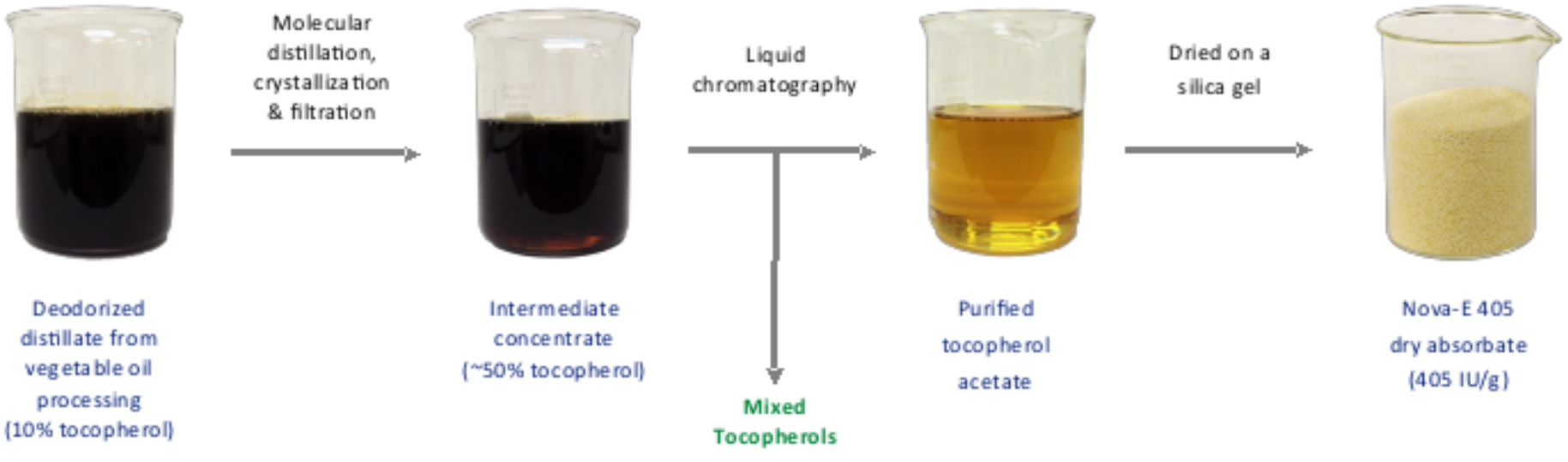
NOVA-E™ NATURAL-SOURCE VITAMIN E USAGE GUIDE

ADM Nova-E™ Natural-Source Vitamin E is produced by extracting α-tocopherol from oilseeds and then stabilizing the molecule as α-tocopheryl acetate for use in animal feed. Synthetic vitamin E has always held a cost advantage compared with vitamin E extracted from natural plant sources. Just within the last few years, however, science has shown that the chemical differences between naturally-sourced and synthetic vitamin E vary greatly in their impact on health of humans and livestock. This guide will help the user understand the biology of Nova-E and aid in developing a supplementation strategy that optimizes the return on investment for this unique molecule.

Processing time = 90 days



Facts about the production of Nova-E:

Natural-source vitamin E represents about 5% of the total vitamin E market.

It takes almost three months to isolate and process Nova-E into feed-grade, d-α-tocopheryl acetate.

One ton of Nova-E 405 requires processing of three million pounds of vegetable oil or about 7,000 acres of soybeans.

The unique biology of natural-source, Nova-E:
Internet check: Querying "RRR" and "tocopherol" in any search engine will generate extensive information for further education.

The molecular tail of α-tocopherol has three chiral carbons that can be rotated to either the left (S-form) or right (R-forms) to create eight *stereoisomers* of α-tocopherol. In natural-source vitamin E, all carbons are rotated to the right, hence the term RRR-α-tocopherol. Synthetic vitamin E contains all eight possible stereoisomers, occurring at 12.5% each.

BIOLOGICAL IMPLICATIONS:
The liver discards 50% of synthetic vitamin E. Alpha-tocopherol Transfer Protein (ATTP) selectively retains the carbon-1 right-handed molecules. This means that the four R-forms (RRR, RRS, RSR, RSS) are retained by ATTP whereas the four L-forms (SSS, SSR, SRS, SRR) are all excreted in about 24 hours (Figure 1). Across species, extensive research shows natural-source vitamin E is at least 2X more potent than synthetic vitamin E and natural-source vitamin E may be legally labeled for this potency in humans, as discussed below.

Cellular membranes may poorly retain non-natural stereoisomers. Even beyond the 50% loss of S-form stereoisomers due to liver ATTP selection, some agricultural species show still greater preferences for natural-source vs synthetic α-tocopherol, as evidenced by tocopherol accumulation in various tissues. This may relate to how well cellular membranes retain the conserved R-forms over longer periods of time. Research in dairy cattle given an injection of synthetic vitamin E (Jensen, 2005) shows that, although it takes several days, the other three carbon-1 right-handed stereoisomers (RSS, RSR, RRS) are eventually cleared from the body; whereas, the RRR form is apparently retained (Figure 2).

AAFCO labeling of natural-source Nova-E:
Both Nova-E and virtually all synthetic vitamin E used in animal feed are sold as stabilized α-tocopherol acetate. Supplemental vitamin E acetate may appear on a feed label in three ways:

- ***Synthetic vitamin E*** can be listed as ***dl***-α-tocopherol acetate
- ***Natural-source Nova-E*** can be listed as ***d***-α-tocopherol acetate
- ***Vitamin E supplement*** can be used for any vitamin E source over 10,000 IU per lb

AAFCO labeling and potency for Nova-E vs synthetic vitamin E: A 2X potency for natural-source vs synthetic vitamin E acetate is now recognized for humans by the Institute of Medicine (2000) and

Figure 1

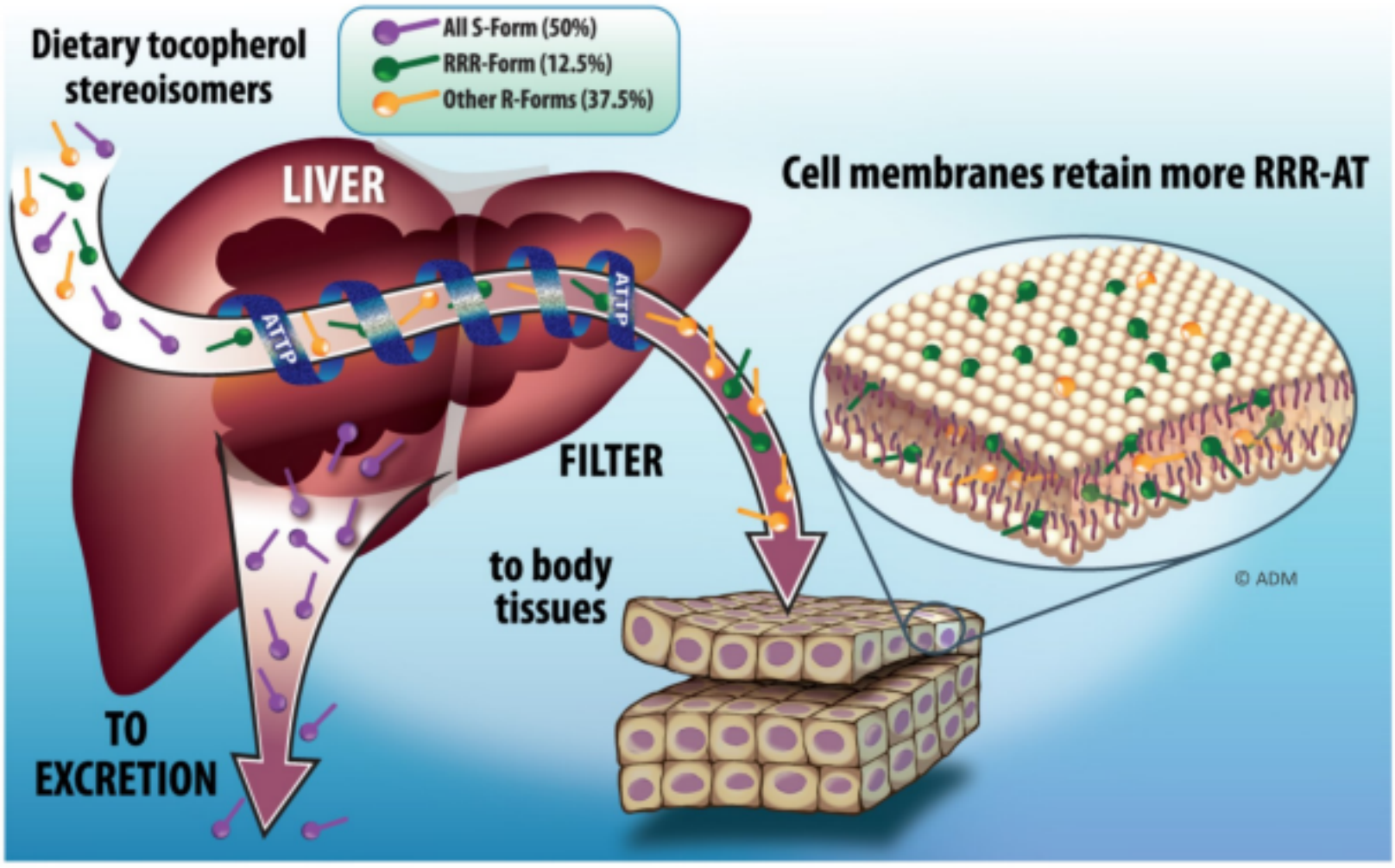
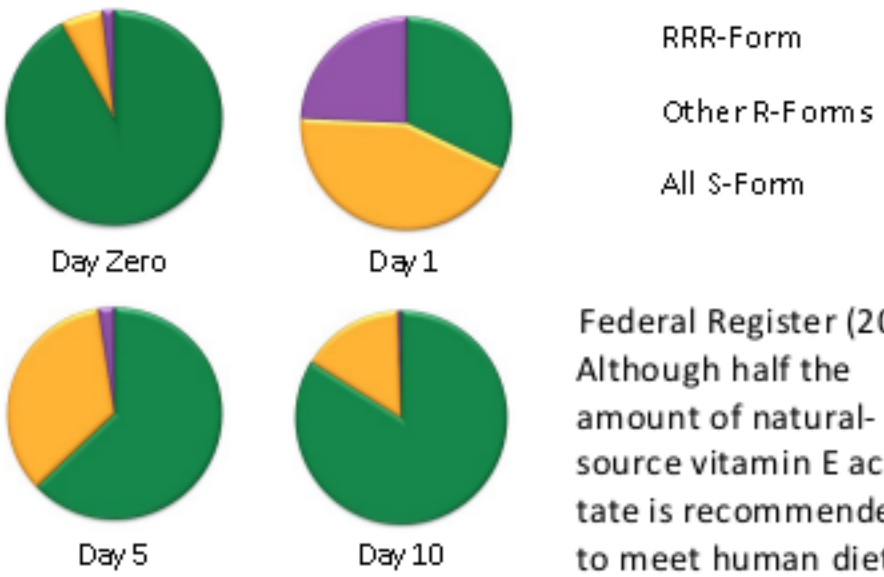


Figure 2

Blood stereoisomer distribution after injecting lactating cows with a pulse-dose of 2.5 grams of synthetic vitamin E
(Jensen, 2005)



Federal Register (2014). Although half the amount of natural-source vitamin E acetate is recommended to meet human dietary requirements, human food supplement labeling may not fully reflect this change for some time. In labeling of livestock feed, the 1.36 IU/mg potency value or natural-source vitamin E acetate is not likely to be modified by FDA/AAFCO in the foreseeable future.

All ADM Nova-E products will be labeled in IU, based on the 1.36 conversion factor. As such, blended products containing Nova-E should also be labeled accordingly. Unfortunately, all research literature references the potency of RRR-α-tocopherol acetate in terms of multiples of potency per milligram of active vitamin relative to synthetic vitamin E. To easily relate to the value proposition of Nova-E for feed usage, research-based multiples can be multiplied by 0.735 to obtain relative potency per AAFCO IU, as shown in Table 1.

- **Synthetic (dl-α-tocopherol acetate):**
  1 milligram = 1.00 IU vitamin E activity
- **Natural-source (d-α-tocopherol acetate):**
  1 milligram = 1.36 IU vitamin E activity

Practical chemical and physical attributes of Nova-E:

Dry Nova-E is a vitamin E absorbate.

Feed-grade Nova-E is dried identically to synthetic vitamin E by absorbing the active oil onto a silica gel. Physical handling is identical to synthetic vitamin E.

Nova-E has equal stability as synthetic vitamin E.

Nova-E is chemically identical to synthetic vitamin E for all aspects of shelf-life and stability and will be equal to that observed for synthetic vitamin E acetate.

Laboratories cannot differentiate Nova-E from synthetic!

Detection of differences in chiral rotation cannot be accomplished by standard AOAC laboratory methods. Standard laboratories will assume all α-tocopherol activity is synthetic vitamin E acetate and use a 1.0 multiplier. As such, vitamin laboratories must be informed of the concentration of naturally-sourced, d-α-tocopherol acetate, so that the appropriate 1.36 multiplier can be applied to the proportion of the blend that is Nova E.

Applying the value of Nova-E:

The scientific literature most often reports the relative potency of natural-source vitamin E in terms of potency ratios or "multiples" which are typically 2 to 3 times higher for natural-source than synthetic vitamin E on a milligram for milligram basis (Table 1). These multiples are largely based on blood and tissue accumulation of tocopherol in animals fed vitamin E acetate in studies where naturally-sourced or synthetic forms of vitamin E were directly compared.

Here are some general guidelines that can be used with Table 1 to apply the value of Nova E:

Using the IU shown on the label for straight products (Nova E 405, Nova E 450), Nova E will cost approximately 2.0 to 2.5 times more per IU than synthetic vitamin E.

Nova E may have slightly less value for use in creation of high tocopherol end-products, such as meat, milk, and eggs. The goal of these applications is simple accumulation of tissue tocopherol, regardless of stereoisomer form, rather than optimum animal health.

The highest value level for Nova E may be a blend with synthetic vitamin E. Tissues appear to vary greatly in their relative abilities to discriminate among the synthetic vitamin E stereoisomers. As such, a blend may be the best economic compromise between the general antioxidant roles for vitamin E stereoisomers in feed and less critical tissues and the health-critical roles for the RRR stereoisomer in tissues which exhibit a high level of discrimination against non-natural vitamin E stereoisomers.

Table 1. Predicted potency and other health value considerations for Nova-E in livestock and poultry

Possible multiples of potency for Nova-E vs synthetic vitamin E for use in formulation*

Specie	Per milligram	Per I.U. Shown on label	Criteria or references	Special applications
Poultry	2.0	1.5	Ognik and Wertelecki, 2012; Field experience	Breeders
Swine	2.5	1.8	Howard et al., 1990; Lauridsen et al., 2002; Yang et al., 2006; Shelton et al., 2014	Mulberry heart; health challenges
Dairy	3.0	2.2	Eicher et al., 1997; Hidiroglou et al., 1997; Flick, 1997; Jensen et al., 2005; Meglia et al. 2006; Weiss et al., 2009	Preweaning calves; health challenges
Beef cattle	2.5	1.8	Hidiroglou et al., 1988	Health challenges
Horses	3.5	2.6	Field experience; Pagan, 2006; Kane, 2009	Health challenges; exercise recovery; neural myopathy

*Much of the scientific literature discusses the relative potency of RRR-α-tocopherol vs synthetic vitamin E in terms of potency ratios which are typically two to three times higher (multiples) on a milligram for milligram basis. The multiples given above for different species are based primarily on blood and tissue accumulation of tocopherol in animals fed either naturally-sourced or synthetic vitamin E acetate.

Nova-E product options:

Nova-E 450 (642572AJ)	204,300 IU/lb, d-alpha-tocopheryl acetate
Nova-E 405 (642570AJ)	183,708 IU/lb, d-alpha-tocopheryl acetate
Super E 20 (79210014)	10,000 IU/lb, d-alpha-tocopheryl acetate 10,000 IU/lb, dl-alpha-tocopheryl acetate

Key References

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Product information is only applicable to domestic (U.S.) market.

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