Photochemical Stabilization of Fortified Salt to Treat Lymphatic Filariasis and Iodine Deficiency Disorder

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Cargill Salt Group

WORLD SALT SYMPOSIUM

June 19-21, 2018 Park City UT, USA

University of Notre Dame Haiti Program is a world leader in the fight against Lymphatic Filariasis, working in Haiti since 1993

Cargill Salt - University of Notre Dame Haiti Program

Salt Project Mission

Ministering in Christ's name, we will eliminate LF and prevent IDD in Haiti through the production and distribution of co-fortified salt.

Strategy

We provide fortified salt competitively in the retail, foodservice, food-service segments while providing unfortified salt profitably in the industrial segment.

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Lymphatic Filariasis and Iodine Deficiency Disorders

- LF is a “neglected tropical disease” affecting 120 million people in 83 countries
  - Elephantiasis
  - Pain
  - Disfigurement
  - Social ostracism
- Iodine Deficiency Disorders
  - World’s most prevalent cause of cognitive impairment
  - In 2011, the WFP estimated 72% of children in Haiti suffered from IDD

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Cargill Salt Group Partnership with UNDHP

- Cargill working with CSC Plant in Port-au-Prince, Haiti
- Providing technical and engineering support for the processing of solar salt from Haiti and Bonaire
- Providing business development support

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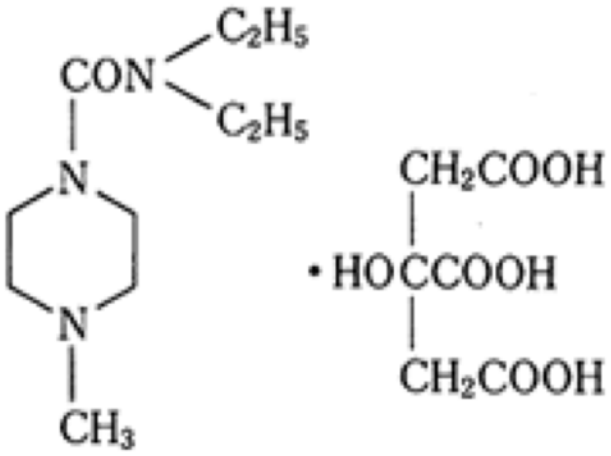
Fortification Agents



- Diethylcarbamazine Citrate (DEC)
- Effective LF treatment
- Citrate salt of free base DEC (weak acid)

KIO_3

- Potassium Iodate
- Iodizing agent

DEC + KIO_3 Stability Issues

- Co-fortified salt would sometimes turn deep yellow (inconsistently)
- Sometimes the yellow color would vanish over time
- Color change only occurred in salt fortified with both DEC and KIO_3
- Customers would not buy a yellow salt – problem needed to be solved
- Investigation revealed exposure to sunlight through transparent plastic bags was driving the color change.
- Yellow color was extractable with water and tested positive for iodine (starch test)
- Color changes arising from changes in iodine speciation

Color of Iodine Species

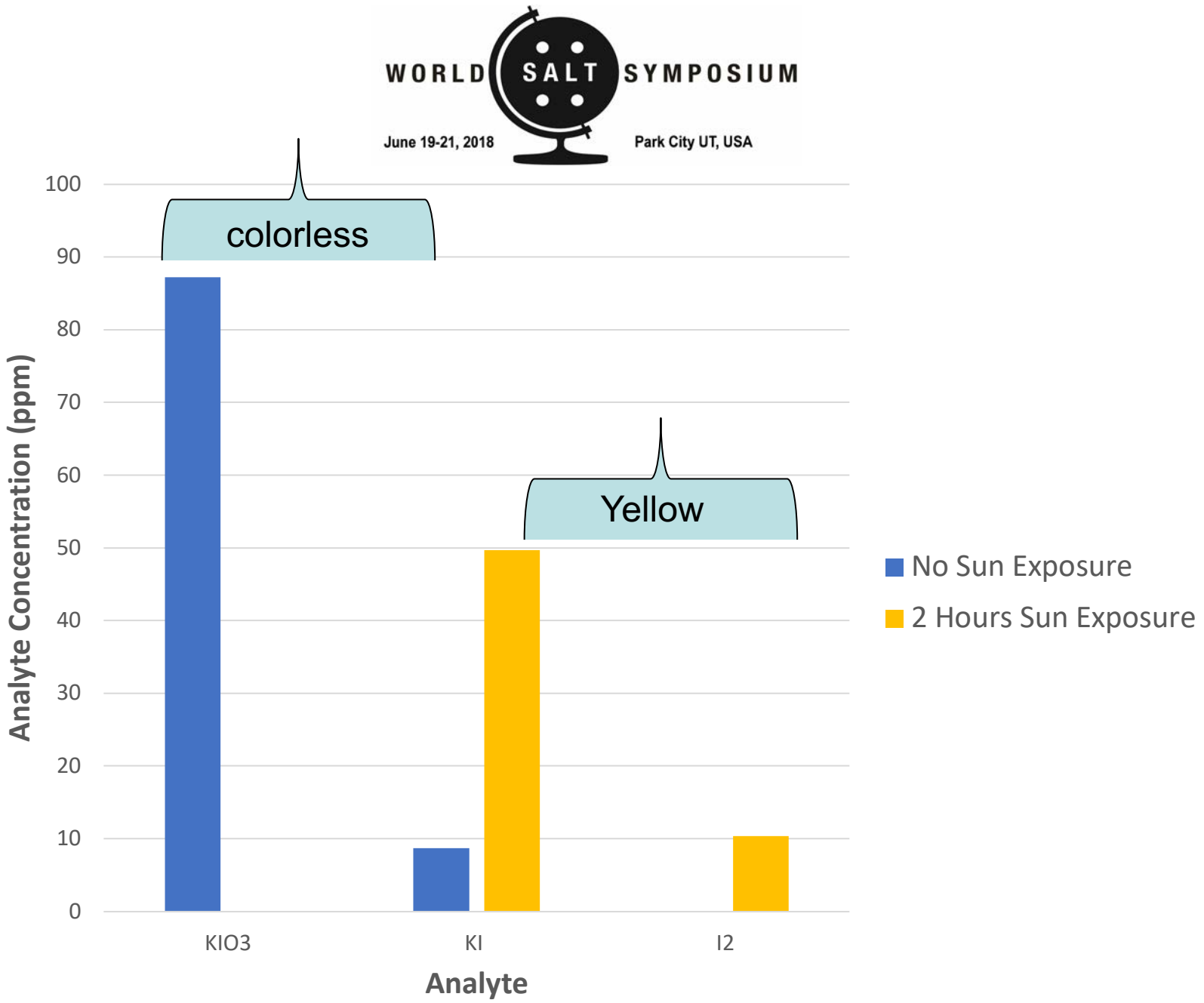
IO_3^-	Colorless
I^-	Colorless
I_2	Yellow
$I_2 + I^- \rightleftharpoons I_3^-$	Yellow

Proposed Mechanism of Color Change: IO_3^- is progressively photochemically reduced by DEC

	Iodine Ox. State	Color
IO_3^-	+5	Colorless
↓		
I_2	0	Yellow
↓		
$I_2 + I^- \longrightarrow I_3^-$	-1/3	Yellow
↓		
I^-	-1	Colorless

Precedence for this Mechanism

- IO_3^-(aq) is photochemically reduced in the presence of humic acid (Saunders, et. al. 2012)
- IO_3^-(aq) is photochemically reduced to I^-(aq), but organic matter is essential for the reaction (Spokes, et. al. 1996)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colorless
Yellow
Analyte Concentration (ppm)
100
90
80
70
60
50
40
30
20
10
0
KIO3
KI
I2
Analyte
No Sun Exposure
2 Hours Sun Exposure

Solution

The reduction of IO_3^- is thermodynamically favorable under acidic conditions (provided by DEC)

$$IO_3^-(aq) + 6H^+(aq) \longrightarrow \tfrac{1}{2}\, I_2(aq) + 3H_2O \quad E^0 = 1.195\ V$$

Adjusting the DEC stock solution to alkaline pH with NaOH makes the reduction thermodynamically unfavorable and stabilizes the DEC + IO_3^- fortification

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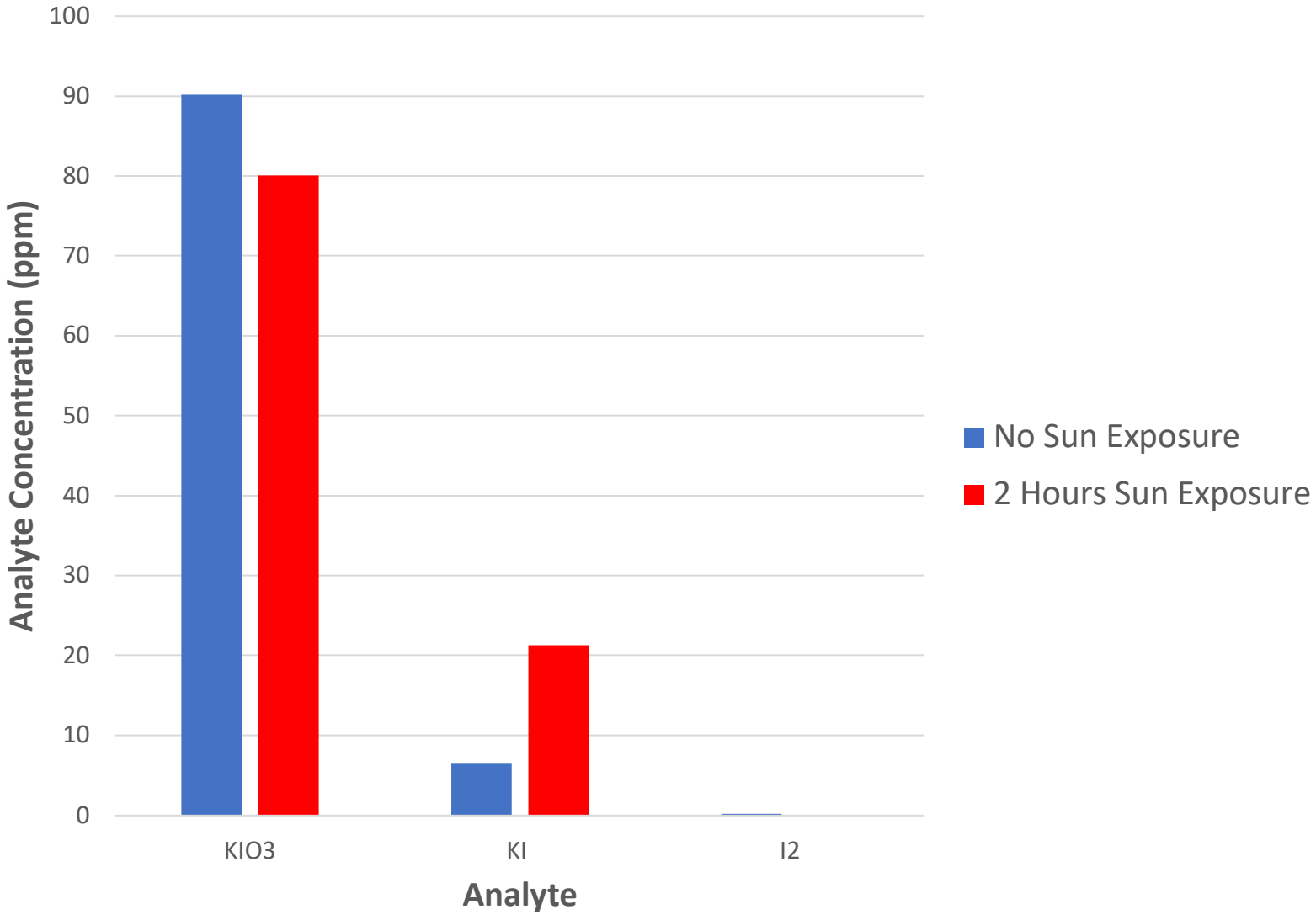

Some Practical Considerations

- In principle DEC/KIO_3 stock solution can be pH adjusted with any suitable base, but NaOH probably most convenient
- Na_2CO_3 is lower cost but pH is limited to ~ 7.2 + effervescence issues
- DEC citrate solubility is higher than free base
- Stock solution DEC concentration must be lower at higher pH – will impart higher moisture to the salt
- If opaque packaging is cost effective, the pH adjustment may not be necessary

Modification of DEC Analytical Method

- Prior method involved back HCl titration of DEC Citrate
- If DEC is pH adjusted this will no longer work
- A simple, accurate method is needed for quality control at Haiti plant
- Solution – within buffer zone DEC pH will be ~ independent of concentration
- Thus titrant volume between two discrete points in buffer zone will be proportional to DEC concentration

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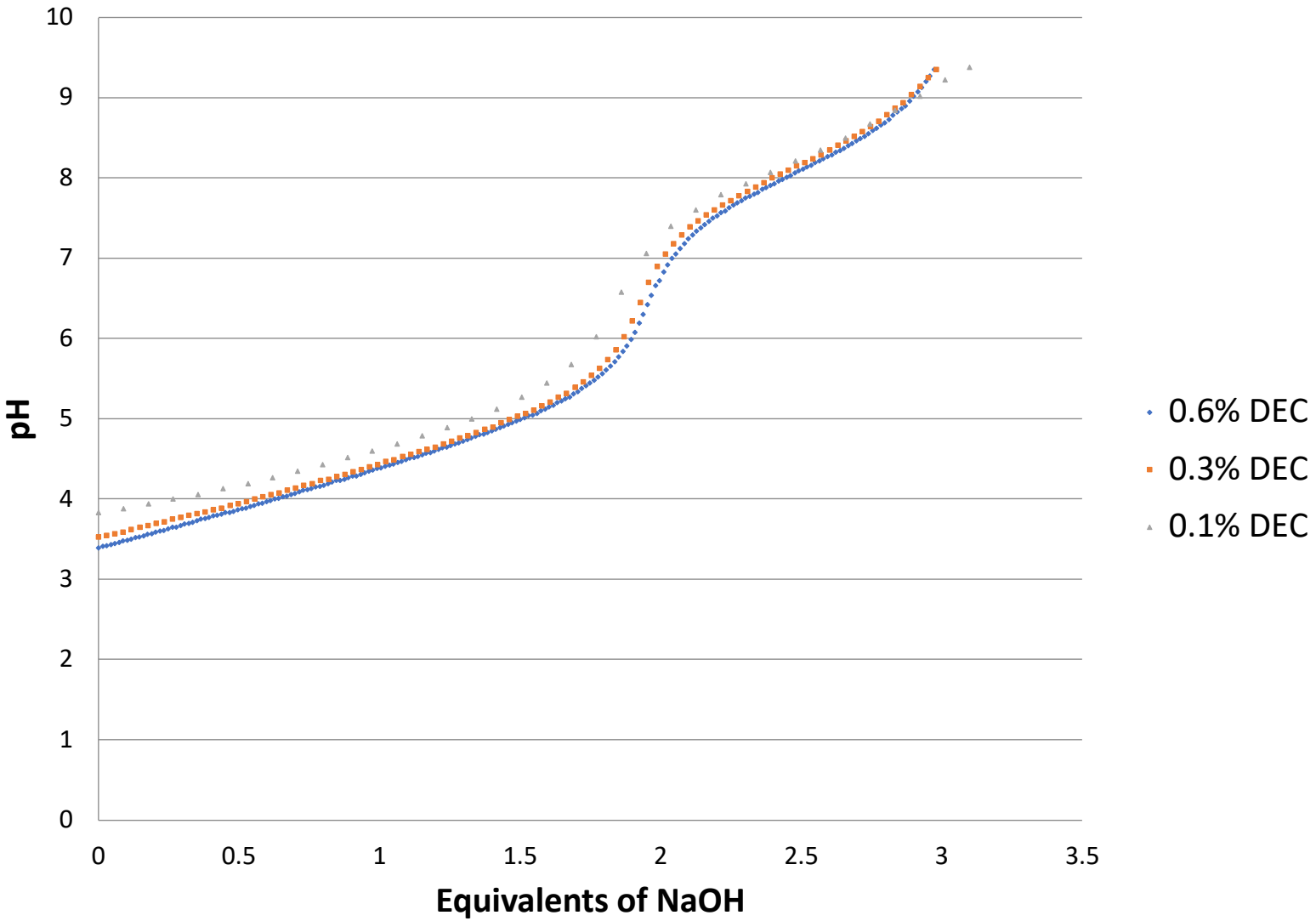

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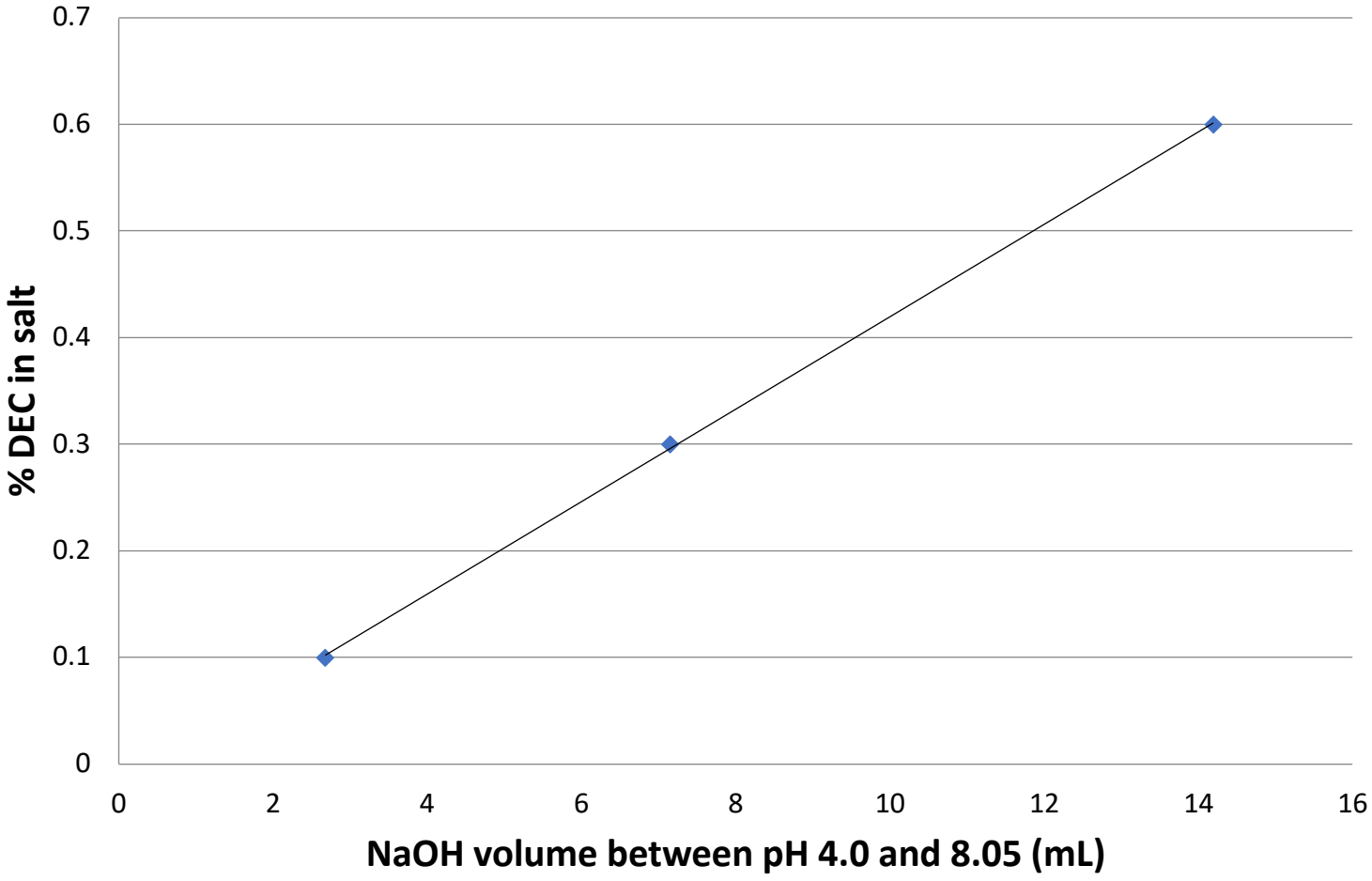
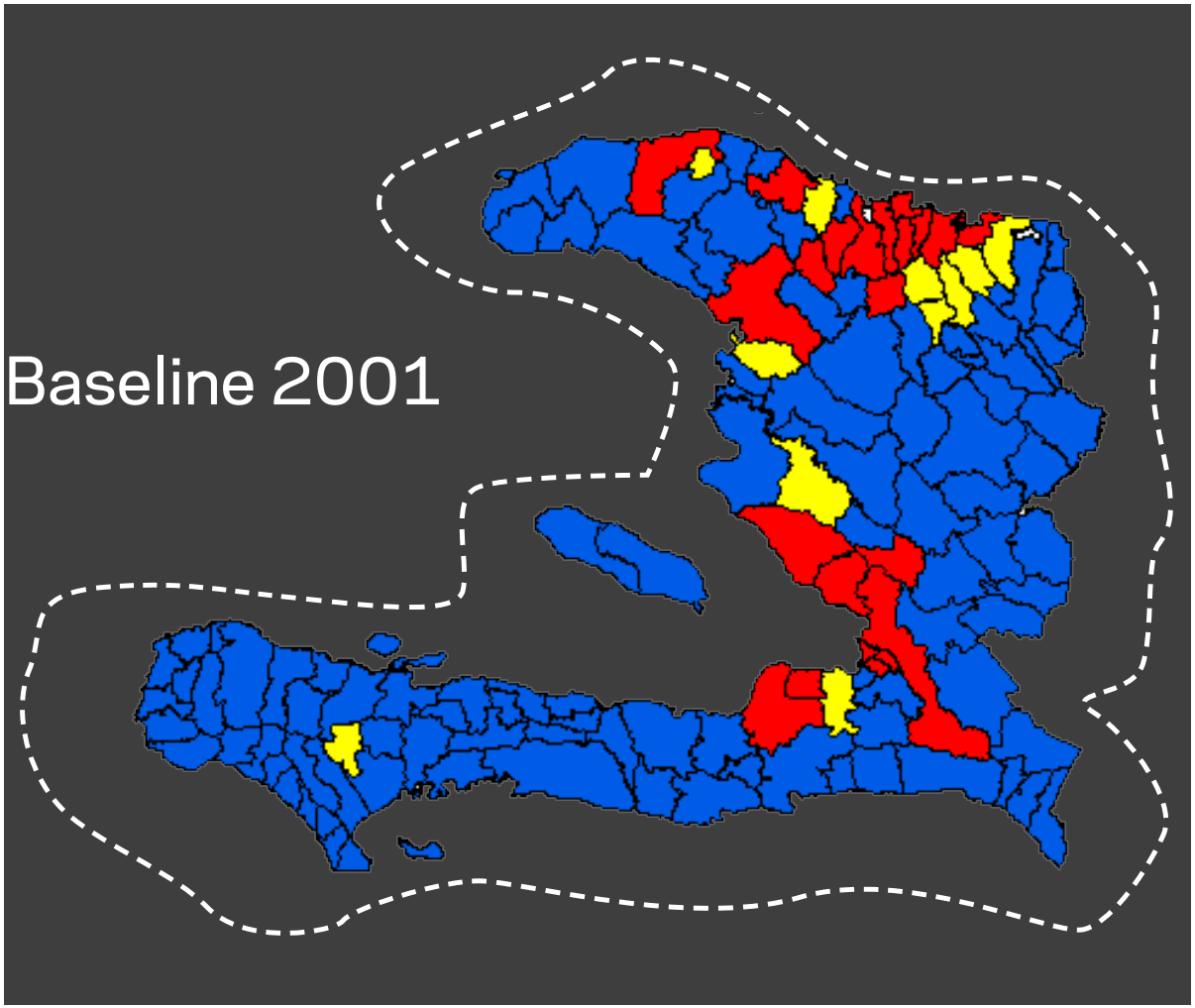


2001: LF was endemic in all 140 communes



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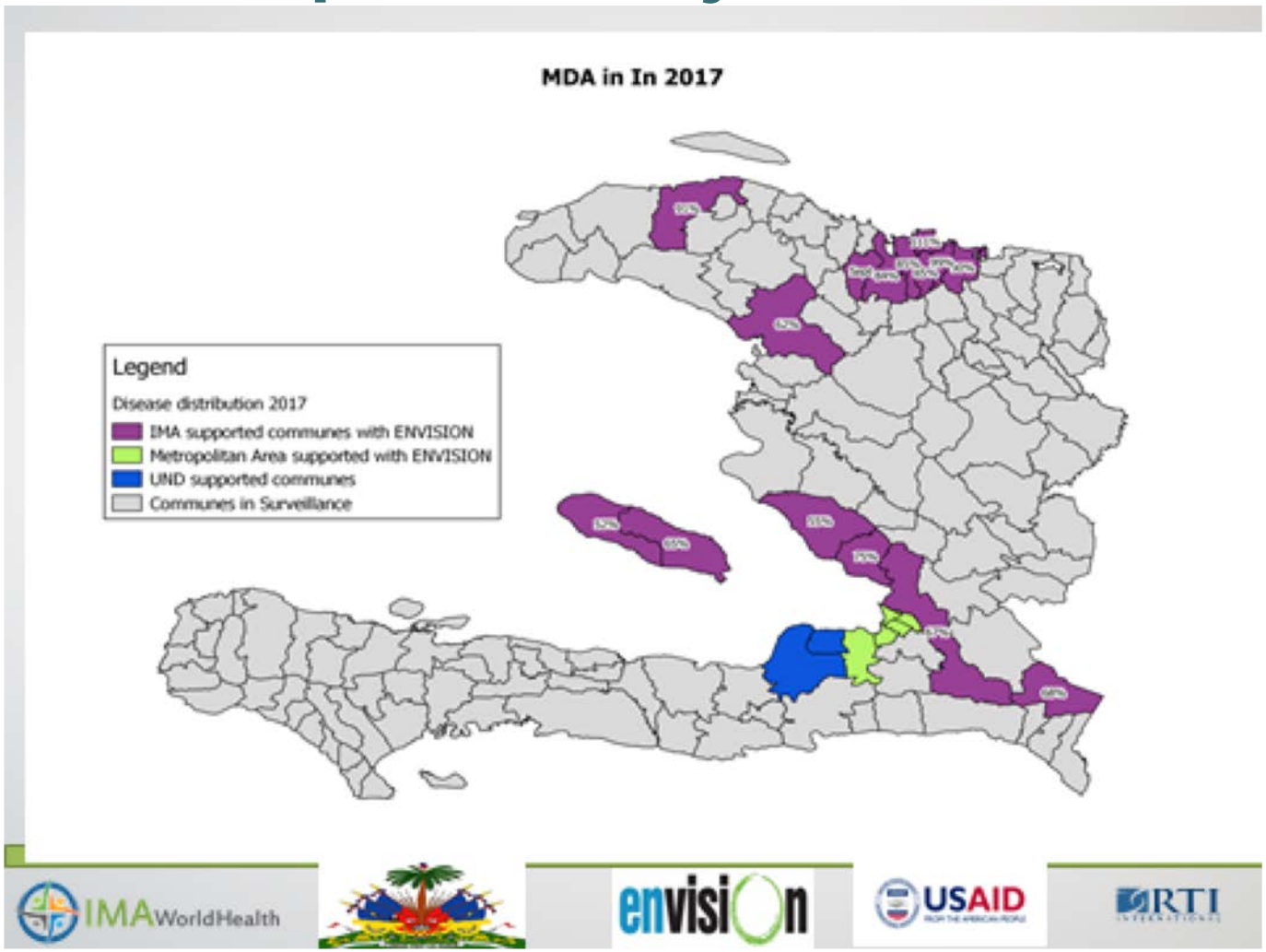
2017: LF present in just 23 communes



Conclusions

- Salt co-fortified with IO_3^- and DEC will turn yellow when exposed to sunlight
- Yellow color is caused by a progressive photochemical reduction of IO_3^- to I_2 and I^-
- Product can be stabilized by adjusting pH of DEC/KIO_3 stock solution to 7.5 or higher
- Since implementing this change, the Haiti CSC plant has been successfully manufacturing stable product
- pH adjusted product can be analyzed for DEC using a simple acid/base titration requiring only a pH meter to an accuracy of +/- 0.01% DEC

Conclusions

- Significant progress has been made
- We are on track to eliminate LF and prevent IDD in Haiti
- Since 2013 over 22 million doses of DEC have been distributed via salt
- Certification of Haiti as LF free is estimated 2020-2022
- Lessons learned in Haiti can be a valuable resource for the more than 60 countries actively working to eliminate LF