ClinicalTrials.gov ID: NCT04342689

Last Approved: 6/22/2020

Document: Protocol w SAP

HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
(2017-1)

Protocol Title: The Role of Resistant Potato Starch in COVID-19 Infection

Principal Investigator: Sherry Mansour, MD, MS (PI)

Version Date: 4-22-2020

Clinicaltrials.gov Registration #: NCT 04342689

Study Intervention: Potato-based dietary starch; Bob's Red Mill®

Clinicaltrials.gov registration #: NCT 04342689 **pre-assigned IND:** 149839, FDA exempt us from IND regulations with an IND Discretion Enforcement in place.

Multicenter: University of Michigan (Mary M. Riwes)

INSTRUCTIONS

This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:**

1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library.

2. If a section or question does not apply to your research study, type "Not Applicable" underneath.

3. Once completed, upload your protocol in the "Basic Information" screen in IRES IRB system.

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SECTION I: RESEARCH PLAN

Section 1. Statement of Purpose: State the scientific aim(s) of the study, or the hypotheses to be tested.
The coronavirus disease-19 (COVID-19) pandemic has caused significant distress, and grief around the world. Given the rising numbers of infected individuals in the United States (US) and need for hospitalization in at least 14% of infected patients (1), there is substantial strain on the health care system. Identifying ways to ameliorate the progression and severity of this infection and preventing hospitalization is critical in preventing break in capacity and overwhelming the healthcare system.
Currently, it is believed that COVID-19 infected patients undergo two phases of illness; viral replication and the more fatal phase of inflammation. Preventing the inflammatory phase has the potential to decrease hospitalization, use of ventilation and mortality. Accordingly, we are proposing to identify the role of resistant potato starch (a natural dietary supplement) in preventing the progression to the inflammatory phase through its immunomodulatory effects on the gut microbiome.
To enhance generalizability, we have designed a multicenter study in varying geographical regions within the US, involving patients who tested positive and are not in need of hospitalization. Using a randomized phase III clinical trial design, we will enroll 1500 COVID-19 positive patients who are not hospitalized, to be randomized to receiving 2 tablespoons (~20 grams) of resistant potato starch (RPS) twice daily for 14 days vs. placebo (2 tablespoons of non-resistant, digestible starch twice daily). We will evaluate the relationship between RPS and the primary outcome of hospitalization and the secondary outcomes of time to clinical recovery (TTCR) defined as return to normal body temperature, and alleviation of major presenting symptoms (myalgia, cough, shortness of breath, and GI symptoms) maintained for 72 hours and peak symptom severity score adapted from the influenza literature (2).
The dietary starch produced by Bob's Red Mill® is a commercially available low-digestible carbohydrate. It is entirely plant based and not genetically modified. It is gluten free. Potato-based starch contains 40 calories per 12 grams and no additional dietary nutrients, vitamins or sodium (labeling information). Corn-based starch contains 30 calories per 8 grams and no additional nutrients, vitamins or sodium (labeling information).
Starch has been well studied within the dietary and nutritional literature and has been demonstrated safe. (3-5). In addition, it has previously been administered to healthy human volunteers at the University of Michigan as part of HUM00118951 and HUM00094242– Linking the Structure and Function of the Gut Microbiome. These studies have revealed minimal adverse events and no serious adverse events in these subjects.
Moreover, it is being administered to allogeneic hematopoietic cell transplant (allo HCT) patients at the University of Michigan as part of HUM00112318 under IND 132208- Dietary manipulation of the microbiome-metabolomic axis for mitigating graft versus host disease (GVHD) in allo HCT patients. This study has revealed minimal adverse events and no serious adverse events in these subjects.
Probable Duration of Project: State the expected duration of the project, including all follow-up and data analysis activities. We anticipate a 12-month study duration, whereby the first six months will focus on RPS administration and data collection and the remaining six months on analysis and manuscript generation.

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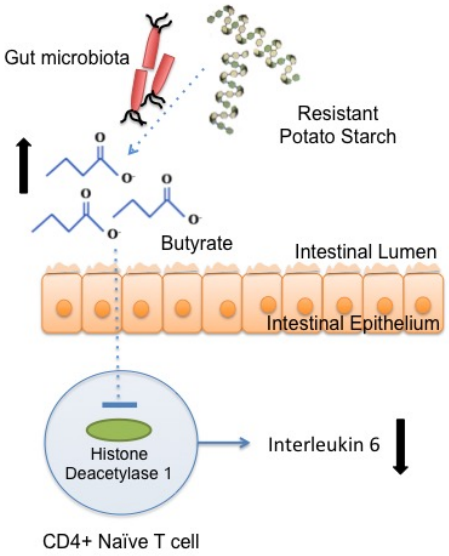
Section 2. Background: Patients suffering from COVID-19 have been shown to have significant inflammation resembling cytokine release syndrome (CRS) (6). It is thought that this inflammatory phase persisting even after viral suppression is what leads to the more fatal phase of COVID-19.(7,8). One of the most commonly elevated markers in COVID-19 patients has been shown to be interleukin (IL)-6.(6,7). To this effect an IL-6 inhibitor known as Tocilizumab, usually used in the treatment of inflammatory conditions including CRS, has been used to help modulate and reduce this exaggerated inflammatory response in COVID-19 patients (9). Tocilizumab is mainly used and studied in hospitalized patients who are showing signs of increased inflammation, but more research on interventions to slow the onset of inflammation and decrease hospitalizations in COVID-19 patients is needed. **Towards this effort, we propose to study the effects of RPS on the rate of hospitalizations in COVID-19 patients who have not yet required hospitalization. Decreasing hospitalization rates is vital in preventing the current burden on our healthcare system and will minimize exposure of healthcare workers to this highly infectious disease.** The rationale for using RPS to mitigate COVID-19 hospitalizations is based on the ability of resistant starch to decrease IL-6 in humans (**Figure 1**).(10,11). Furthermore, others, as well as our group. have shown that resistant starch increases butyrate levels (12-14), which in turn has been shown to reduce IL-6 production and overall inflammation (15). Additionally butyrate has also been shown to specifically decrease lung inflammation in animal models by suppressing inflammatory cytokine production (**Figure 2**) (16-20). As butyrate is produced in higher amounts in the gastrointestinal tract, it can be absorbed into the bloodstream and has been shown to have significant amelioration of lower respiratory infections and inflammation in humans (21). It has also been postulated that butyrate decreases Angiotensin Converting Enzyme 2 (ACE2) receptor expression, which is the main entry mechanism for COVID-19 into epithelial lung cells (16-19). Our preliminary data shows that within one week of being on RPS therapy (~20 grams twice daily), participants' stool butyrate levels increases (14). As RPS is a commonly used nutritional supplement, often used in gluten free cooking and baking, it offers minimal risk to participants in this proposed work. Furthermore, we have encountered only minimal adverse events and no serious adverse events from its use in our preliminary data in allo HCT patients (HUM00112318 under IND 132208) (14). Hence, we propose to enroll 1500 COVID-19 positive patients, who are being monitored in the outpatient setting, to receive 2 tablespoons (~ 20 grams) of RPS twice daily for 14 days vs. placebo to test **our hypothesis that RPS will reduce rate of hospitalization in COVID-19 patients**. Our primary outcome of interest will be rate of hospitalization for COVID-19 related complications and our secondary outcomes will be TTCR and symptom severity score (2). If our hypothesis is proven, this simple, minimal risk intervention, will have the potential to reduce healthcare burden and improve patient outcomes.

Figure 1. Schematic of the effect of RPS on lowering IL-6



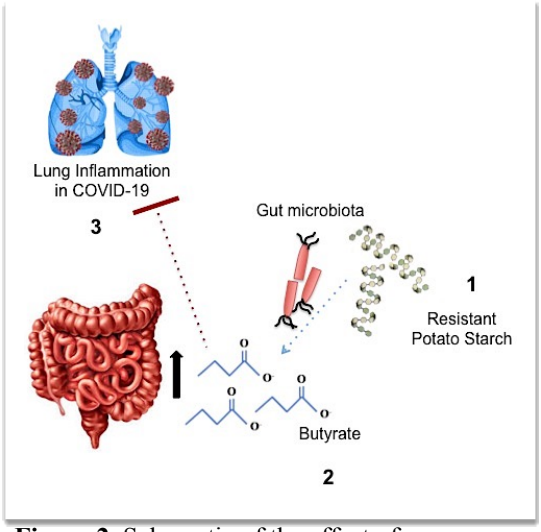


Figure 2. Schematic of the effect of RPS on lung inflammation

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Section 3. Preliminary Data

•RPS is potent at increasing butyrate levels in stool of healthy humans, compared to other forms of dietary resistant starch. Published data showed that administration of defined quantities of RPS induces production of butyrate from the microbiota in 20 healthy volunteers (12) (**Figure 3**).

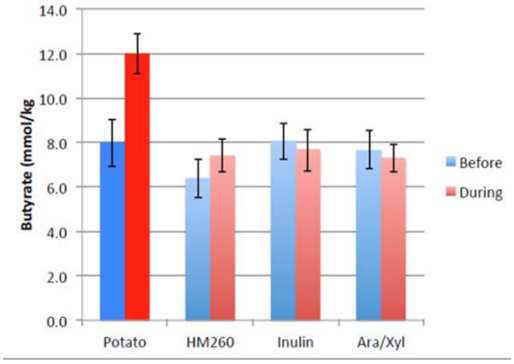

Figure 3. *Fecal butyrate levels before (blue) and after (red) RPS ("Potato") or other commercially available dietary resistant starch preparations*

•RPS alters stool butyrate levels in allo HCT patients. Our published preliminary data showed that administration of RPS in a pilot study increased stool butyrate levels in allo HCT recipients (14) (**Figure 4**).

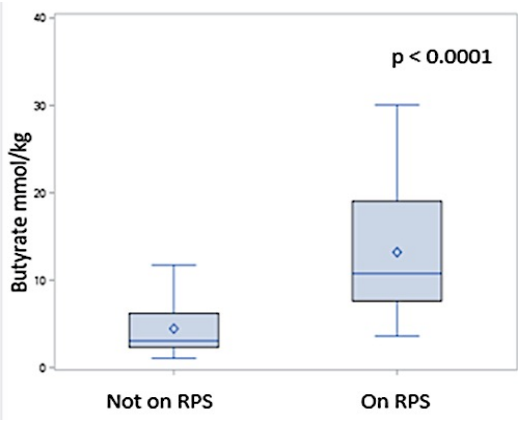

Figure 4. *Effect of RPS on allo HCT recipients' stool butyrate levels.*

•Butyrate inhibits IL-6. Human endothelial cells pretreated with butyrate and then stimulated with lipopolysaccharide (LPS) and tumor necrosis factor-alpha (TNF-α) had significant reductions in IL-6 compared to endothelial cells without butyrate pretreatmet (15) (**Figure 5**).

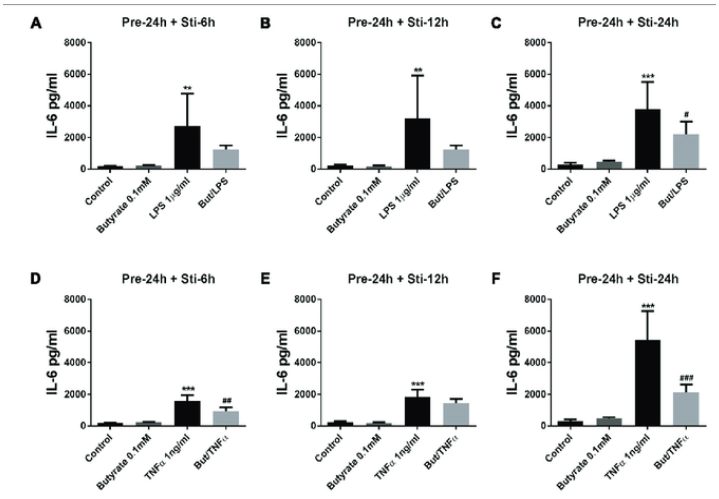

Figure 5. *Effects of butyrate on IL-6 release.* ***(A–F)*** *The effects of butyrate on IL-6 release with 24 h pre-incubation and 6, 12, or 24 h stimulation.* ***(A–C)*** *Butyrate combined with LPS.* ***(D–F)*** *Butyrate combined with TNFα. N = 4, $^{**}p < 0.01$, $^{***}p < 0.001$ compared with control group. $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ compared with LPS or TNFα group.*

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•**Butyrate is associated with less viral lower respiratory tract infections.** Increased abundance of butyrate producers in the intestinal microbiome (which is correlated with higher stool butyrate levels) was associated with less viral lower respiratory tract infections in allo HCT recipients (21) (**Figure 6**)

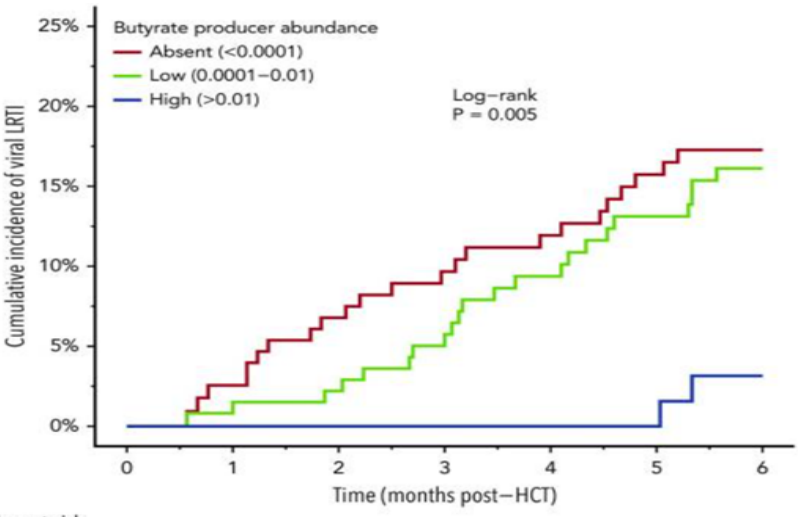


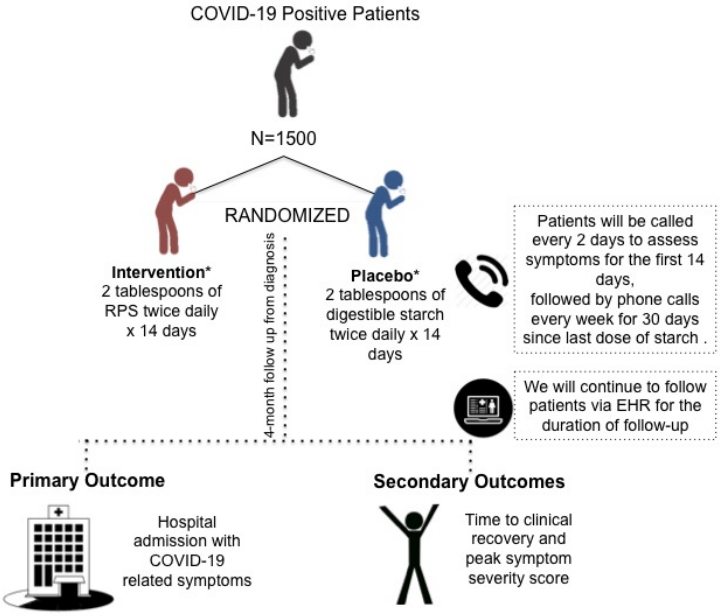
***Figure 6**. Increased butyrate producers are associated with reduction in viral lower respiratory tract infections*

Section 4. Research Plan:

Study Design.

This is a multicenter phase III randomized, placebo controlled, double blinded, clinical trial enrolling 1500 COVID-19 positive patients who are being managed as outpatients to investigate the role of RPS in incident hospitalization after COVID-19 diagnosis as well as the secondary outcomes of TTCR and symptom severity score. Participants will be enrolled from multiple sites. Patients will be identified via Electronic Health Record (EHR) using a real time compiled list of COVID-19 positive patients at University of Michigan, and will similarly be identified via an EHR compiled list at other sites. Initial screening will be conducted via review of the EHR and will be followed up by a telephone call to obtain informed consent and to confirm inclusion and exclusion criteria (**Table 1**). If subjects agree to participate in the study via phone and meet the inclusion criteria, an informed consent document will be sent to patients electronically for subjects to sign digitally via SignNow. Upon receipt of subject's informed consent documentation with approval to participate in our study, pre-packaged Bob's Red Mill® RPS vs. pre-packaged placebo consisting of iso-caloric digestible Bob's Red Mill® corn starch (non-resistant starch) will be delivered to their home, with printed instructions (**see**

***Figure 7.** Trial Design*



attached instructions) on how to take the RPS or placebo for the duration of the trial. Patients will be asked to take 2 tablespoons (~20 grams) of RPS in water or juice or applesauce (any cool substance to make it palatable) twice daily for 14 days with the same instructions for the placebo arm. Patients will be called every 2 days while taking RPS to assess symptoms and adverse events via a pre-specified questionnaire (**see attached questionnaire**) for the first 14 days and then will be called weekly until 30 days after the last dose of treatment. Patients are then followed via EHR to complete the 4-months follow up from the time of diagnosis (ie. COVID test positive) **(Figure 7**). Of note, the placebo will be identical in appearance and packaging as the RPS. Both food ingredients, placebo and RPS, are isocaloric (approximately 140 calories per day from either food ingredient). The placebo has been safely used as a control in human clinical trials (NCT 02763033, NCT01939600, NCT01708694).

Inclusion and Exclusion Criteria:

Table 1. Inclusion and Exclusion criteria:

Inclusion criteria	Participants >18 years of age with COVID-19 positive status who are monitored in the outpatient setting and are English speaking.
Exclusion criteria	Inflammatory bowel disease, history of gastric bypass surgery, active Clostridium difficile infection, active participation in another COVID-19 intervention trial, any physical or psychological condition that, in the opinion of the investigator, would pose unacceptable risk to the patient or raise concern that the patient would not comply with protocol procedures. We will also exclude reported allergy to potato starch or corn starch or difficulty swallowing in order to prevent any aspiration risk or anyone on IL-6 inhibitors (such as Tocilizumab)

Primary Objectives

-To assess the effect of RPS on hospitalization rates in COVID-19 infection

Primary Outcome Measure:

Hospitalization for a COVID-19 related admission during the first month of follow up.

A COVID-19 related admission is defined as the following:

•Presenting symptoms of fever or shortness of breath or myalgia or cough or hypoxia.

•Admission diagnosis of hypoxic respiratory failure, pneumonia, vial pneumonia.

•Death prior to hospitalization thought to be secondary to COVID-19 will also be defined as an event.

All hospital admissions will be reviewed and adjudicated by site PI to ensure that the hospitalization is a COVID-19 related admission.

Secondary Objectives

-To access the effect of RPS on time to clinical recovery (TTCR)

Secondary Outcome Measure:

TTCR will be defined as a return to normal body temperature to 97°F -99°F as reported by the patient, and resolution of any major presenting symptoms (myalgia, cough, shortness of breath, GI symptoms) maintained for 72 hours.

-To assess the effect of RPS on symptom severity score

Secondary Outcome Measure:

Symptom severity score (2): This will be evaluated using a subjective self-reporting questionnaire (see section 15: Appendices) around eight symptoms, which include:

1) Shortness of breath at rest or on exertion
2) Fatigue
3) Myalgia/ muscle aches
4) Feverishness
5) Cough
6) Headaches
7) GI symptoms
8) Inability to taste or smell

Participants will rate each of their symptoms on an ordinal scale as follows:

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absent (0), mild (1), moderate (2), or severe (3). These symptom ratings will be added to define the symptom severity score with a possible score range of 0–24 points.
Inquiry regarding symptom severity score will take place during phone questionnaires with patients performed Q2 days for 14 days from start of treatment then weekly until 30 days from last dose of treatment.

Exploratory Objectives
To understand whether RPS has an effect on Emergency Room (ER) visits without admission.
Among those who end up hospitalized, we will explore whether RPS has an effect on:
1. Oxygen requirement
2. Need for mechanical ventilation
3. Duration of ventilation
4. Length of hospital stay
5. Levels of inflammatory markers routinely ordered as part of clinical care (CRP, LDH, D-dimer, Ferritin, Il-6)
6. Rates of discharge

SUBJECT ELIGIBILITY
Subjects must meet all of the selection criteria to be enrolled to the study. Study treatment may not begin until a subject has been consented and meets the eligibility criteria.

Inclusion Criteria (please also refer to **Table 1**)
Participants >18 years of age with who are:
1. COVID-19 test positive status
2. Monitored in the outpatient setting

Exclusion Criteria
1. Inflammatory bowel disease
2. History of gastric bypass
3. Active Clostridium difficile infection
4. Active participation in another COVID-19 intervention trial
5. Any physical or psychological condition that, in the opinion of the investigator, would pose unacceptable risk to the patient or raise concern that the patient would not comply with protocol procedures
6. Reported allergy to potato-based starch or corn-based starch
7. Difficulty swallowing in order to prevent any aspiration risk
8. Currently taking any IL-6 inhibitors such as Tocilizumab for any disease condition

SUBJECT SCREENING, ENROLMENT, AND RECRUITMENT
This study will be conducted at multiple sites. Patients >18 years of age with COVID-19 positive status and who are being monitored in the outpatient setting will be approached by phone. IRB-approved informed consent must be obtained from patients prior to the initiation of treatment on this protocol. After informed consent is obtained and prior to the initiation of protocol therapy, all patients satisfying the inclusion/exclusion criteria must have eligibility confirmed by the PI or Co-I of the study team at each site. The patient will not be considered enrolled in the study until all information is confirmed by the PI or Co-I.
Screen Failures
Participants who are consented to participate in the clinical trial, who do not meet one or more criteria required for participation in the trial during the screening procedures, are considered screen failures. Screen failures will not be re-screened.
Randomization
We will use stratified (by site) permuted block randomization and will generate randomization lists to be sent to the investigational pharmacy for packaging of starch and delivery to the designated participants.
Blinding
The study will be double blinded to patients and investigators. The study team will include investigational pharmacists who will package the intervention RPS and placebo starch into packages labeled per FDA guidelines,

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and will not share the labeling key code with any of the other study members who are performing the study. Labeling will also comply with labeling regulations under 21 CFR 312.6. As aforementioned in section 4.2 above, we will use stratified (by site) permuted block randomization and will generate randomization lists to be sent to the research staff members who will package the starch to deliver the designated packages to participants
.

Subject Recruitment and Retention

Subjects will be identified via the use of an EHR compiled list of COVID-19 positive patients who are outpatients. We will use medical records to obtain phone numbers. We will contact patients via phone and before discussing any material pertaining to the study, we will first inform the patients that this call is regarding a research study and if they would like they can opt out, to ensure that the option of opting out is given to the patient as early as possible. If the patient agrees to hear information regarding the study, we will provide an oral presentation of the study. Additionally, we will also post flyers at testing centers to give participants information about the study and the option to opt out. After presenting the study to patients by phone, an informed consent document will be sent to the patient electronically for subjects to sign digitally. After informed consent is obtained, screening to ensure that participants meet the inclusion/ exclusion criteria will be performed via phone and EHR. All follow up will be via phone calls and EHR review. The above plan was put together in order to limit contact with COVID-19 positive patients as the alternative of approaching and following the patients in person will put the research staff and the community at large at risk as it will promote the spread of this highly infectious virus by bringing these patients to the health system.

Drug Information

• This study investigates a food source that is being used as a drug but FDA offered a Discretionary Exemption to the IND application. While there are many potential sources for a potato-based or corn-based starch, we have chosen to use starch produced by Bob's Red Mill® because it is easily commercially available, economical and previously well tolerated in our preliminary data

•Some possible side effects to starch are flatulence (gas), abdominal bloating and chalky taste in the mouth. However, the majority of patients do not experience any symptoms when ingesting the dietary supplement. Below are the symptoms that may be experienced from the starch listed as possible, infrequent, and rare:

Possible 10-25 %: flatulence (gas), bloating, chalky taste in your mouth after drinking the starch, which resolves quickly

Infrequent 5-10 %: abdominal cramps, diarrhea, nausea, vomiting

Rare <5%: allergy to starch

Although very minimal adverse events and no serious adverse events were observed in our preliminary data, we have compiled a list of possible adverse events that will need to be reported to the safety monitoring coordinators.

• Contraindications

No contraindications to administration of this investigational agent other than the exclusion criteria noted. Specifically, should an enrolled subject develop one of the exclusion criteria (ie active Clostridium difficile infection or IBD) after enrollment and initiation of the study, they will be allowed to continue on study treatment. Meeting the primary end point of hospitalization is considered a contraindication to continue with the investigational agent.

The only concomitant medications prohibited on the study are anti-IL 6 inhibitors such as Tociluzimab, which is one of the exclusion criteria. This is usually a medication started as inpatient so we don't anticipate our patient population will be prescribed this drug after enrollment and while on investigational agent, since subjects will only continue to receive the investigational agent if they are not hospitalized.

• Interaction with other medications

As a dietary supplement and component of normal dietary intake, there are no anticipated interactions with other medications.

• Storage and stability: Store at room temperature, 59 °F to 86 °F. Avoid extremes of temperature. No need for refrigeration

• Preparation and Dispensing: Mix 2 tablespoons of dietary starch (~20 grams) with any amount water, juice, applesauce or any other cool substance to make palatable. Starch substance should not be heated or warmed

• Other administration instructions: No regulation for administration of starch with or without other food or medications. As this is a commercially available food product, subjects can keep any remaining product at the end

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of study. We will determine compliance via questionnaire that will be utilized during phone follow ups. Doses should be administered twice daily. Although we suggest the doses be spread apart to minimize any potential GI disturbance, there is no limit as to how closely together doses can be given. For example, doses do NOT need to be given 12 hours apart and instead can be given at times that feel comfortable to the subject
• Missed doses should be documented by the research team during phone follow up
• Missed doses should simply be skipped with no need to make up this dose at a later time
• Availability: Commercially Available. Potato starch and corn starch packages will be provided for the study free of change by Bob's Red Mill. Please see product specifications (**attached**)
.All starch for this study has been freely donated by Bob's Red Mill with no expectations or contracts. The starch has already been shipped to both sites.

• Nutritional label:

DESCRIPTION VIDEOS RECIPES RELATED PRODUCTS REVIEWS NUTRITIONAL INFO

Nutrient Facts
Serving Size: 1 Tbs(12g)
Servings Per Container: 56

	Amount Per Serving	% Daily Value
Calories	40	
Calories from Fat	0	
Total Fat	0 g	0 %
Saturated Fat	0 g	0 %
Trans Fat	0 g	0 %
Cholesterol	0 mg	0 %
Sodium	0 mg	0 %
Total Carbohydrate	10 g	3 %
Dietary Fiber	0 g	0 %
Sugars	0 g	N/A
Protein	0 g	0 %
Vitamin A		0 %
Vitamin C		0 %
Calcium		0 %
Iron		0 %

* Percent Daily Values (DV) are based on a 2000 calorie diet. Your daily values may be higher or lower depending on your calorie needs.

Ingredients:
potato starch

*Manufactured in a facility that also uses tree nuts and soy

Packaging and Delivery of potato starch (active) and corn starch (placebo) (600 grams and 500 grams respectively):
As this is a double blinded randomized control trial, investigators and participants will not be made aware of participant allocation to intervention or placebo starch.
To ensure blinded study design, as well as safe packaging and shipment of starch the following steps will take place:
-Starch was delivered from Bob's Red Mill free of change to:
Yale Investigational Pharmacy (55 Park Street, New Haven, Ct)
- Similarly, starch was delivered from Bob's Red Mill free of charge to Michigan site.
- Only the pharmacist will hold the labeling key and will repackage the starch. The manufacturer packaging will be removed and the starch will be emptied into a pre-labeled freezer ziploc bag. To ensure secure packaging of starch, each amount (either 600 or 500 grams depending on type of starch) will be double bagged for safety. Labeling will comply with labeling regulations.
- Starch packages will be repackaged and labeled at Yale's investigational drug services (IDS) who will be responsible for dispensing the starch, keeping drug accountability logs and compliance with any relevant state requirements. Research study team will package the starch at University of Michigan and the IDS at Michigan will dispense and ship the starch accordingly.
-A generated list of enrolled participants randomized to intervention or placebo by stratified permuted block randomization will be given to IDS who will ship starch based on patient allocation.

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Treatment Dosage and Administration

RPS or placebo will be administered at ~20 grams (2 tablespoons) once daily for days 1-3 and then twice daily for days 4-14, (**Table 2**).

Intervention and Placebo:

Table 2. Intervention and Placebo

Intervention	Study Product, Dose, Route Regimen	Food Source (used as a drug): Potato based dietary starch, Bob's Red Mill®, ~20 grams (2 tablespoons) orally twice daily. (start with 2 tablespoons once daily for 3 days, followed by twice daily on days 4 to 14 to minimize GI symptoms)
	Duration of Administration	14 days
Placebo	Study Product, Dose, Route Regimen	Food Source (used as a drug): Corn based dietary starch by Bob's Red Mill, ~20 grams (2 tablespoons) orally twice daily. (start with 2 tablespoons once daily for 3 days, followed by twice daily on days 4 to 14)
	Duration of Administration	14 days

• Storage and stability: Avoid extremes of temperature. No need for refrigeration.
• Preparation and Dispensing: Mix 2 tablespoons of dietary starch (~20 grams) with any amount water, juice, applesauce or any other cool substance to make palatable. Starch substance should not be heated or warmed.
• Other administration instructions: No regulation for administration of starch with or without other food or medications. As this is a commercially available food product, subjects can keep any remaining product at the end of study. We will determine compliance via questionnaire that will be utilized during phone follow ups (**see attached questionnaire**). Doses should be administered twice daily. Although we suggest the doses be spread apart to minimize any potential GI disturbance, there is no limit as to how closely together doses can be given. For example, doses do NOT need to be given 12 hours apart and instead can be given at times that feel comfortable to the subject.
• Missed doses should be documented by the research team during phone follow up
• Missed doses should simply be skipped with no need to make up this dose at a later time.
• Availability: Commercially Available

Toxicities and Dosing Delays/Dose Modifications

• This study investigates a food source used as a drug but has been given Discretion Exemption from the FDA. While there are many potential sources for a potato-based or corn-based starch, we have chosen to use starch produced by Bob's Red Mill® because it is easily commercially available, economical and previously well tolerated in our preliminary data.
• Starches are regulated by the Food and Drug Administration (FDA). The FDA's Select Committee on GRAS (Generally Recognized as Safe) Substances published an opinion in 1979 that stated: "There is no evidence in the available information on unmodified or pregelatinized corn, high amylose corn, waxy maize, wheat, milo (also called grain sorghum starch), rice, potato, tapioca or arrowroot starch that demonstrates or suggests reasonable grounds to suspect a hazard to the public when they are used at levels that are now current or that might reasonably be expected in the future" (SCOGS 1979).
• Drug Interactions: None known
• As starch is a natural nutritional supplement used for gluten free baking and cooking, we anticipate none to minimal risk to participants. Some possible side effects to starch are flatulence (gas), abdominal bloating and chalky taste in the mouth. However, the majority of patients do not experience any symptoms when ingesting the dietary supplement. Below are the symptoms that may be experienced from the starch listed as possible, infrequent, and rare:

Possible 10-25 %: flatulence (gas), bloating, chalky taste in your mouth after drinking the starch, which resolves quickly

Infrequent 5-10 %: abdominal cramps, diarrhea, nausea, vomiting

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Rare <5%: allergy to starch
Although very minimal adverse events and no serious adverse events were observed in our preliminary data, we have compiled a list of possible adverse events that will need to be reported to the safety monitoring coordinators (**Table 3**).
• Drug Interactions: None known
Table 3. Possible adverse events secondary to dietary starch use that will need to be reported to safety monitor

Adverse events related to Resistant Potato Starch (RPS)	• Allergy to potato or corn based starch • Persistent* Abdominal cramping or pain • Nausea or vomiting • Diarrhea • Persistent Bloating • Persistent Flatulence	All will be reported within 1 to 5 days to safety monitoring coordinator of event becoming known to PI at each site.

*Persistent symptoms will be defined as lasting 72 hours or longer

• If persistent side effects related to the investigational agent occur, a dose reduction can be made to once daily instead of twice daily dosing at the discretion of the PI or Co-I. If intolerability continues, despite decreasing the frequency of dosing, the investigational agent may be held for up to 3 days. Investigational agent can also be held for up to 3 days if the patient is unable to take oral intake for any reason. If investigational agent is held longer than 3 days, subject will be removed from treatment and included with an intention to treat protocol.
• The study intervention will be discontinued if patient meets the primary study endpoint of hospitalization

The Placebo uses corn starch. A potential risk although rare is allergy to corn. We will in screening ask about the potential subjects' exposure to corn and any reaction or avoidance of corn. Allergies to corn are extremely rare and there are no recent literature documenting specific rates, but one study from 1950 showed a very low rate of 0.16% (DOI:https://doi.org/10.1016/0021-8707(50)90098-0).

Concomitant Medications/Treatments
The only concomitant medications prohibited on the study are anti-IL 6 inhibitors such as Tociluzimab which is one of the exclusion criteria. Tociluzimab is usually started as an inpatient so we don't anticipate our patient population will be prescribed this medication while on study, since subjects will only continue to receive the investigational agent (starch) if they are not hospitalized.

Other Modalities or Procedures:
Only English-speaking patients will be mailed an instruction sheet with their investigational agent.
Duration of Therapy
Treatment will continue for 14 days, or until one of the following criteria apply:

- Hospitalization
- Death
- Persistent adverse event(s) leading to the investigational agent to be held for longer than 3 days
- Subject voluntarily withdraws from treatment **OR**
- General or specific changes in the subject's condition render the subject unacceptable for further treatment in the judgment of the investigator

Off Treatment Criteria
Patients will be removed from protocol therapy when any of the criteria listed above. The reason for ending protocol therapy and the date the patient was removed from treatment will be documented. All patients who discontinue treatment should comply with protocol specific follow-up procedures. The only exception to this requirement is when a subject withdraws consent for all study procedures or loses the ability to consent freely.

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Duration of Follow-Up
Subjects will be followed for 4 months from positive COVID-19 test or until death, whichever occurs first. Subjects will be followed for adverse events for at least 30 days after the last dose of study drug. Subjects removed from treatment for persistent adverse events thought to be due to interventional treatment will be followed until resolution or stabilization of the adverse event

Off Study Criteria
Patients can be taken off study at any time at their own request, or they may be withdrawn at the discretion of the investigator for safety, behavioral or administrative reasons. The reason(s) for discontinuation from study will be documented and may include:
•Patient withdraws consent (termination of treatment and follow-up);
•Loss of ability to freely provide consent through imprisonment or involuntary incarceration for treatment;
•Patient is unable to comply with protocol requirements;
•Investigators judge continuation on the study would not be in the patients best interest;
•Lost to Follow-up. If a research subject cannot be located to document hospitalization, the subject may be considered "lost to follow-up." All attempts to contact the subject during the four-month period must be documented.
•Termination of the study by any of the participating IRBs or FDA.
•Patient completes protocol treatment and follow-up criteria.

Subject Replacement
If subject needs to go off study after randomization, protocol dictates that subject cannot be replaced given the intention to treat nature of the protocol.

Screening baseline procedures
Assessments performed exclusively to determine eligibility for this study will be done only after obtaining informed consent. Assessments performed for clinical indications (not exclusively to determine study eligibility) such as COVID testing may be used for baseline values even if the studies were done before informed consent was obtained.
All screening procedures must be performed within 7 days prior to registration unless otherwise stated. The screening procedures include:
1 Informed Consent
2 Medical history: Complete medical and surgical history
3 Demographics: Age, gender, race, ethnicity
4 Review subject eligibility criteria
5 Review previous and concomitant medications
6 Adverse event assessment

Procedures during treatment and follow up procedures
Assessment for primary objective of hospitalization at one month via phone and EHR:
Every 2 days phone questionnaires (**see attached questionnaire**) and EHR review for the first 14 days followed by once weekly phone call and EHR review to complete a month follow up from last dose of treatment.

Assessment for secondary objectives of TTCR and symptom severity score via phone and EHR:
Every 2 day phone questionnaires (**see attached questionnaire**) and EHR review for the first 14 days followed by once weekly phone call and EHR review to complete a month follow up from last dose of treatment.

Assessment of exploratory objectives
EHR review to complete 4 months follow up from COVID positive test

Safety and Tolerability
Analyses will be performed for all subjects having received at least one dose of study drug.
*Assessment of adverse events (**outlined in Table 3 above**)*

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Every 2-day phone questionnaires (**Table 4**) and EHR review for the first 14 days followed by once weekly to complete a month follow up from last dose of treatment. Subjects will be followed for adverse events for at least 30 days after the last dose of study treatment. Subjects removed from treatment for persistent adverse events thought to be due to interventional treatment will be followed until resolution or stabilization of the adverse event.

Table 4: Time and Events

	Pre-Study	**Treatment Period/ Phone follow-up (14 days)**		**Follow-Up Period with phone and electronic medical record (EHR) review**			
Observations	Enrollment	Day 1-14	Every 2 days day 0-14	Every 7 days through Day 30 from last dose of treatment	Day 60 +/- 7 days	Day +90 +/- 7 days	Day 120 +/- 7 days
Informed Consent (phone)	X						
Assessment of co-morbidities	X						
Study Agent		X	X				
Side Effects	X		X	X			
Phone Symptom Questionnaire			X	X			
Assessment of medication use	X		X				
Assessment of Hospitalization			X	X			
EHR review	X	X	X	X	X	X	X

Section 5. Subject Population: Provide a detailed description of the types of human subjects who will be recruited into this study.

Participants >18 years of age with COVID-19 positive status and who are English speaking and do not require hospitalization. Upon enrollment participants cannot be hospitalized and cannot be actively enrolled in any other interventional trials. Participants with any allergy to potato or corn starch or inability or difficulty swallowing solids/liquids will also be excluded. For full inclusion and exclusion criteria, please refer to **Table 1** above.

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Section 6. Subject classification: Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement. N/A
NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes ☐ No ☒

Section 7. Inclusion/Exclusion Criteria: What are the criteria used to determine subject inclusion or exclusion?
Assessments performed exclusively to determine eligibility for this study will be done only after obtaining informed consent. Assessments performed for clinical indications (not exclusively to determine study eligibility) such as COVID testing may be used for baseline values even if the studies were done before informed consent was obtained.
All screening procedures must be performed within 7 days prior to registration unless otherwise stated. The screening procedures include:
1 Informed Consent
2 Medical history: Complete medical and surgical history
3 Demographics: Age, gender, race, ethnicity
4 Review subject eligibility criteria
5 Review previous and concomitant medications
6 Adverse event assessment

Section 8. How will **eligibility** be determined, and by whom?
This study will be conducted at multiple sites. Patients >18 years of age with COVID-19 positive status and who are being monitored in the outpatient setting will be approached by phone. IRB-approved informed consent must be obtained from patients prior to the initiation of treatment on this protocol. After informed consent is obtained and prior to the initiation of protocol therapy, all patients satisfying the inclusion/exclusion criteria must have eligibility confirmed by the PI or Co-I of the study team at each site. The patient will not be considered enrolled in the study until all information is confirmed by the PI or Co-I. Both the EHR and phone calls on enrollment will be used to assess eligibility criteria.

Section 9. Risks: Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.
There is minimal risk to our intervention as RPS is a natural nutritional source often used for gluten free baking and cooking. Similarly, corn starch should offer minimal risk as a placebo to study participants. There is some inconvenience to participants, as we will monitor their progress via phone calls every two days to assess their symptoms via a phone questionnaire.

While there are many potential sources for a potato-based or corn-based starch, we have chosen to use starch produced by Bob's Red Mill® because it is easily commercially available, economical and previously well tolerated in our preliminary data.

Adverse Reactions
Only mild adverse reactions and no serious adverse reactions have been noted with the previous administration of this dietary supplement to a group of healthy volunteers (HUM00118951 and HUM00094242 from the University of Michigan) or to allo HCT patients (HUM00112318 from the University of Michigan). Some possible side effects to starch are flatulence (gas), abdominal bloating and chalky taste in the mouth. However, the majority of patients do not experience any symptoms when ingesting the dietary supplement. Below are the symptoms that may be experienced from the starch listed as possible, infrequent, and rare:
Possible 10-25 %: flatulence (gas), bloating, chalky taste in your mouth after drinking the starch, which resolves quickly

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Infrequent 5-10 %: abdominal cramps, diarrhea, nausea, vomiting
Rare <5%: allergy to starch
Although no serious side effects were observed in our preliminary data, we have compiled a list of possible adverse events that will need to be reported to the safety monitoring coordinators (**Table 3 above**).

Section 10. Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.
To minimize risk of GI discomfort, the participants will work up to the full dose of starch during the initial 3 days of study.

Section 11. Data and Safety Monitoring Plan: Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)

a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal risk
b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? Minimal risk
c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates

Adverse event (AE) monitoring and reporting is a routine part of every clinical trial and is done to ensure the safety of subjects enrolled in the studies as well as those who will enroll in future studies using similar agents. Data on adverse events will be collected from the time of the initial study treatment through 30 days after the last dose. Any serious adverse event that occurs more than 30 days after the last study treatment and is considered related to the study treatment must also be reported. Serious Adverse Events (SAEs) will continue to be followed until:

- Resolution or the symptoms or signs that constitute the serious adverse event return to baseline;
- There is satisfactory explanation other than the study [treatment or intervention] for the changes observed; or
- Death.

The investigator is responsible for the detection, documentation, grading and assignment of attribution of events meeting the criteria and definition of an AE or SAE. The **definitions** of AEs and SAEs are given below. It is the responsibility of the principal investigator to ensure that all staff involved in the trial is familiar with the content of this section.

Any medical condition or laboratory abnormality with an onset date before initial study treatment is considered to be pre-existing in nature. Any known pre-existing conditions that are ongoing at time of study entry should be considered medical history.

All events meeting the criteria and definition of an AE or SAE, as defined below, occurring from the initial study treatment through 30 days following the last dose of study treatment must be recorded as an adverse event in the subject's source documents and on the CRF regardless of frequency, severity (grade) or assessed relationship to the study treatment.

In addition to new events, any increase in the frequency or severity (i.e., toxicity grade) of a pre-existing condition that occurs after the subject begins study treatment is also considered an adverse event.

Review of AE and SAE data will be performed on a routine basis by the Data and Safety Monitoring Board (DSMB).

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Definitions

1. Adverse Event

Adverse Event Definition

An adverse event (AE) is any untoward medical occurrence in a subject participating in an investigational study or protocol regardless of causality assessment. An adverse event can be an unfavorable and unintended sign, symptom, syndrome or disease associated with or occurring during the use of an investigational product whether or not considered related to the investigational product.

2. Serious Adverse Event

An adverse event is considered "serious" if, in the view of the investigator, it results in any of the following outcomes:

- Death
  If death results from (progression of) the disease, the disease should be reported as event (SAE) itself.

- A life-threatening adverse event
  An adverse even is considered 'life-threatening' if, in the view of either the investigator [or sponsor], its occurrence places the subject at immediate risk of death. It does not include an adverse event that, had it occurred in a more severe form, might have caused death.

- Inpatient hospitalization or prolongation of existing hospitalization for $\geq$ 24 hours.

- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions

- A congenital anomaly/birth defect

- Important medical event

Any event that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, it may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition of "Serious Adverse Event". Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home; convulsions that do not result in inpatient hospitalization or the development of drug dependency or drug abuse.

Previously planned (prior to the informed consent) surgeries should not be reported as SAEs unless the underlying medical condition has worsened during the course of the study. Preplanned hospitalizations or procedures for preexisting conditions that are already recorded in the subject's medical history at the time of study enrollment should not be considered SAEs. Hospitalization or prolongation of hospitalization without a precipitating clinical AE (for example, for the administration of study therapy or other protocol-required procedure) should not be considered SAEs. However, if the preexisting condition worsened during the course of the study, it should be reported as an SAE.

3. Expected Adverse Events

An adverse event (AE) is considered "expected" if:

- For approved and marketed drugs or devices, those adverse events are described in the approved Package Insert (Label).
- In clinical research studies, information on expected adverse events is also summarized in the protocol and in the consent document.

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4. Unexpected Adverse Event

An adverse event (AE) is considered "unexpected" if it is not described in the Package Insert, in published medical literature, in the protocol, or in the informed consent document.

Adverse Event Characteristics

1. Terms and Grading

The severity or grade of an adverse event may be measured using the following definitions:

Mild: Noticeable to the subject, but does not interfere with subject's expected daily activities, usually does not require additional therapy or intervention, dose reduction, or discontinuation of the study.

Moderate: Interferes with the subject's expected daily activities, may require some additional therapy or intervention but does not require discontinuation of the study.

Severe: Extremely limits the subject's daily activities and may require discontinuation of study therapy, and/or additional treatment or intervention to resolve.

2. Attribution of the AE

The investigator or co-investigator is responsible for assignment of attribution.

- Definite – The AE *is clearly related* to the study treatment/intervention.
- Probable – The AE *is likely related* to the study treatment/intervention.
- Possible – The AE *may be related* to the study treatment/intervention.
- Unlikely – The AE *is doubtfully related* to the study treatment/intervention.

Unrelated – The AE *is clearly NOT related* to the study treatment/intervention.

Reporting of AEs and SAEs for this study

In the event of an adverse event, the first concern will be for the safety of the subject. Investigators are required to report any SAE, whether expected or unexpected, and which is felt by the investigator to be reasonably or possibly related to or caused by the study treatment. All events meeting these criteria will be reported for the time period beginning with any amount of exposure to study treatment until 30 days from the last dose of treatment. We will **report expected or unexpected SAEs to the IRB that are deemed related to the investigational agent** according to the reporting requirements of the IRB. **Adverse events will be reported according to the IRB reporting guidelines.**

Reporting of Unanticipated Problems

Unanticipated problem: Per FDA Procedural Guidance for Clinical Investigators, Sponsors, and IRBs (January 2009), A serious problem that has implications for the conduct of the study (requiring a significant and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, or informed consent).

Upon becoming aware of any incident, experience, or outcome (not related to an adverse event) that may represent an unanticipated problem, the investigator should assess whether the incident, experience, or outcome represents an unanticipated problem. The incident, experience, or outcomes is considered unanticipated if it meets all of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency);
2. Related or possibly related to participation in the research; and
3. Suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized.

Unanticipated problem Reporting: Per 21 CFR 312.66, 312.53 (c)(1)(vii), and 56.108(b)(1), should an Unanticipated problem occur during the investigation, the investigator will promptly report all unanticipated problems involving risks to human subjects or others to the IRB /FDA.

Reporting of Pregnancy

N/A

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Stopping Rules
During the interim statistical analysis, we will analyze the efficacy of RPS in relation to the primary outcome of hospitalization. If there is a significant difference between the two arms with p-value of <0.01, we will not continue the study.

Data and Safety Monitoring
Briefly, the principal investigator from each site will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews every week throughout the duration of the study. During the review process the principal investigators will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.
The principal investigators, or the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and adverse events are not anticipated. In the unlikely event that such events occur, reportable events (expected or unexpected SAEs that are deemed related to the investigational agent and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs)) will be reported by the research coordinator to the PI as soon as they occur , followed by a written report within 7 calendar days of the Principal Investigator becoming aware of the event to the IRB and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all reportable SAEs and UPIRSOs that occur during the conduct of this research project through regular study meetings via video-conferences, and emails. The protocol's central safety research monitor will be informed of any reportable SAEs or UPIRSOs within 48 hours of the event becoming known to the principal investigators.

Data Safety Monitoring Committee (DSMC)
The study specific DSMC consisting of Mike Simonov (Physician and Statistician), Mary Savoye (Registered Dietician), and Yasemin Kavak (Research Coordinator) will meet monthly or more frequently depending on the activity of the protocol. The discussion will include matters related to the safety of study participants (reportable SAEs and UPIRSOs), validity and integrity of the data, enrollment rate relative to expectations, characteristics of participants, retention of participants, adherence to the protocol (potential or real protocol deviations) and data completeness. A protocol specific DSMC report will be completed and signed by the site Principal Investigator or by one of the co-investigators and sent to the DSMC quarterly. The DSMC will act in an advisory capacity to monitor participant safety, evaluate the progress of the study, to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses. All the above members of the DSMC are independent of the study team and are not on the IRB protocol.

In the event of an AE, the first concern will be for the safety of the subject. As potato and corn starch are natural food products used for gluten free baking and cooking, we anticipate none to minimal risk to participants. As starch is a natural nutritional supplement used for gluten free baking and cooking, we anticipate none to minimal risk to participants. Some possible side effects to starch are flatulence (gas), abdominal bloating and chalky taste in the mouth. However, the majority of patients do not experience any symptoms when ingesting the dietary supplement. Below are the symptoms that may be experienced from the starch listed as possible, infrequent, and rare:
Possible 10-25 %: flatulence (gas), bloating, chalky taste in your mouth after drinking the starch, which resolves quickly
Infrequent 5-10 %: abdominal cramps, diarrhea, nausea, vomiting
Rare <5%: allergy to starch
Although very minimal adverse events and no serious adverse events were observed in our preliminary data, we have compiled a list of possible adverse events (**see table 3)** that will need to be recorded by the research team at each site, reported to the research safety monitor and included on the quarterly reports to the protocol specific DSMC for the time period beginning with any amount of exposure to study treatment through at least 30 days after the last dose of study treatment.

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As aforementioned, the site PI will be informed of SAEs and UPIRSOs as soon as they occur by the study coordinator and will notify the protocol's central safety research monitor within 48 hours of becoming aware of the event. Reportable SAEs and UPIRSOs will be reported to the local IRB according to the local IRB reporting guidelines. These events will be included on the quarterly reports to the protocol specific DSMC. Ad hoc reviews by the study specific DSMC will occur if there are unforeseen frequent SAEs.

Content of DSMC report (to be sent to the protocol specific DSMC quarterly and at time of interim analysis):
•Actual versus expected enrollment figures that illustrate recruitment and participation status
•Data tables that summarize demographic and baseline clinical characteristics
•Data quality tables that capture missing data
•Aggregate tables of AEs, SAEs, UPIRSOs, and prortocol deviations
•Listings of AEs, SAEs, UPIRSOs, and protocol deviations
***Responsibilities of protocol specific DSMC may include*:**
•Reviewing the research protocol, and informed consent documents.
•Evaluating the progress of the study on an ongoing basis including periodic assessments of data quality, participant recruitment, accrual and retention, participant risk versus benefit, performance of study site(s), and other factors that can affect the outcome.
•Considering the impact of factors external to the study when new information, such as scientific or therapeutic developments becomes available that may affect safety of participants, their willingness to participate in the study or the ethics and conduct of the study.
•Reviewing UPIRSO, SAE, AE, and protocol deviation reports.
•Reporting any problems with study conduct or performance to the IRB.
•Ensuring the measures to ensure the confidentiality of study data and results are appropriate.
•Reviewing and evaluating requests for protocol modifications/amendments.
•Reviewing before study initiation the stopping rules and plans for interim analyses presented in the protocol. These plans outline the conditions under which a study may be stopped (e.g., difficulties in recruitment, retention, obtaining outcome measures or other issues).
•Reviewing the interim analyses and/or accumulating data at the specified interval(s), and as appropriate and make a recommendation to continue, terminate or modify the study based on observed benefit or harm in accordance with the planned stopping rules.

Section 12. For multi-site studies for <u>which the Yale PI serves as the lead investigator</u>: How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed?

Multicenter Coordinating Plan.
We will have routinely scheduled video-conferences with all sites every two weeks to discuss any reported events or unanticipated problems. Our calls will include all study team members including students, research coordinators and all PIs.

In order to coordinate and ensure ongoing communication, accurate data collection, and secure file sharing we will have developed the following plan:

As mentioned, there will be video-conference with PIs, and study team members every two weeks. Initially the meetings will focus on study enrollment to discuss any issues meeting enrollment targets or capturing the patient population. During these meetings, a research assistant will take notes of key points that were discussed and will distribute this email to all study members.

Both Yale and Michigan sites will use Yale OnCore to input all data. Michigan coordinators will be given access to the Yale OnCore/EDC and will sign a material transfer agreement with Yale. All data will be analyzed at Yale and will be saved on a secure server at a Yale desktop located at 60 Temple St, suite 6c, New Haven CT 06510.

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Yale will be the central data analysis site. All data will be analyzed by s a full time statistician at the Program of Applied Translational Research (Yu Yamamoto; main statistician). The Michigan site will input their data into the OnCore portal at Yale and all data will be analyzed at Yale. Michigan will draft and sign a material transfer agreement with Yale.

Yale will serve as the Data Coordinating Center, to ensure that all data is accurate, valid and securely stored. Research Coordinators (led by Tanima Arora) will have meetings every 2 weeks to ensure the process of data collection and storage is done systematically across all sites. Any unanswered questions on these meetings will be brought up to the PIs during the every 2-week calls for this multicenter study.

As Yale is the primary site and the Yale PI is the primary PI, we will assure IRB review at Michigan (other site) and will collect all adverse events and UPIRSOs in the review as detailed under Data Safety Monitoring Committee.

Audits and Inspections
The DSMC can request a 'for cause' quality assurance audit of the trial if the committee identifies a need for a more rigorous evaluation of study-related issues.

The FDA has offered a Discretion Exemption to our IND application. However, other regulatory authority may also wish to conduct an inspection of the study, during its conduct or even after its completion. If an inspection has been requested by a regulatory authority, the study staff must immediately inform IRB, Medical School Regulatory Affairs, MIAP, and the Research Pharmacy (if providing study drug).

The local site investigator at Michigan will immediately inform the Data Coordinating Center, Yale, if such a request has been made.

Protocol Deviations
A protocol deviation is defined as noncompliance with the clinical trial protocol. The noncompliance may be either on the part of the subject, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

Specific deviation plan for this protocol: Deviations in study treatment administration from protocol treatment plan will be recorded and reported to the IRB. Deviations in follow up procedures for the primary and secondary outcomes from protocol follow-up procedures will be recorded and reported to the IRB. Deviations in follow up procedures for exploratory outcomes from protocol follow-up procedures will be recorded but not reportable to IRB since follow up for exploratory outcomes, while important, is optional.

All deviations must be addressed in study source documents, reported to the central research safety monitor within 2 weeks of identification, and reported quarterly to the DSMC. IRB reportable protocol deviations must be sent to the IRB per their policies. The site investigator is responsible for reporting deviations to the local IRB according to local IRB reporting guidelines.

Subject information and Consent
Study team member will explain to each subject (or legally authorized representative) the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved and any discomfort it may entail. Each subject will be informed that participation in the study is voluntary and that he/she may withdraw from the study at any time and that withdrawal of consent will not affect his/her subsequent medical treatment or relationship with the treating physician.

We will contact patients via phone to perform an oral presentation of the study. After presenting the study to patients by phone, an informed consent document will be sent to the patient electronically for subjects to sign digitally. The plan of obtaining informed consent virtually was formulated in order to limit contact with COVID-19 positive patients as the alternative of approaching the patients in person will put the research staff and the community at large at risk as it will promote the spread of this highly infectious virus by brining these patients to the health system.

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No subject can enter the study before his/her informed consent has been obtained.

The informed consent process and form are considered to be part of the protocol, and will be submitted for IRB approval.

Section 13. What provisions are in place for management of interim results?
Interim analysis plans:
Once our enrollment target for the secondary outcomes is reached (n~200), the DSMB and Yu Yamamoto (Bio Satistician) will perform an interim analysis to assess safety, feasibility, utility, futility, and treatment effect.
Interim analysis 1(safety):
All adverse events will be summarized and the independent data safety monitoring committee (DSMC) will make recommendations regarding continuation of recruitment.
Interim analysis 2 (feasibility):
Study enrollment, follow up and any withdrawals from the study will be summarized and discussed by IDSMC to see if the degree of missing data is acceptable and if any further efforts need to be taken to optimize enrollment and follow up. Successful feasibility will be defined as more than 60% of patients took at least 50% of their prescribed doses (as directed by study team).
Interim analysis 3 (treatment effect):
We will analyze the efficacy of RPS in relation to the primary outcome of hospitalization. If there is a significant difference between the two arm with p-value of <0.01, we will not continue the study. For data quality and integrity, we will also analyze the efficacy of RPS in relation to the secondary outcomes of TTCR and symptom severity score to assess efficacy and ensure no increase in harm in the intervention arm.

Section 14. Statistical Considerations: Describe the statistical analyses that support the study design.
Study design/Study outcomes measures: We will conduct a double-blinded, randomized clinical trial comparing RPS (~20g twice daily for 14 days) with placebo (non-resistant starch) in 1500 adults (age ≥18 years old) with COVID-19 diagnosis (defined by a positive swab) who are being managed in the outpatient setting. The primary outcome is hospital admission due to COVID-19 related complications. The secondary outcomes are TTCR and symptom severity score. We also will investigate some exploratory outcomes such as ER visits without admission, and among those hospitalized, we will explore differences in oxygen requirement, need for mechanical ventilation, duration of ventilation, length of hospital stay, levels of inflammatory markers routinely ordered as part of clinical care (CRP, LDH, D-dimer, Ferritin, Il-6), and rates of discharge between the RPS and placebo arms.
Sample size and accrual: Assuming a 14% admission rate in the placebo group, we calculated that a sample size of 1362 (we will enroll 1500 to account for 10% loss to follow up) will be required to provide 80% power (with a two-sided alpha level of 0.04 to detect an absolute reduction in hospital admission rates of 5% or more in the RPS group. **The primary analysis will be based on the intention-to-treat principle, with all patients included in their assigned group.**
For our secondary outcomes, assuming a TTCR of about 14 days in the placebo group with standard deviation of 5 days, we calculated that a sample size of 196 would be required to provide 80% power (with a two-sided alpha level of 0.05) to detect an absolute reduction in TTCR by 2 days or more in the RPS group. For the outcomes of symptom severity score, we assumed that the placebo group would have a peak score of 20 with a standard deviation of 5 points, and we calculated that a sample size of 32 patients would be required to provide 80% power (with a two-sided alpha level of 0.05) to detect an absolute reduction in symptom severity score of 5 points or more in the RPS group.
Total accrual between all sites is 1500 patients. Depending on accrual rates, some sites may accrue more than other sites with a total goal of 1500 patients.
Data analysis plan: The primary outcome of hospital admission rates will be compared with the use of Pearson's chi-square test. The secondary outcomes of TTCR and symptom severity score will be compared in the two groups by means of a two-sample t-test. Adjusted measures and subgroup effects for the primary and secondary outcomes will be analyzed with the use of logistic regression and linear regression, respectively. Generalized estimating equations and linear mixed models will be used to test for an interaction between treatment group and

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site in primary and secondary outcomes, respectively. The alpha level will be set at 0.05 for all analyses, 95% confidence intervals will be calculated, and all comparisons will be two-tailed.

Interim analysis plans:

Once our enrollment target for the secondary outcomes is reached (n~200), we will perform an interim analysis to assess safety, feasibility and treatment effect.

Interim analysis 1(safety):

All adverse events will be summarized and the independent data safety monitoring committee (DSMC) will make recommendations regarding continuation of recruitment. None of the DSMC members will be on our IRB protocol or the study team.

Interim analysis 2 (feasibility):

Study enrollment, follow up and any withdrawals from the study will be summarized and discussed by IDSMC to see if the degree of missing data is acceptable and if any further efforts need to be taken to optimize enrollment and follow up. Successful feasibility will be defined as more than 60% of patients took at least 50% of their prescribed doses (as directed by study team).

Interim analysis 3 (treatment effect):

We will analyze the efficacy of RPS in relation to the primary outcome of hospitalization. If there is a significant difference between the two arm with p-value of <0.01, we will not continue the study. For data quality and integrity, we will also analyze the efficacy of RPS in relation to the secondary outcomes of TTCR and symptom severity score to assess efficacy and ensure no increase in harm in the intervention arm.

Yale will be the central data analysis site. All data will be analyzed by a full time statistician at the Program of Applied Translational Research.

Use of Placebo:

If use of a placebo is planned, provide a justification which addresses the following:

a) Describe the safety and efficacy of other available therapies. If there are no other available therapies, state this. As there are no current treatments for COVID-19, there is no other safe or efficacious therapy that we can use instead of placebo.

b) State the maximum total length of time a participant may receive placebo while on the study.
14 days.

c) Address the greatest potential harm that may come to a participant as a result of receiving placebo.
There should be no harm incurred by participants receiving placebo, which is corn starch (non-resistant digestible starch).

d) Describe the procedures that are in place to safeguard participants receiving placebo.
We will perform interim analysis for efficacy to determine if early study termination may be needed if there is evidence of benefit in the intervention arm that precludes us to continue the study ethically.

4. **Continuation of Drug Therapy After Study Closure ☒Not applicable to this project**

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SECTION III: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. **Targeted Enrollment: Give the number of subjects:**
   a. Targeted for enrollment at Yale for this protocol: 500
   b. If this is a multi-site study, give the total number of subjects targeted across all sites: *1500*

2. **Indicate recruitment methods below.** Attach copies of any recruitment materials that will be used.

☒ Flyers	☐ Internet/web postings	☐ Radio
☐ Posters	☐ Mass email solicitation	☒ **Telephone**
☐ Letter	☐ Departmental/Center website	☐ Television
☒ **Medical record review***	☐ Departmental/Center research boards	☐ Newspaper
☐ Departmental/Center newsletters	☐ Web-based clinical trial registries	☐ Clinicaltrails.gov
☐ YCCI Recruitment database	☒ Social Media (Twitter/Facebook):	
☒ Other: Testing Sites		

*** Requests for medical records should be made through JDAT as described at**
http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx

3. **Recruitment Procedures:**
a. Describe how potential subjects will be identified. Via the use of a Joint Data Analytics Team (JDAT) compiled list of COVID-19 positive patients who are outpatients, we will contact patients via phone calls to ensure inclusion criteria and obtain phone consent. We will also post IRB-approved informational flyers at testing sites and on social media platforms.
b. Describe how potential subjects are contacted. Mainly via medical record review and phone calls.
c. Who is recruiting potential subjects? PIs and research assistants via phone.

4. **Assessment of Current Health Provider Relationship for HIPAA Consideration:**
Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?
☐Yes, all subjects
☒Yes, some of the subjects
☐No

If yes, describe the nature of this relationship. The PIs may be involved in the clinical care of the participants if they eventually become hospitalized, but at time of enrollment it is unlikely that any PIs will be involved in the care of the patient.

5. **Request for waiver of HIPAA authorization:** (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)
Choose one:
☐ For entire study
☒ For recruitment/screening purposes only
☐ For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

   i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data: To limit contact with COVID-19 positive patients, the only way to request their permission to participate in our study will be via phone calls. To obtain phone numbers and do initial screening to ensure that participants meet the inclusion criteria we will have to access their medical records.

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Approaching the patient directly will put the research staff at risk and the community at large as it will promote the spread of this highly infectious virus.

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data: We will obtain phone consent to commence the study and will ask patients to sign a formal consent form via email if feasible. Bringing the patients to a health care facility to ensure obtaining a singed authorization will put the research staff at risk and the community at large as it will promote the spread of this highly infectious virus.

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. **Process of Consent/Assent:** Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.
   Study team member will explain to each subject (or legally authorized representative) the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved and any discomfort it may entail. Each subject will be informed that participation in the study is voluntary and that he/she may withdraw from the study at any time and that withdrawal of consent will not affect his/her subsequent medical treatment or relationship with the treating physician.

   We will contact patients via phone to perform an oral presentation of the study. After presenting the study to patients by phone, an informed consent document will be sent to the patient electronically for subjects to sign digitally. The plan of obtaining informed consent virtually was formulated in order to limit contact with COVID-19 positive patients as the alternative of approaching the patients in person will put the research staff and the community at large at risk as it will promote the spread of this highly infectious virus by brining these patients to the health system.

   No subject can enter the study before his/her informed consent has been obtained.

   The informed consent process and form are considered to be part of the protocol, and will be submitted for IRB approval.

7. **Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent:** Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.
   Every patient will be assessed for capacity by ensuring that they have understanding of the research and are able to repeat back what we discussed in a manner that expresses understanding. Any patients on heavy pain medications will not be eligible for immediate consenting.
8. **Non-English Speaking Subjects:** Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.
   We do not anticipate that any non-English speaking subjects will be enrolled.

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Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. **Please review the guidance and presentation on use of the short form available on the HRPP website.**

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☒Not Requesting any consent waivers

☐Requesting a waiver of signed consent:

☐ **Recruitment/Screening only** (if for recruitment, the questions in the box below will apply to recruitment activities only)

☐ **Entire Study (**Note that an information sheet may be required.)

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☐ NO ☐
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☐ NO ☐

OR

- Does the research pose greater than minimal risk? YES ☐ NO☐
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☐

☐ Requesting a waiver of consent:

☐ **Recruitment/Screening only** (if for recruitment, the questions in the box below will apply to recruitment activities only)

☐ **Entire Study**

For a full waiver of consent, please address all of the following:

- Does the research pose greater than minimal risk to subjects?
  - ☐ Yes *If you answered yes, stop. A waiver cannot be granted.*
  - ☐ No
- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☐
- Why would the research be impracticable to conduct without the waiver? *Write here*
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date? *Write here*

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SECTION IV: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research? We will need subjects' demographics such as age, sex, race, height, weight, and BMI.

2. How will the research data be collected, recorded and stored? We will store all data on the protected/secure/encrypted Yale G drive/server. Other sites will send collected data securely via Yale secure file transfer.

3. How will the digital data be stored? Yale desktop computer.

4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?
   All information will be stored on a secured Yale drive. No personal laptops or computers will be used to store any of this information.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.
   This information will be kept for five years. After that time it will be destroyed or de-identified, meaning we will replace the identifying information with a code that does not directly identify the participant. The principal investigator (PI) will keep a link that identifies the participant to the coded information, but this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify the participant will remain confidential. The research team will only give this coded information to others to carry out this research or to investigators approved for use of banked data.

6. If appropriate, has a Certificate of Confidentiality been obtained? NA

SECTION V: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)
If our hypothesis is proven, this simple, minimal risk intervention, will have the potential to reduce healthcare burden and improve the outcomes of COVID-19 positive patients.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?
   NA, research participation is completely voluntary. As there are no current approved treatments for COVID-19, there are no other standard of care treatments that participants can receive.
   Participants may change their mind at any time. They are free to choose not to take part in this study. If they begin the study and later change their mind, they can withdraw at any time. Refusing to participate will involve no penalty or loss of benefits to which they are otherwise entitled (such as their health care outside the

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study, the payment for their health care and their health care benefits). It will not harm their relationship with their own doctors. If they decide to withdraw from the study, they may withdraw by telling the study staff or sending written notice to the address provided in the consent form.
Dr. Sherry Mansour, PO Box 208029, New Haven, CT 06520, (203) 737-3363
Payments for Participation (Economic Considerations): Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.
none

2. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.
   None

IMPORTANT REMINDERS

Will this study have a billable service? **Yes** ☐ **No**☒

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? **Yes** ☐ **No** ☒

If you answered "no" to question 4a, or "yes" to question 4b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. **By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.**

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Attachments:

Appendix A: Phone Questionnaire

COVID-19 Symptom Severity Questionnaire[1]

Hello "*Enrolled subject*"

I would like to assess the severity of your COVID-19 symptoms. Please consider the severity of each symptom based on the following scale: absent, mild, moderate, or severe, to the best of your ability. Remember, If you experience severe symptoms, like shortness of breath, at any point during your evaluation for COVID-19, please call 911 to be emergently evaluated by a healthcare provider.

A. Over the past 2-3 days:

	Absent	Mild	Moderate	Severe
1) Do you have loss of taste or smell?				
2) Do you have any bellyaches, diarrhea, or nausea/vomiting?				
3) Do you have a cough?				
4) Are you short of breath or wheezy on rest or exertion?				
5) Do you have a fever or feel feverish?				
6) Are you experiencing fatigue?				
7) Do you have a headache?				
8) Do you have muscle aches, pains, or cramps?				

B. What medication are you on currently?

Name of drug	Dose	Frequency	Newly started within the past 2-3 days (Y/N)

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C. Have been taking your starch as instructed? Y/N

If No, could you let us know why?

D. Have you experienced any side effects from the starch? Y/N

If yes, could you tell us about your symptoms?

This concludes the questionnaire. You will be contacted every 2 days to review your symptoms. If you have questions regarding your health or diagnosis of COVID-19, please contact your healthcare provider.

Reference

1. VanWormer JJ, Sundaram ME, Meece JK, *et al.* A cross-sectional analysis of symptom severity in adults with influenza and other acute respiratory illness in the outpatient setting. *BMC Infect Dis* 2014; **14:** 231.

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Appendix B: Instruction which will be sent to patient with the study treatment

Dear Study Participant,
Please take two tablespoons of the delivered starch once daily for three days. On the fourth day, please start taking two tablespoons of the delivered starch twice daily until day number 14.

You can place the starch in any cool substance such as water, juice, or applesauce to make it more palatable. Please stir constantly while drinking and some residue may form on the bottom without stirring.

Of note, it is not essential that you space out the two tablespoons by 12 hours, if you prefer you can take all 4 tablespoons at the same time.

Please repeat the above steps for 14 days. By the end of 14 days you should have completed all the bag starch content.

DAILY ON DAYS 1, 2 and 3.

DAILY

FROM DAY 4 to DAY 14.

We thank **YOU** for volunteering to participate in this study during such a difficult time for the whole world. We are working together to fight this pandemic, and we thank you for being the most integral part of this fight. Your contribution to science will help us win this fight. We wish you health and a speedy recovery.

Sincerely,
Study Team

Appendix C: Potato starch product specification

Original draft: 2/18/2016
Revision date: 1/7/2020
Approved by: zeast

Revised by: zeast
Revision #: 11
Document #: FG SPEC 1444 GF POTATO STARCH

BOB'S RED MILL NATURAL FOODS, INC.

Product Specification

Product Name: GF POTATO STARCH

Product Number: 1444

Product Description:	*GF POTATO STARCH are made from starch that has been extracted from potatoes, processed in accordance with 21 CFR Part 117 subpart B and in compliance with state and federal requirements for food safety and quality.*
Ingredients:	*Potato Starch.*
Allergens:	*No Allergens. Manufactured in a facility that also uses tree nuts and soy.*
Gluten Free:	*This product is a gluten-free food. In accordance with the Codex Alimentarius' established threshold for gluten contamination, this product contains less than 20 ppm gluten.*

Physical Properties

Appearance:	*White powder.*
Aroma:	*Neutral with no rancid or off-odors.*
Flavor:	*Clean with no rancid or undesirable flavors.*

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Original draft: 2/18/2016
Revision date: 1/7/2020
Approved by: zeast

Revised by: zeast
Revision #: 11
Document #: FG SPEC 1444 GF POTATO STARCH

Nutrition Facts	
Serving size	100g
Amount per serving	
Calories	**327.00**
	% Daily Value*
Total Fat 0.00g	0%
Saturated Fat 0.00g	0%
Trans Fat 0.00g	
Cholecterol 0.00mg	0%
Sodium 38.70mg	2%
Total Carbohydrate 81.80g	30%
Dietary Fiber 0.00g	0%
Total Sugars 0.00g	
Includes 0.00g Added Sugars	0%
Protein 0.00g	
Vitamin D 0.00mcg	
Calcium 19.20mg	
Iron 0.48mg	
Potassium 60.00mg	

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

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Certifications

Kosher:	*Certified by OK Kosher Certification of Brooklyn, New York*
Non-GMO:	*Verified by the Non-GMO Project.*
3rd Party Food Safety Audit:	*Certified by NSF International, Safe Quality Food (SQF) Level II, Food Safety Code for Manufacturing Edition 8.0*
Country of Origin:	*Germany, Netherlands, United States of America*
Shelf Life:	*When handled under recommended storage, the product has a 730 day shelf life for optimum flavor and quality. Shelf life is printed on each package and case using a "Best By" date. The "Best By" date is the production date plus the determined appropriate shelf life time. The "Best By" date is displayed as Day/Month/Year and is printed with the format of DD/MM/YYYY*

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Appendix D: Corn starch product specification

Original draft: 2/18/2016
Revision date: 1/3/2020
Approved by: zeast

Revised by: zeast
Revision #: 5
Document #: FG SPEC 1146 GF CORN STARCH

BOB'S RED MILL NATURAL FOODS, INC.

Product Specification

Product Name: GF CORN STARCH

Product Number: 1146

Product Description:	*GF CORN STARCH are made from endosperm of corn kernels, processed in accordance with 21 CFR Part 117 subpart B and in compliance with state and federal requirements for food safety and quality.*
Ingredients:	*Cornstarch.*
Allergens:	*No Allergens. Manufactured in a facility that also uses tree nuts and soy.*
Gluten Free:	*This product is a gluten-free food. In accordance with the Codex Alimentarius' established threshold for gluten contamination, this product contains less than 20 ppm gluten.*

Physical Properties

Appearance:	*Fine white powder.*
Aroma:	*Clean and fresh with no rancid or off-odors.*
Flavor:	*Clean and fresh with no rancid or undesirable flavors.*

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Original draft: 2/18/2016
Revision date: 1/3/2020
Approved by: zeast

Revised by: zeast
Revision #: 5
Document #: FG SPEC 1146 GF CORN STARCH

Nutrition Facts	
Serving size	100g
Amount per serving	
Calories	**362.00**
	% Daily Value*
Total Fat 1.00g	1%
Saturated Fat 0.40g	2%
Trans Fat 0.01g	
Cholesterol 0.00mg	0%
Sodium 0.00mg	0%
Total Carbohydrate 87.60g	32%
Dietary Fiber 1.30g	5%
Total Sugars 0.00g	
Includes 0.00g Added Sugars	0%
Protein 0.70g	
Vitamin D 0.00mcg	
Calcium 14.50mg	
Iron 0.00mg	
Potassium 1.13mg	

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

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Revision date: 1/3/2020
Approved by: zeast

Revised by: zeast
Revision #: 5
Document #: FG SPEC 1146 GF CORN STARCH

Certifications

Kosher:	*Certified by OK Kosher Certification of Brooklyn, New York*
3rd Party Food Safety Audit:	*Certified by NSF International, Safe Quality Food (SQF) Level II, Food Safety Code for Manufacturing Edition 8.0*
Country of Origin:	*Mexico, United States of America*
Shelf Life:	*When handled under recommended storage, the product has a 730 day shelf life for optimum flavor and quality. Shelf life is printed on each package and case using a "Best By" date. The "Best By" date is the production date plus the determined appropriate shelf life time. The "Best By" date is displayed as Day/Month/Year and is printed with the format of DD/MM/YYYY*

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