DE NOVO CLASSIFICATION REQUEST FOR
RELIZORB™

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Enzyme Packed Cartridge: The enzyme packed cartridge is an *ex vivo* prescription device that is used in enzymatic hydrolysis of macronutrients into their essential nutrient forms at the time of delivery. The device consists of an outer casing containing an inert polymer with a covalently bound enzyme through which nutritional formula is directed. The device fits in line with enteral feeding systems.

NEW REGULATION NUMBER: 21 CFR 876.5985

CLASSIFICATION: II

PRODUCT CODE: PLQ

BACKGROUND

DEVICE NAME: RELIZORB™

SUBMISSION NUMBER: DEN150001

DATE OF DE NOVO: DECEMBER 17, 2014

CONTACT:

ALCRESTA, INC.
ONE NEWTON EXECUTIVE PARK
SUITE 202
NEWTON, MA 02462

INDICATIONS FOR USE

RELIZORB™ is indicated for use in adults to hydrolyze fats in enteral formula.

LIMITATIONS

The sale, distribution, and use of the device are restricted to prescription use in accordance with 21 CFR §801.109.

RELIZORB™ is for use with enteral feeding only. The "Feed Only" lettering on the RELIZORB™ purple outlet is there to identify that the RELIZORB™ cartridge is intended for connection to enteral feeding lines only.

Medications should not be administered through the RELIZORB™ cartridge. Do

not add medications to the enteral feed line in between the pump and RELIZORB™ (before RELIZORB™). The passage of medications through RELIZORB™ may adversely affect the medications or the ability of RELIZORB™ to hydrolyze fats.

Do not re-use RELIZORB™. RELIZORB™ is a single-use product. Re-use may result in contamination of the product. If re-used, RELIZORB™ may not effectively hydrolyze fats.

Enteral formulas containing insoluble fiber should NOT be used. Insoluble fiber may clog the RELIZORB™ cartridge.

The use of RELIZORB™ along with porcine pancreatic enzyme replacement therapy (PERT) has not been investigated. The appropriate dose and administration of PERT should be evaluated on an individual basis. Patients should continue to follow physician's guidance and PERT product labeling when used in conjunction with RELIZORB™.

The use of RELIZORB™ has not been studied in patients with exocrine pancreatic insufficiency (b) (4) RELIZORB™ has not been evaluated in pediatric populations.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS, AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The RELIZORB™ device is a point-of-care accessory designed to fit in series with currently used enteral feeding circuits. During the submission process, the device was also known as the Enteral Feeding In-Line Cartridge (EFIC). Therefore, the subject device may be referred to as EFIC in some figures within this document. RELIZORB™ is designed to hydrolyze (break down) fats present in enteral formulas from triglycerides into fatty acids and monoglycerides to allow for their absorption and utilization by the body. This breakdown of fats by the RELIZORB™ is intended to mimic the function of the enzyme lipase in patients who do not excrete sufficient levels of pancreatic lipase. The subject device is shown below in Figure 1. The RELIZORB™ is comprised of a cylindrical, hollow (b) (4) cartridge with a single inlet port and a single outlet port connection.

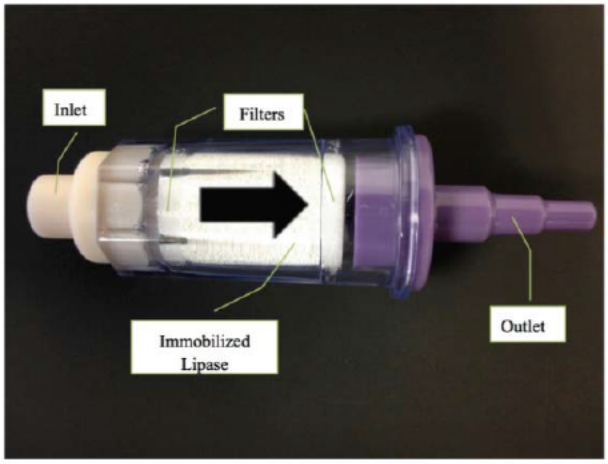

Figure 1. Photograph of the RELIZORB™ device.

RELIZORB™ is packed with polymeric beads that have lipase enzyme immobilized on the surface. This lipase enzyme is Generally Regarded as Safe (GRAS) [redacted (b) (4)]. The chemical action of the lipase enzyme is shown in Figure 2, where triglyceride molecules are broken into constituent monoglycerides and fatty acids. The food contacting substance (FCS) of the RELIZORB™ are [redacted (b) (4)] beads manufactured using [redacted (b) (4)] process. The FCS was an effective notification [redacted (b) (4)]. The lipase enzyme is chemically bound to the FCS and is intended to remain within the cartridge.

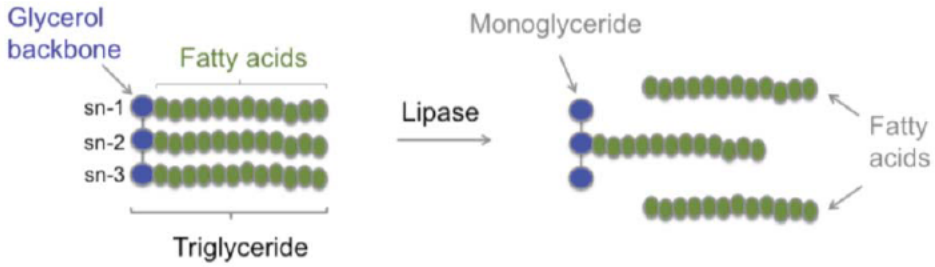

Figure 2. The lipase enzyme breaks down triglycerides into monoglycerides and fatty acids.

RELIZORB™ is an intermediary between an enteral feeding source (infusion pump) and an implanted feeding tube, as shown in Figure 3. The distal end of compatible infusion pump administration sets (Figure 3A) should have a stepped connector (Christmas tree). This connector plugs into the proximal end of the RELIZORB™ device (Figure 3B). The distal end of the RELIZORB™ (Figure 3C) connects to the enteral funnel of an extension set (Figure 3D). This extension set connects to an enteral feeding tube on the patient, such as a nasogastric or gastrostomy tube.

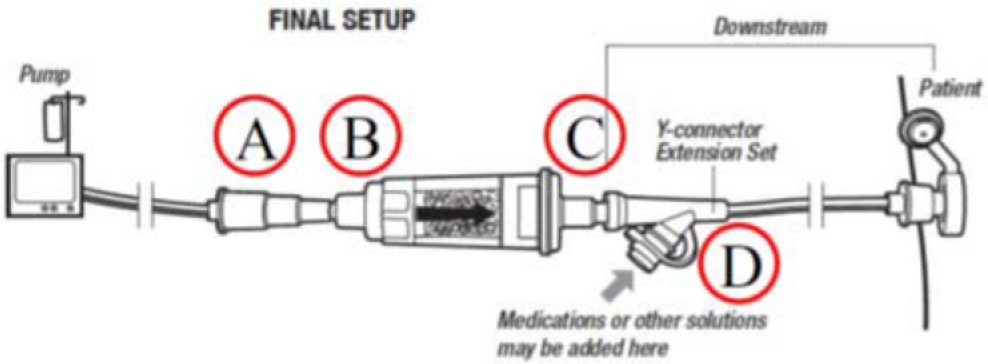

Figure 3. Illustration showing a proposed enteral feeding circuit with RELIZORB™.

SUMMARY OF NON-CLINICAL/BENCH STUDIES

Non-clinical/bench studies conducted on the RELIZORB™ to demonstrate a reasonable assurance of safety and effectiveness of the device are summarized in the sections below.

BIOCOMPATIBILITY/MATERIALS

The RELIZORB™ cartridge is constructed using a [redacted] (b) (4) housing, [redacted] (b) (4) inlet connector, [redacted] (b) (4) outlet connector, and [redacted] (b) (4) filters. The food contacting materials are the acrylic copolymer beads, lipase enzyme, and [redacted] (b) (4) stabilizer.

All materials within the RELIZORB™ have indirect contact with the patient's gastrointestinal tract. The RELIZORB™ is categorized as a permanent (>30 days) contact device that is externally communicating. The following biocompatibility testing was conducted on the final RELIZORB™ device in Table 1.

Test	Purpose	Results
Cytotoxicity – MEM Elution Test (ISO 10993-5: 2009 [redacted] (b) (4)	To assess the biological activity of L-929 mouse fibroblast cells after exposure to extracts prepared from the final RELIZORB™ device.	Non-cytotoxic
Irritation – Intracutaneous reactivity (ISO 10993-10: 2010)	To determine if extracts from the final RELIZORB™ device produce an irritation reaction when injected intracutaneously in the rabbit model.	Non-irritating
Sensitization – Guinea Pig Maximization Test (ISO 10993-10: 2010)	To determine the potential for sensitization of extracts prepared from the final RELIZORB™ device using the guinea pig animal model.	Non-sensitizing
Acute systemic toxicity (ISO 10993-11: 2010)	To determine the potential for acute systemic toxicity of extracts prepared from the final RELIZORB™ device by injections into mice.	Not systemically toxic
Genotoxicity – In Vitro Gene Mutations in Bacteria (Ames Assay, ISO 10993-3: 2003 [redacted] (b) (4))	To determine the potential mutagenic activity of extracts prepared from the final RELIZORB™ device by measuring reversion rates in bacteria.	Non-mutagenic
Genotoxicity – In Vitro Mouse Lymphoma (ISO 10993-3: 2003 [redacted] (b) (4)	To determine if extracts prepared from the final RELIZORB™ device induce forward mutations at the thymidine kinase locus.	Non-mutagenic

Test	Purpose	Results
Genotoxicity – In Vivo Mouse Micronucleus Assay (ISO 10993-3:2003 (b) (4)	To determine the potential for extracts prepared from the final RELIZORB™ device induce micronuclei formation in immature polychromatic erythrocytes in the bone marrow of mice.	Non-mutagenic

Table 1. RELIZORB™ Biocompatibility Testing.

The sponsor justified that for non-polar extractions, sesame oil would be degraded by the lipase enzyme. Because the sponsor did leachability testing on the lipase enzyme from the beads, the sponsor used a surrogate bead for non-polar extractions. This approach was deemed acceptable by FDA.

PERFORMANCE TESTING – BENCH

The sponsor conducted bench tests to demonstrate mechanical integrity, package integrity, enzyme activity, and that RELIZORB™ can be integrated into existing enteral feeding circuits. Table 2 summarizes each of the bench tests.

Test	Purpose	Acceptance Criteria	Results
Torque strength	To determine the torque necessary to separate the small bore connectors from the cartridge body at both the distal and proximal ends of RELIZORB™.	The sponsor estimated the clinical force that RELIZORB™ may encounter and built in a three-fold safety factor. The sponsor defined a passing result as a torque at separation higher (b) (4)	RELIZORB™ met the acceptance criteria for this test.
Tensile strength	To determine the force required to separate the device small bore connectors from the cartridge using a linear tensile force.	RELIZORB™ shall have a linear tensile (b) (4) break.	RELIZORB™ met the established acceptance criteria.
Air leakage test	To establish that the RELIZORB™'s material bonds would not fail or leak when challenged with pressurized air.	RELIZORB™ material bonds shall not leak when challenged with (b) (4) compressed air.	RELIZORB™ did not leak when pressurized with air. The device met the acceptance criteria.
Filter integrity	To ensure that the FCS/enzyme beads are retained within the cartridge. The sponsor connected RELIZORB™ to an enteral feeding circuit and subjected the device to the maximum pump flow rate for five minutes. The sponsor conducted this test in both a forward and	RELIZORB™ should not allow for beads (b) (4) to pass the filter and leave the cartridge.	RELIZORB™ allowed for five particles to leave the cartridge in three repetitions in the forward flow direction. RELIZORB™ allowed one particle to exit the cartridge in the reverse flow direction. Out of these six particles, only one had a diameter (b) (4) The sponsor investigated the

Test	Purpose	Acceptance Criteria	Results
	reverse flow orientation The sponsor collected any potential escaped particles during this test using a (b) (4) filter.		source of this particle using spectroscopy and concluded that it was a contamination from their testing laboratory. The Agency reviewed the sponsor's data and agrees with their justification. Because the sponsor did observe some particles exiting the cartridge, FDA considered clinical or toxicological adverse events resulting from escaped particles. A clinical assessment determined that so few escaped beads would likely pass in a patient's stool. Additionally, the sponsor submitted acceptable biocompatibility data and the FCS-enzyme complex are acceptable for use in foods. Based on these assessments, this is an acceptable result.
Fat hydrolysis	Using a simulated enteral circuit, this test is to determine the amount of free fatty acids (FFA) that RELIZORB™ produces by enzymatic hydrolysis. The sponsor used a commercially available colorimetric assay to determine the amount of free fatty acids produced by RELIZORB™ after simulated use.	RELIZORB™ should produce (b) (4) FFA per serving.	The sponsor submitted bench testing data demonstrating that RELIZORB™ breaks down ≈90% of fats in most enteral formulas. The sponsor added these results to their labeling. This is an acceptable result.
Unconjugated lipase analysis	The sponsor evaluated the potential leaching of the lipase enzyme from the beads. The sponsor extracted the beads for (b) (4) at room temperature.	There were no formal acceptance criteria for this test. The sponsor measured the lipase concentration using a (b) (4)	Using several lots, the sponsor observed (b) (4) leaching by the BCA assay and (b) (4) leaching by absorbance. Based on the biocompatibility testing and the GRAS status of lipase, there are no safety concerns with this small amount of enzyme released.
Assessment of impact to other nutrients	Using simulated use conditions, the sponsor flowed enteral formula through their device. The sponsor analyzed	There were no formal acceptance criteria for this bench test. The sponsor conducted a nutritional analysis of	After exposure to RELIZORB™, there was no meaningful difference for any vitamins or minerals. This is an acceptable result.

Test	Purpose	Acceptance Criteria	Results
	nutritional components such as vitamins and minerals to ensure that RELIZORB™ does not adversely affect other nutrients in enteral formula.	vitamins and minerals.	
Flow rate	The sponsor conducted this test to ensure that RELIZORB™ does not restrict the flow of formula using an enteral feeding pump.	The presence of RELIZORB™ in an enteral feeding circuit should not affect the flow rate of formula.	There were no statistical differences between the flow rate with or without RELIZORB™ in the enteral feeding line. This result is acceptable.
Liquid leakage test	After simulated feeding, the sponsor inspected material joints to determine if the device leaked during priming or flow rate testing.	RELIZORB™ should not leak under normal and worst-case conditions.	The sponsor used two formulas and two different enteral feeding pumps. In all cases, the sponsor did not observe any leaking from any material joints.
Pump alarm verification	After performing flow rate testing, the sponsor kinked the tubing while the pump was in run mode to verify that the flow error alarm works both before and after RELIZORB™.	RELIZORB™ shall not cause pump alarm failure.	The sponsor verified that the flow alarm sounds if the tubing becomes occluded before or after the RELIZORB™. This is an acceptable result.

Table 2. RELIZORB™ Bench Testing.

In accordance with the recommendations outlined in the guidance document "Safety Considerations to Mitigate the Risks of Misconnections with Small-bore Connectors Intended for Enteral Applications," mechanical misconnection testing was conducted and a warning is included in the labeling to reduce the risk of misconnection.

SHELF LIFE/STERILITY

RELIZORB™ is provided non-sterile in a foil package. RELIZORB™ is a single use only device that is disposed of after each use. The identified shelf life for RELIZORB™ is six months. (b) (4) . (b) (4)

In support of the six-month shelf life, the sponsor completed several tests using real-time aged devices after simulated shipping. The shelf life tests have identical acceptance criteria to those identified in the Performance Testing – Bench section.

- Fat hydrolysis
- Tensile strength
- Filter integrity
- Flow rate
- Package integrity
    - Visual inspection

- Peel strength (ASTM F88)
- Bubble leak test (ASTM F2096)

The sponsor reported fat hydrolysis conversions that were in agreement with their baseline data:

	TwoCal HN	Peptamen
t=0	51%	85%
t=1 month	44%	89%
t=3 months	49%	84%
t=6 months	47%	92%

Table 3. Fat hydrolysis results (% conversion of fats).

Because there was no meaningful difference between the baseline and aged product, the Agency determined that the fat hydrolysis results were acceptable. The tensile strength, filter integrity, and flow rate were not compromised after aging. After simulated shipping, the clean barrier for the RELIZORB™ was not compromised. The six-month shelf life is acceptable.

PERFORMANCE TESTING – ANIMAL

The sponsor completed four animal tests using exocrine pancreatic insufficient (b) (4) (b) (4) pig models. (b) (4) The four animal studies are summarized below.

1. Chronic Porcine Study

Protocol

The purpose of this study was to determine if the absorption of long-chain polyunsaturated fatty acids (LCPUFAs) is enhanced when formulas were pre-hydrolyzed with soluble microbial lipase. (b) (4)

The pigs were monitored for a reduction of total and PUFA fecal fats, and change in coefficient of fat absorption (% CFA). The pigs were also monitored for an increase in arachidonic acid (AA) and docosahexaenoic acid (DHA) in plasma and tissues such as the liver, retina, heart, and fat. This result is consistent with increased absorption of LCPUFAs. After the study endpoint, the sponsor performed necropsy of study animals to harvest specified tissues, such as the liver, retina, heart, fat, red blood cells, hippocampus, cerebellum, and brain cortex.

Results

There were no adverse clinical effects or pathologic macroscopic findings in the gut or liver after seven days of administration. Both the RO and CV pre-hydrolyzed formulas increased the absorption of LCPUFA as reflected by reduced total stool fat, fecal AA, and DHA. The sponsor included a summary showing the %CFA for the control and treated groups. The sponsor's data supports their conclusion that the enriched diets enhanced fat absorption with an improvement in %CFA of 20-30% in comparison to controls.

WEEK	CFA% (MEAN ± SD)		
	CONTROL	CV LIPASE	RO LIPASE
CONTROL	66.5±7.8	51.7±14.3	76.9±1.9
TREATMENT	67±5.8	86.6±4.3*	87.1±3.5*
P value		0.002	0.003

Shown is a mean (± SD) CFA values during Control and Treatment weeks for Control, CV and RO groups. Difference was consider significant *p<0.05 for comparison between Control and CV and RO groups during treatment week, n=3/arm

Table 4. Mean of 24 hour %CFA during 3 consecutive days (Study 1).

2. Chronic Porcine Study

Protocol

The sponsor tested the safety and effectiveness of continuous feeding of the RO lipase enzyme in the (b) (4) porcine model over six weeks. The sponsor used the same lipase bound beads that are packed into the final device in this study. (b) (4) During the study, the sponsor measured total and PUFA fecal fats, %CFA, and AA and DHA levels in both plasma and tissue. At study termination, the sponsor completed a gross postmortem examination of tissue and a blinded GLP histopathology examination.

Results

The sponsor reported food intake and body weight of all pigs. The formula intake and body weight were the same for all (b) (4) pigs. In contrast, the (b) (4) control pigs grew 2-4 kg per week. The sponsor observed a 38% and 53% reduction in omega-3 and omega-6 fecal LCPUFA in (b) (4) pigs treated with the RO enzyme. Similarly, the sponsor reported a 66% and 50% respective reduction in fecal AA and DHA levels for (b) (4) pigs treated with RO enzyme. These data suggest that the inability for (b) (4) pigs to absorb fat was reversed by feeding with pre-hydrolyzed formula treated with the lipase enzyme. Additionally, the pigs fed a pre-hydrolyzed diet had a more normalized blood lipid profile, improved consumption of LCPUFA, and improved Vitamins A and E absorption.

The sponsor harvested the cranial alimentary, GI tract, and the liver to send the samples for a blinded, GLP histopathology examination. The sponsor included analyses on the tongue, esophagus, stomach, small intestines, large intestines, liver,

and liver fat. The pathologist found no safety signals relative to the consumption of the lipase enzyme. The pathologist had the following observations:

- Increased periportal fat in the liver (all study animals).
- Inflammatory lesions in the liver, stomach, and tongue of (b) (4) animals, but not healthy control animals.
- An increase in distribution and severity of inflammatory lesions in EPI animals compared to healthy control animals.

The sponsor's findings seemed related to the pigs' (b) (4) status and not the (b) (4) treatment group. Some of the findings showed milder and less frequent issues in the treatment (b) (4) animals in comparison to (b) (4) controls. The observations noted in the (b) (4) treatment group were not related to the treatment itself and were of low incidence. The histopathological examination followed GLP regulations and was complete. Because the pathologist's findings were also peer reviewed, this study supported the accuracy of the sponsor's conclusions.

3. 12 Day Efficacy study with Gastrostomy Tube Feeding

Protocol

The sponsor conducted a simulated use study of RELIZORB™. The sponsor did nightly gastrostomy tube feeding over 12 days in the (b) (4) porcine model. (b) (4) During the last three days of the study, the sponsor collected two 24 hour stool and urine samples. On the last day after overnight fasting, the sponsor collected blood samples for protein and fat profiles, as well as DHA and eicosapentaenoic acid (EPA) measurements.

Results

The sponsor did not report any adverse events during this study. While the food intake between (b) (4) control and (b) (4) treatment pigs was similar, the sponsor reported a statistically significant decrease in the stool weight for the treatment group ($p=0.014$). The sponsor reported a statistically significant increase in %CFA, as shown in Figure 4.

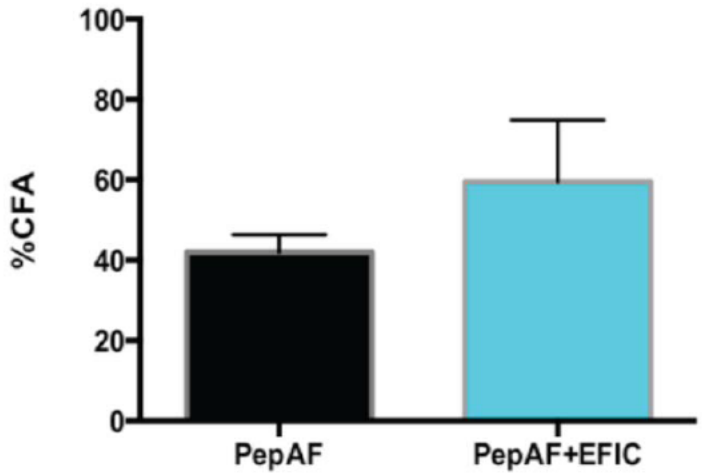

Figure 4. Improved fat absorption expressed as %CFA for EFIC/RELIZORB™ (p=0.036, Study 3).

4. **24 Hour Pharmacodynamics Study**

Protocol

The sponsor conducted a 24 hour, randomized, cross-over study in 11 pigs to assess the pharmacodynamics of gastrostomy tube feeding using a prototype of the RELIZORB™ device through a gastrostomy tube. While the sponsor used a device prototype for the treatment arm, this prototype was nearly identical in form and function to the finished device. (b) (4) The sponsor collected baseline samples and at several time points after tube feeding began. (b) (4)

Results

Due to the short study duration, food consumption and body weight were not endpoints. The sponsor reported a statistically significant improvement in fat absorption in the treatment arm in comparison to the control. The plasma omega-3 fat (DHA and EPA) concentrations over 24 hours are shown in Figure 5. The sponsor reported a statistically significant ($p < 0.05$) increase in plasma omega-3 fats when using RELIZORB™ in comparison to formula that was not pre-hydrolyzed with RELIZORB™.

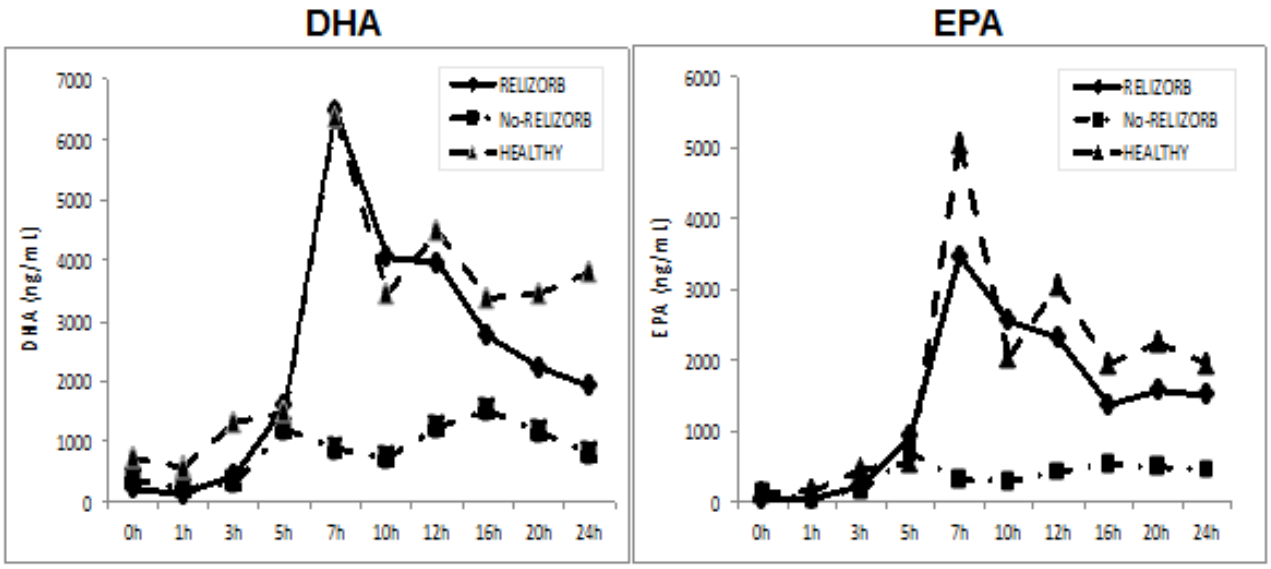

Figure 5. Plasma DHA and EPA concentration over 24h period after single administration of hydrolyzed formula (500 mL) using RELIZORB™ in a porcine model of exocrine pancreatic insufficiency(b) (4)

The sponsor completed a proof of concept (Study 1), safety (Study 2), and a simulated use study (Study 3) using the same enzyme as the finished device. These studies demonstrated safety using the enzyme and simulated use conditions. The sponsor demonstrated improvements in fat absorption and Vitamins D and E absorption in these studies. The sponsor also observed increased concentrations of LCPUFAs in several organs after the studies were completed. The Agency expects these results would also be seen in humans using pre-hydrolyzed formula due to the nutritional benefits observed from fat hydrolysis in the literature.

HUMAN FACTORS TESTING

The sponsor conducted a human factors summative protocol in the submission. This study evaluated both the clinical care setting with trained operators and the home care setting with lay users. The sponsor conducted a subjective assessment on the performance of the critical tasks. The sponsor noted clinician errors after they neglected to change the device after one feeding session versus institutional policies that change feeding sets after 24 hours. This resulted in an update to the directions for use with a precaution that the device is for single use only. Based on the low risk of injury to the patient, the Agency determined that the sponsor's human factors activities are adequate.

LABELING

The sponsor provided labeling that includes the physician's instructions for use, patient guide, and package labels for the RELIZORB™.

The labeling is acceptable and meets the requirements of 21 CFR §801.109 for prescription devices. The patient guide also follows the principles identified in the FDA Guidance Document *Medical Device Patient Labeling.*

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of Enzyme Packed Cartridges and the measures necessary to mitigate these risks.

Identified Risk	Mitigation Measure
Adverse tissue reaction	• Biocompatibility testing • Non-clinical testing • *In vivo* testing • Labeling
Mechanical failure - Deprivation of care - Device clogging - Filter becomes dislodged and releases beads into enteral formula	• Non-clinical testing • Shelf life testing • Labeling
Reduced enzymatic effect	• Non-clinical testing • *In vivo* testing • Shelf life testing • Labeling
Use error	• Human factors testing • Labeling
Infection	• Shelf life testing • Labeling

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the Enzyme Packed Cartridge is subject to the following special controls:

1. The patient contacting components of the device must be demonstrated to be biocompatible.

2. *In vivo* testing must be performed and must demonstrate that the device causes neither an adverse tissue response nor adverse performance.

3. Non-clinical testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be demonstrated:

   (A). Mechanical testing to demonstrate that the device can withstand clinical forces.
   (B). Flow rate and leakage testing to demonstrate that the device does not impede the flow of enteral formula.
   (C). Demonstration of enzymatic effect on intended macronutrient.
   (D). The amount of enzyme that exits the cartridge must be characterized.
   (E). Validation that the device does not adversely impact the nutritional composition of enteral formula.

(F). Validation that the device does not impede flow alarms on enteral feeding pumps.

4. Human factors testing must be performed to characterize use error risks.

5. Performance data must support shelf life by demonstrating package integrity and device functionality over the identified shelf life.

6. Labeling must include the following:

   (A). A detailed summary of *in vivo* testing pertinent to use of the device, including device-related adverse events.
   (B). A detailed summary of compatible formulas that is supported by non-clinical testing, including the expected enzymatic conversion as a percentage.
   (C). Detailed instructions on how to place the device into an enteral feeding circuit.
   (D). A warning regarding the possibility for misconnections.
   (E). Expiration date or shelf life.

7. Patient labeling must be provided and must include:

   (A). Relevant warnings, precautions, adverse effects, and complications.
   (B). A description of the device and how it operates.
   (C). Instructions on how to correctly use the device.
   (D). The benefits and risks associated with the use of the device.

BENEFIT/RISK DETERMINATION

The observed risks of the device are based on the animal studies described above. The sponsor did not include any clinical data. The sponsor presented safety data from four different porcine studies. The sponsor did not observe any adverse events in their animal studies. Since the sponsor's small bore connector is based on a legacy design, there is a risk for misconnection with devices from other healthcare applications.

The observed probable benefits of the device are also based on nonclinical laboratory and animal study data as described above. The sponsor demonstrated in laboratory testing that the device was able to hydrolyze >90% of fat in most enteral formulas. The four preclinical animal studies appeared to provide benefit to pigs displaying clinical signs of exocrine pancreatic insufficiency (b) (4) when fed a diet pre-hydrolyzed by the lipase enzyme manually or through the RELIZORB™ device. In their animal studies, the sponsor demonstrated that treating (b) (4) pigs using RELIZORB™ led to increases in total fat absorption, improved update of omega-3 fatty acids in plasma, and improved Vitamin D and E levels. FDA expects these benefits would also be seen using pre-hydrolyzed formula due to the nutritional benefits observed from fat hydrolysis in the literature.

Additional factors to be considered in determining probable risks and benefits for the RELIZORB™ include:

- The cumulative data from the animal studies were robust. They were designed logically, systematically, and built on each other. The first two studies did not use the device. The

pigs in the first study were fed soluble lipase enzyme, while the second study used the beads bound with lipase in a mesh bag. The final two studies used a device prototype that was functionally equivalent to the final device.

- Study 2 had a safety endpoint and the histopathology was conducted at a GLP pathology lab under blinded conditions. Study results were peer-reviewed prior to release of final study report.
- Study 4 was a randomized, blinded, cross-over study.
- Patients can have abdominal cramps, steatorrhea (loose, greasy, foul-smelling voluminous stools), and malnutrition with weight loss. The condition is currently treated with oral administration of pancreatic enzyme replacement therapy tablets (PERTs).
- Human factors testing and clear labeling help mitigate risks.
- The device is beneficial because no enteral formulas currently contain pre-hydrolyzed fat.

In conclusion, given the available information above, the data support that the probable benefits for the RELIZORB™ device to hydrolyze fats in enteral formula outweigh the probable risks. The device provides probable benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The De Novo request for the RELIZORB™ is granted and the device is classified under the following:

Product Code:	PLQ
Device Type:	Enzyme Packed Cartridge
Class:	II
Regulation:	21 CFR 876.5985