic and export markets.
- Standard dosage of 0.16%.
- Total normalized active substance content was less than 100 mg/kg (ppm).
- Declared preservation requirements are for a minimum of 6 months
- Some of this wetblue has now been stored for well over 1 year with continued good preservation.

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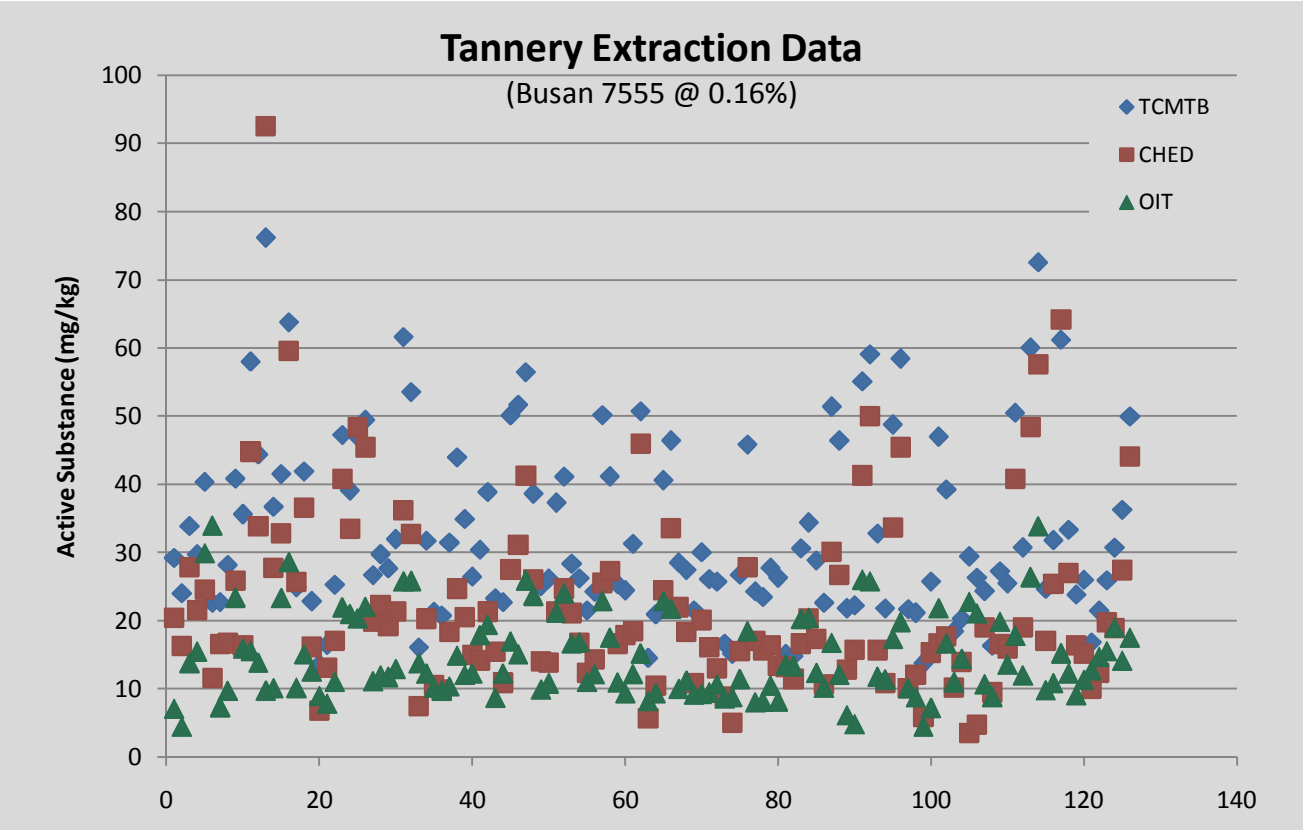
Case Study: ANZ

Sample Size	Dosage %	Normalized Extraction Values			EC @ 4 weeks	EC @ 8 weeks
		TCMTB	CHED	OIT		
126	0.16	33.2 STD = 13.4	22.5 STD = 13.6	14.7 STD = 6.2	10 / 10	9.6 / 9.8



- Tannery that produces wetblue for export from fresh bovine hides.
- Dosage is 0.16% with single addition
- Performance expectation is > 6 months
- Program has been running for ~ 2 years

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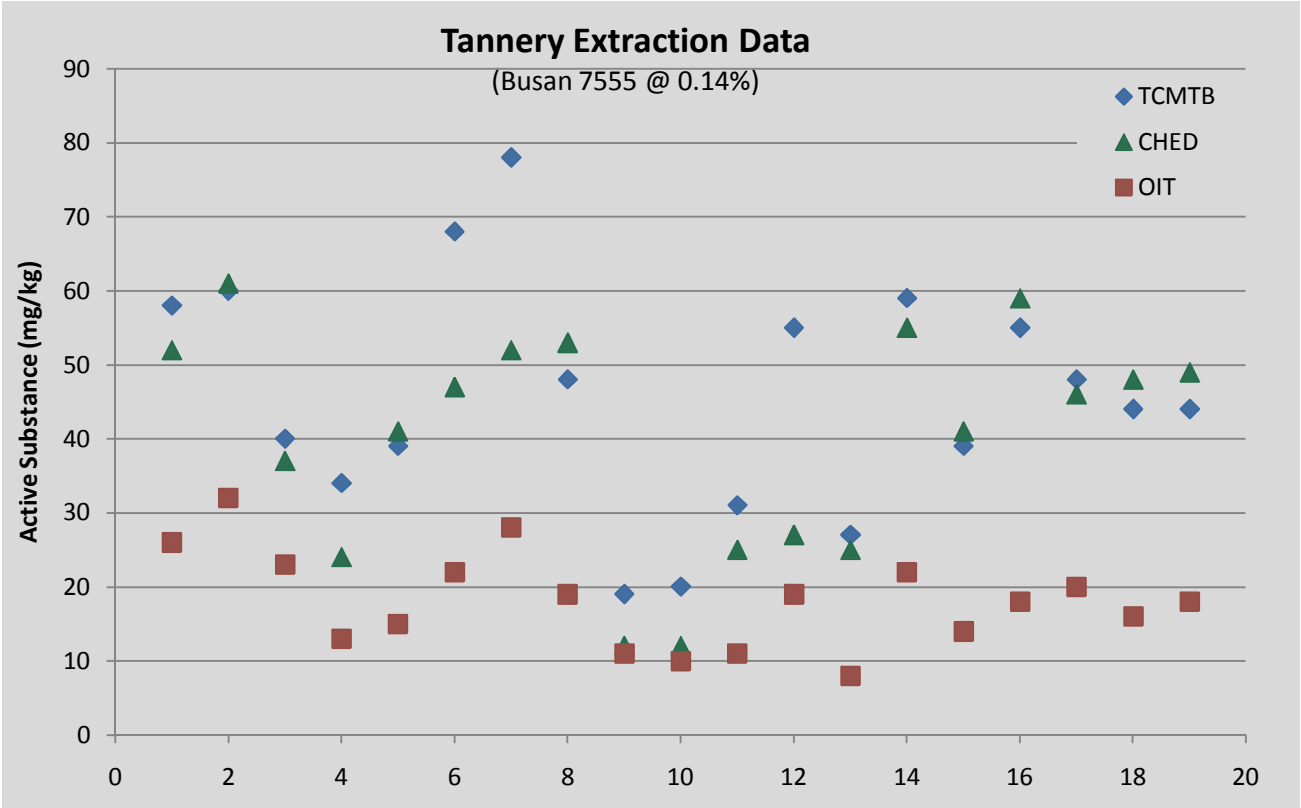
Case Study: South America

Sample Size	Dosage %	Normalized Extraction Values			EC @ 4 weeks	EC @ 8 weeks
		TCMTB	CHED	OIT		
19	0.14	45.6 STD = 15.7	40.3 STD = 15.2	18.2 STD = 6.4	10 / 10	10 / 10



- Processes fresh hides to wetblue for export.
- Good uptake of actives
- Dosage 0.14%
- Performance expectation > 6 months
- Program has been running for about one year

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CHED

- A new antifungal agent for the leather industry
- Highly effective against common leather fungi
- Works alone
- Works in synergistic combination
- Sets a new standard for low levels of residual active substance in leather
- Proven in production on different substrates around the world
- Toxicity & environmental fate data indicate that CHED has a favorable profile
- Registration of CHED in countries with strict regulatory requirements is in progress

Thank You

Acknowledgements:
• Buckman R&D worldwide
• Buckman SoCone & ANZ

CHED = S-chloromethyl-S'-hexylcyanodithiocarbimate

Buckman