

# Changes in Pediatric Hospital Wide Thickening Protocol in Response to Events and Evidence

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## Thickeners and Necrotizing Enterocolitis

Thickeners:

- Used in pediatric population to allow safe bottle feeding, prevent aspiration, and avoid feeding tube placement
- Commonly used thickeners include products such as Simply Thick, Thick-It, rice cereal and oatmeal cereal
- Xanthum gum thickeners, such as Simply Thick, was preferred for infants due to its low caloric density, consistent texture and stable molecular structure among breastmilk enzymes

Necrotizing Enterocolitis:

- Death of intestinal mucosa caused by intestinal ischemia, infection, or translocation of bacteria which trigger excessive immune response and GI tissue death<sup>1,3</sup>
- Leading cause of morbidity and mortality in neonates<sup>1,3</sup>
- Occurs in 0.3% of live births, with 13% of those affecting term infants and 87% affecting preterm infants<sup>3</sup>
- Incidence increases with decreasing birth weight and gestational age, affecting 7% of very low birth weight infants<sup>3</sup>

Cases have potentially linked use of xanthum gum thickeners with necrotizing enterocolitis (NEC)

## Evidence to Support Policy Change

Case review and rigorous studies show strong evidence that xanthum gum thickeners may increase risk of NEC in infants

Case Review of FDA Reported NEC After Use of SimplyThick

- Review of these cases showed distinct features, different from most previous infant NEC cases<sup>1</sup>
  - Median onset of NEC at 66 days of life - 21 days later than latest age of infant NEC, per largest cohort study to date<sup>1,2</sup>
  - 50% of cases developed NEC at home - without other medical risks, most cases of infant NEC develop in the hospital<sup>1</sup>
  - EN initiated 43 days prior to NEC onset - NEC usually develops quickly after initiation of EN, with 48 hours<sup>1,8</sup>
- These distinct features suggest development of NEC must have been due to an additional factor, beyond the usual risk factors of NEC. The only known commonality among these cases is the use of SimplyThick<sup>1</sup>.

Is There a Potential Mechanism?

Yes, SimplyThick may predispose infants to GI mucosal injury and NEC through accumulation of short-chain fatty acids (SCFA) produced by bacterial metabolism of xanthum gum<sup>1,4,5</sup>.

Supporting Evidence for Potential Mechanism

- Studies from healthy adults showed increase in fecal SCFA production after ingestion of 15g of xanthum gum<sup>5</sup>
- Production of some SCFA is expected in infants and adults due to bacterial fermentation of carbohydrates<sup>4,6</sup>
- Excessive production of organic acids such as SCFA may exceed the absorptive capacity of the colon<sup>6,7</sup>
- High concentrations of organic acids significantly lower the pH of the intestinal lumen which may cause intestinal injury<sup>4</sup>
- Intra-luminal admin of SCFAs in newborn rats induced intestinal injury pathologically similar to those seen in NEC<sup>4</sup>
- In FDA reported cases of NEC after use of SimplyThick, a median of 13 days passed from introduction of SimplyThick to onset of NEC, sufficient time for intestinal SCFA build-up<sup>1,5</sup>

Ultimately, SimplyThick may lead to excess intestinal SCFA production in infants, leading to increased intestinal pH, mucosal injury and development of necrotizing enterocolitis

### References

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## Events & FDA Issued Warnings

- May 2011 → The FDA was notified of 15 premature infants diagnosed with NEC possibly associated with use of SimplyThick<sup>9</sup>
- May 2011 → The FDA issued a consumer warning against use of SimplyThick in premature infants born <37 weeks gestational age<sup>9</sup>
- September 2012 → 22 infants have been reported to have NEC after use of SimplyThick. The FDA extended the warning to include infants of any gestational age<sup>9</sup>
- Current → FDA maintains warning against SimplyThick for any infant <1 year of gestational age<sup>9</sup>

## Hospital Thickener Policy - July 2011 – PAST POLICY

General Guidelines:

- Use hospital-approved formula thickeners whenever possible. Exceptions must be justified in clinical documentation and ordered through standard, non-formulary special ordering processes

Age & Nutritional Concern	Thickener
Breastfed, non-premature infants (>37 weeks)	Gel-based thickener (i.e. Simply Thick)
Premature infants <37 weeks, or premature infants with corrected age of less than 44 weeks whether hospitalized or discharged home	DO NOT use Simply Thick or xanthum gum
Formula fed infants	Powder based thickener (i.e. Thick It)
Ketogenic, Corn Allergy, Weight Management (Obesity)	Low-carbohydrate, gel-based thickener (i.e. Simply Thick)

- For premature infants born <37 weeks and post-menstrual age <44 weeks, do not use Simply Thick or xanthum gum
- Caution advised with use of any thickener in patients with high risk diagnoses such as gastroschisis, TEF, atresia, pharyngeal cleft

## Hospital Thickener Policy – April 2015 - CURRENT POLICY

General Guidelines:

- Initiating thickened liquids requires physician oversight to assess the risks and benefits of thickened liquids
- Risks and benefits must be communicated, put into clinical context for the family and documented in the medical record
- Use of thickeners in infants outside the guidelines requires clear documentation of the indication in the medical record

Age	Thickeners for Breastmilk	Thickener for Formula
Infant with corrected gestational age <42 weeks	None	None
Infants with corrected gestational age >42 weeks and weighing at least 6 pounds	Gelmix	Infant plain rice or oat cereal Thick-It* Gelmix*
Children >12 months	Simply Thick* Gelmix	Simply Thick** Thick-It Gelmix Infant plain rice or oat cereal

\*if clinically indicated (i.e. failed trial of cereals)  
\*\*Simply Thick is not recommended for any child under the age of 12 years with history of NEC

Special Considerations:

- Enzymes in breastmilk break down molecular structure of cereals and Thick-It
- It is difficult to achieve honey-thick consistency with products safe for infants