

# Summary Report

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## Choline Chloride

### Prepared for:

Food and Drug Administration

Clinical use of bulk drug substances nominated for inclusion on the 503B Bulks List

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## REVIEW OF NOMINATIONS

Choline chloride (UNII code: 45I14D8O27) was nominated for inclusion on the 503B Bulks List by Fagron, American College for Advancement in Medicine (ACAM), McGuff Compounding Pharmacy Services, Inc, American Association of Naturopathic Physicians (AANP), Alliance for Natural Health USA (ANH-USA), and Integrative Medicine Consortium (IMC).

Choline chloride was nominated for oral and intravenous use. Orally choline chloride is used in liver disease including chronic hepatitis and cirrhosis; hypercholesterolemia; depression; memory loss; Alzheimer's disease and dementia; schizophrenia; body building; delaying fatigue in endurance sports; preventing neural tube defects; preventing cancer; Huntington's chorea; Tourette's disease; cerebellar ataxia; complex partial seizures; asthma; and as a supplement in infant formulas. Intravenously choline chloride is used for TPN-associated hepatic steatosis, choline deficiency, and fetal alcohol syndrome.

The nominated formulations include a 0.1 mg/mL injection, a 25-100mg/mL injection, and an injection in various concentrations and formulations in combination with other vitamins, supplements, and/or minerals, refer to Table 7 for the nominated combination formulas. Choline chloride will be administered via intravenous or intramuscular injection.

Reasons provided for nomination to the 503B Bulks List include:

- There are no FDA-approved injectable products containing choline chloride as a single active pharmaceutical ingredient (API) or in combination with other APIs.
- There are no FDA-approved medications to treat choline deficiency.
- Thousands of patients with metabolic disorders are prescribed and use choline chloride as a single preparation or a combination preparation by alternative and naturopathic physicians.

## METHODOLOGY

### *Background information*

The national medicine registers of 13 countries and regions were searched to establish the availability of choline chloride products in the United States (US) and around the world. The World Health Organization, the European Medicines Agency (EMA), and globalEDGE were used to identify regulatory agencies in non-US countries. The medicine registers of non-US regulatory agencies were selected for inclusion if they met the following criteria: freely accessible; able to search and retrieve results in English language; and desired information, specifically, product trade name, active ingredient, strength, form, route of administration (ROA) and approval status, provided in a useable format. Based on these criteria, the medicine registers of 13 countries/regions were searched: US, Canada, European Union (EU), United Kingdom (UK), Ireland, Belgium, Latvia, Australia, New Zealand, Saudi Arabia, Abu Dhabi, Hong Kong, and Namibia. Both the EMA and the national registers of select EU countries (Ireland, UK, Belgium, and Latvia) were searched because some medicines were authorized for use in the EU and not available in a member country and vice versa.

Each medicine register was searched for choline chloride; name variations of choline chloride were entered if the initial search retrieved no results. The following information from the search results of each register was recorded in a spreadsheet: product trade name; active ingredient(s); strength; form; ROA; status and/or schedule; approval date. Information was recorded only for products with strengths, forms, and/or ROA similar to those requested in the nominations.

In addition to the aforementioned medicine registers, the DrugBank database (version 5.1.4) and the Natural Medicines database were searched for availability of over-the-counter (OTC) products containing choline chloride. The availability of OTC products (yes/no) in the US and the ROA of these products were recorded in a spreadsheet. Individual product information was not recorded.

### *Systematic literature review*

#### Search strategy

Two databases (PubMed and Embase) were searched including any date through September 7, 2018. The search included a combination of (choline[TIAB] OR "choline chloride"[TIAB] OR "choline hydrochloride"[TIAB] OR "cholinium chloride"[TIAB]) AND (therapy[TIAB] OR therapeutic[TIAB] OR treatment[TIAB] OR hepat\*[tiab] OR "non-alcoholic fatty liver disease"[TIAB] OR atherosclerosis[TIAB] OR "fetal alcohol spectrum disorder"[TIAB] OR ped\*[TIAB] AND (humans[MeSH Terms] AND English[lang]) NOT autism). Peer-reviewed articles as well as grey literature were included in the search. Search results from each database were exported to Covidence®, merged, and sorted for removal of duplicate citations.

#### Study selection

Articles were not excluded on the basis of study design. Articles were considered relevant based on the identification of a clinical use of choline chloride or the implementation of choline chloride in clinical practice. Articles were excluded if not in English, a clinical use was not identified, incorrect salt form, or if the study was not conducted in humans. Screening of all titles, abstracts, and full-text were conducted independently by two reviewers. All screening disagreements were reconciled by a third reviewer.

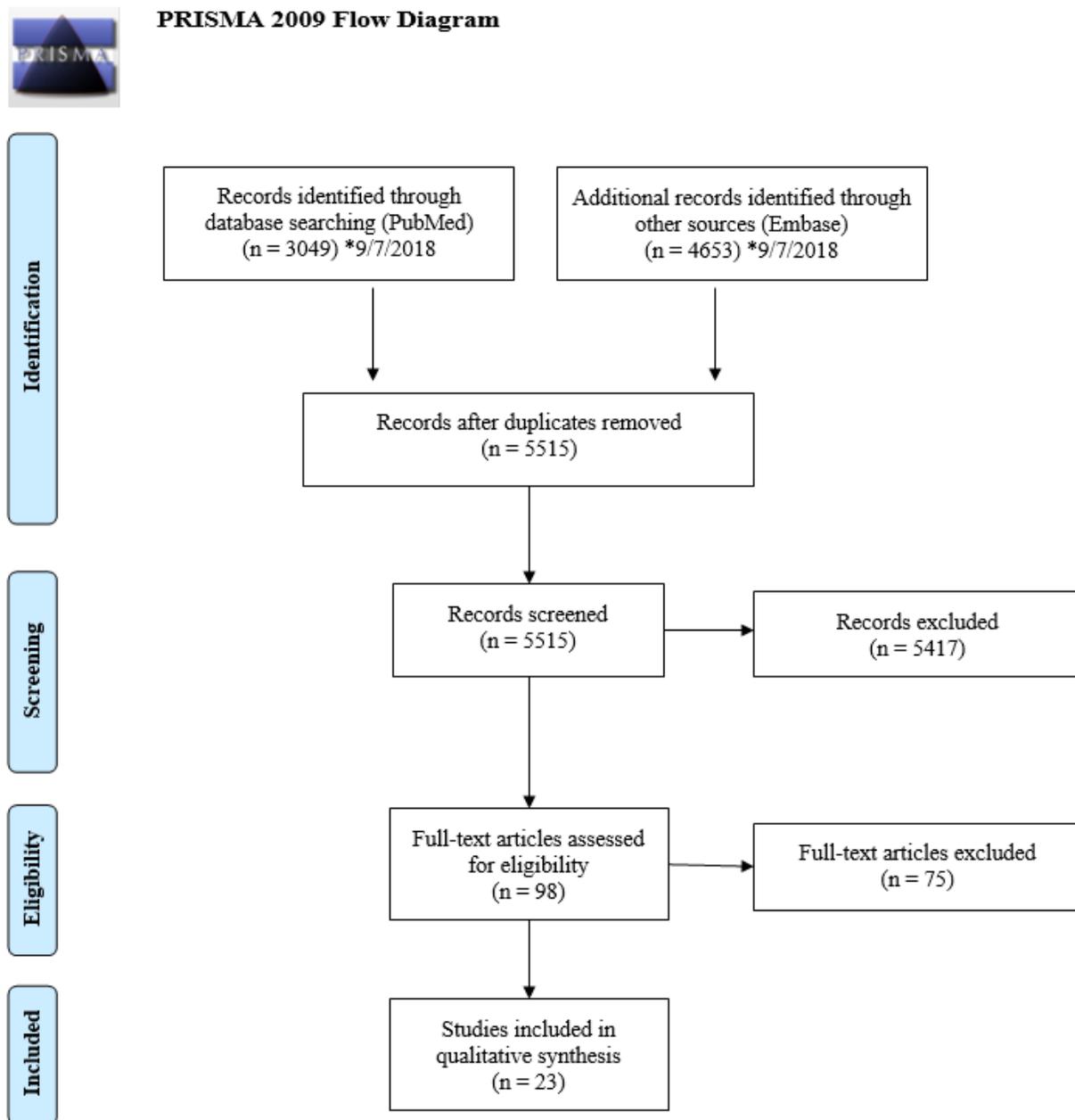
#### Data extraction

A standard data extraction form was used to collect study authors; article title; year published; journal title; country; indication for choline chloride use; dose; strength; dosage form; ROA; frequency and duration of therapy; any combination therapy utilized; if applicable, formulation of compounded products; study design; and any discussion surrounding the use of choline chloride compared to alternative therapies.

#### Results

Please refer to Figure 1.

Figure 1. Summary of literature screening and selection (PRISMA 2009 Flow Diagram)



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).

### *Outreach to medical specialists and specialty organizations*

Using the indications from the nominations and the results of the literature review, nine (9) medical specialties that would potentially use choline chloride were identified: cardiology, hematology, hepatology, naturopathy, neurology, pediatrics, psychiatry, primary care, and pulmonology. Semi-structured interviews were conducted with subject matter experts within these specialties. Interviews lasted from 30-75 minutes and were conducted either via telephone or in-person. Criteria for selecting subject matter experts included recommendations provided by specialty professional associations, convenient geographic location, authorship within the specialty, or referral by an interviewee. Up to nine (9) interviews were conducted per substance. To determine if a formal interview was warranted, medical experts in hepatology, neurology, and psychiatry were provided the list of substances pertinent to their specialty via email. The hepatologist and the psychiatrist replied that they do not utilize any of the substances listed. The neurologist failed to respond to the interview request. One (1) expert was contacted for an interview, of which one (1) accepted and zero (0) declined interviews. The interview was recorded and transcribed via ©Rev.com. QSR International's Nvivo 12 software was utilized for qualitative data analysis. The University of Maryland, Baltimore IRB and the Food & Drug Administration RIHSC reviewed the study and found it to be exempt. Subject matter experts provided their oral informed consent to participate in interviews.

### *Survey*

General professional medical associations and specialty associations for cardiology, hematology, hepatology, naturopathy, neurology, pediatrics, psychiatry, primary care, and pulmonology, identified from the nominations, literature review, and interviews, were contacted to facilitate distribution of an online survey. A Google™ search was conducted to identify relevant professional associations within each specialty. Associations were included if their members are predominantly practitioners, national associations, and organizations focused on practice within the US. Organizations without practicing physicians and state or regional organizations were excluded. The association's website was searched in order to identify the email of the executive director, regulatory director, media director, association president, board members, or other key leaders within the organization to discuss survey participation. If no contact information was available, the "contact us" tab on the association website was used.

An online survey was created using Qualtrics® software (Provo, UT). The survey link was distributed to twelve (12) associations. If an association had more than one (1) substance with indications relevant to that specialty, substances were combined into one (1) survey with no more than 14 substances per survey. Table 1 highlights the associations that agreed to distribute the survey link and Table 2 includes the associations that declined to participate. Additionally, single substance surveys were created and posted on the project website which was shared with survey participants.

Participation was anonymous and voluntary. The estimated time for completion was 30 minutes with a target of 50 responses per survey. The Office of Management and Budget (OMB) approved this project.

Table 1. Participating associations

Specialty	Association
Naturopathy	American Association of Naturopathic Physicians (AANP)
Pediatrics	American Academy of Pediatrics (AAP)
Primary Care	American Association of Environmental Medicine (AAEM)

Table 2. Associations that declined participation

Specialty	Association	Reasons for Declining
Hematology	American Society of Hematology (ASM)	Failed to respond
Hepatology	American Association for the Study of Liver Diseases (AASLD)	Failed to respond
Medicine	American Medical Association (AMA)	Failed to respond
	American Osteopathic Association (AOA)	Failed to respond
Neurology	American Academy of Neurology (AAN)	Failed to respond
Primary Care	American College of Physicians (ACP)	Failed to respond
	American Academy of Family Physicians (AAFP)	Failed to respond
Psychiatry	American Psychiatric Association (APA)	Declined, “we have put this ask to our members and unfortunately, we have not received any information on psychiatrists using compounded products”
Pulmonology	American Thoracic Society (ATS)	Failed to respond

## CURRENT AND HISTORIC USE

### *Summary of background information*

- Choline chloride is not available as an FDA-approved product.
- Choline chloride is not available as an OTC product in the US.
- There is a current United States Pharmacopeia (USP) dietary monograph for choline chloride.
- Choline chloride is not available in any of the foreign regulatory databases searched.

Table 3. Currently approved products – US

*No approved products in the US*

Table 4. Currently approved products – select non-US countries and regions

*No approved products in the selected non-US countries and region*

*Summary of literature review*

- Total number of studies included: 23 studies (6 descriptive, 14 experimental, and 3 observational).
- Most of the studies were from the US (14 studies).
- The most common indication in the US was for tardive dyskinesia followed by memory impairment in the elderly and then hepatic steatosis and Huntington’s disease. From the non-US studies, the most common indication was cerebellar and spinocerebellar ataxia.
- There were no combination products found identical to the nominator’s example combination. One (1) non-nominated combination was found consisting of choline chloride 100mg / folic acid 2mg / heparin sodium 25mg / niacinamide 50mg / vitamin B<sub>12</sub> 15 mcg.
- There were six (6) US studies with compounded products identified for hepatic steatosis, verbal and visual memory improvement, cystinuria, Huntington’s disease, tardive dyskinesia, manic-depressive illness, schizophrenia, and lipotrophic states in cardiovascular disease. Four (4) of the studies utilized choline chloride as an intravenous or intramuscular injection and two (2) studies used and oral solution. One (1) non-US study used a 0.1% oral solution as a compounded product for Huntington’s disease.

Table 5. Types of studies

Types of Studies	Number of Studies
Descriptive <sup>1-6</sup>	6
Experimental <sup>7-20</sup>	14
Observational <sup>21-23</sup>	3

Table 6. Number of studies by country

Country	Number of Studies
Chile <sup>16</sup>	1
Germany <sup>8</sup>	1
India <sup>15</sup>	1
Japan <sup>6</sup>	1
Sweden <sup>7</sup>	1
The Netherlands <sup>2</sup>	1
UK <sup>3,13,14</sup>	3
US <sup>1,4,5,9-12,17-23</sup>	14
Total US: 14 Total non-US Countries: 9	

Table 7. Number of studies by combinations

	Combination Formula	Number of Studies
<b>Nominated</b>	Choline chloride 50mg/ Inositol 50mg/ L-methionine 25mg	0
Others found in literature	Choline chloride 100mg/ Folic acid 2mg/ Heparin sodium 25mg/ Niacinamide 50mg/ Vitamin B <sub>12</sub> 15 mcg <sup>19</sup>	1

Table 8. Dosage by indication – US

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Tardive dyskinesia <sup>1,12,22,23</sup>	150-200mg/kg/day	–	–	Oral	6-8 weeks
	4-20g/day	0.5g/mL	–		29-56 days
Memory impairment in elderly <sup>5,17,20</sup>	9-20g/day	–	–	Oral	7-28 days
Hepatic steatosis <sup>9,10</sup>	1-4g/day	50%	Solution	Intra venous	6-24 weeks
Huntington’s disease <sup>22,23</sup>	4-20g/day	0.5g/mL	Solution	Oral	29-40 days
Cystinuria <sup>21</sup>	3-8g/day	25%	Elixir	Oral	–
Hepatic cirrhosis <sup>4</sup>	1.5-6g/day	–	–	–	–
Infectious hepatitis <sup>4</sup>	20g/day	–	–	–	2-3 weeks
Korsakoff’s syndrome <sup>18</sup>	10.4-18.2g/day	–	–	Oral	3 weeks
Lipotrophic states in cardiovascular disease <sup>19</sup>	2mL	0.1g/mL	Injection	Intramuscular	As needed
Manic-Depressive Illness <sup>22</sup>	4-20g/day	0.5g/mL	–	–	29-40 days
Pernicious anemia <sup>4</sup>	1g/day	5%	Solution	Intra venous	–
Schizophrenia <sup>22</sup>	4-20g/day	0.5g/mL	–	–	29-40 days
Verbal and visual memory improvement <sup>11</sup>	2g/day	–	Solution	Intra venous	24 weeks

Abbreviations: “–”, not mentioned; ROA, route of administration

Table 9. Dosage by indication – non-US countries

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Cerebellar <sup>6,13</sup> and spinocerebellar ataxia <sup>14</sup>	4-12g/day	–	–	Oral	6-12 weeks
	150mg/kg/day			–	–
Asthma (immune inflammation and bronchial hyperreactivity) <sup>15</sup>	3g/day	–	–	Oral	6 months
Edema <sup>2</sup>	3g/day	–	–	Oral	14 days
Hepatic steatosis <sup>8</sup>	3g/day	1g	–	Oral	90 days
Huntington's disease <sup>7</sup>	3-15g/day	–	Solution	Oral	–
Megaloblastic anemias <sup>3</sup>	3-10g/day	–	Solution	Oral	–
	1-10g/day	–		Intravenous	16 days
Nutritional dystrophy <sup>16</sup>	0.32g/day	–	–	Oral	1-53 days

Abbreviations: “–”, not mentioned; ROA, route of administration

Table 10. Compounded products – US

Indication	Publication Year	Compounding Method	Dosage Form	Final Strength
Hepatic steatosis <sup>9,10</sup>	2005, 1995	<ul style="list-style-type: none"> <li>Choline chloride 1-4g added to total parenteral nutrition (TPN)</li> </ul>	Solution	–
Verbal and visual memory improvement <sup>11</sup>	2000	<ul style="list-style-type: none"> <li>Choline chloride 2g added to TPN</li> </ul>	Solution	–
Cystinuria <sup>21</sup>	1954	<ul style="list-style-type: none"> <li>Choline chloride 250g</li> <li>Distilled water 150mL</li> <li>Raspberry syrup 1000mL</li> </ul>	Solution	25%
Huntington’s disease, tardive dyskinesia, manic-depressive illness, schizophrenia <sup>22</sup>	1978	<ul style="list-style-type: none"> <li>Dissolved in distilled water and flavored with strawberry syrup</li> </ul>	Solution	0.5g/mL
Lipotrophic states in cardiovascular disease <sup>19</sup>	1955	<ul style="list-style-type: none"> <li>“Hep-Nine B prepared by The Columbus Pharmacal Company, Columbus, Ohio”</li> <li>Each cc contains:                             <ul style="list-style-type: none"> <li>Heparin Sodium (2500 units) 25mg</li> <li>Choline Chloride 100mg</li> <li>Vitamin B<sub>12</sub> 15mcg</li> <li>Folic Acid 2mg</li> <li>Niacinamide 50mg</li> </ul> </li> </ul>	Solution	100mg/mL

Abbreviation: “–”, not mentioned.

Table 11. Compounded products – non-US countries

Indication	Compounding Method	Dosage Form	Final Strength
Huntington’s disease <sup>7</sup>	<ul style="list-style-type: none"> <li>Choline chloride: 100 mg</li> <li>Liquor pectoralis: 60 mL</li> <li>Distilled water: to 1000 mL</li> </ul>	Solution	0.1%

*Summary of focus groups/interviews of medical experts and specialty organizations*

Two (2) interviews were conducted with the same person. A Medical Doctor (MD) specializing in hepatology, an MD specializing in psychiatry, and an MD specializing in psychiatry were provided the list of substances pertinent to their specialty via email, which included choline chloride. Per the hepatologist, choline chloride has no indication in liver disease. The psychiatrist does not use choline chloride. The neurologist failed to respond to the interview request.

Table 12. Overview of interviewees

Interviewee	Level of Training	Specialty	Current Practice Setting	Experience with Choline Chloride	Interview Summary Response
NAT_01B, NAT_02	ND	None	Private practice	Yes	<ul style="list-style-type: none"> <li>Sometimes uses supplements like lecithin or phosphatidylcholine that contains choline chloride; more experience with choline only.</li> </ul>

Abbreviation: ND, Naturopathic Doctor

- Use of choline chloride
  - Interviewee stated “we use that [choline chloride] in our brain IVs, so IV form, and then we would use it for neurodegenerative illnesses, and then as a repletion if we do a vitamin/mineral analysis.”
  - Uses in an IV formulation for antiaging
  - Uses supplements, like lecithin or phosphatidylcholine, that contain choline chloride
- Administration of choline chloride
  - Intravenous administration
  - Weight-based dosing
- Need for office-stock
  - Interviewee stated stocks in office however did not supply any additional details regarding the need

*Summary of survey results*

Table 13. Characteristics of survey respondents [29 people responded to the survey<sup>a</sup>]

<b>Board Certification</b>	<b>MD</b>	<b>ND</b>	<b>PharmD</b>	<b>No Response</b>
Anesthesiology	7	0	0	0
Critical Care Medicine	3	0	0	0
Clinical Pharmacology	1	0	0	0
Gastroenterology	1	0	0	0
Fellow of the American Board of Naturopathic Oncology	0	1	0	0
Hospice & Palliative Medicine	1	0	0	0
Naturopathic Doctor	0	6	0	0
Naturopathic Physician	0	5	0	0
Pediatrics	4	0	0	0
Pediatric Anesthesiology	3	0	0	0
No Board Certification	1	2	1	0
No Response	0	0	0	7

Abbreviations: MD, Doctor of Medicine; ND, Naturopathic Doctor; PharmD, Doctor of Pharmacy

<sup>a</sup>Some respondents reported more than one terminal clinical degree or board certification.

Table 14. Types of products used, prescribed, or recommended

<b>Types of Products</b>	<b>Respondents, n (N=2<sup>a</sup>)</b>
Compounded	1 <sup>b</sup>
FDA-approved	0
Over-the-counter	0
Dietary	1
Unsure	0
No response	0

<sup>a</sup>Out of 29 respondents, two (2) reported using, prescribing, or recommending choline chloride products.

<sup>b</sup>One (1) respondent used in combination: “Choline chloride 50mg / Inositol 50mg / L-methionine 25mg”.

Table 15. Compounded use of choline chloride in practice

*No survey respondents provided this information*

Table 16. Indications for which choline chloride is considered a standard therapy

<b>Indication</b>	<b>Standard Therapy</b>	
	<b>Compounded, n (N=1)</b>	<b>Non-Compounded, n (N=1)</b>
Prenatal support	0	1
No response	1	0

Table 17. Reasons for using a compounded product instead of any FDA-approved products

<b>Reasons</b>
“fat metab”

Table 18. Change in frequency of compounded choline chloride usage over the past 5 years

	<b>Respondents, n (N=1)</b>
No - use has remained consistent	0
Yes - I use it LESS often now	0
Yes - I use it MORE often now	1

Table 19. Do you stock non-patient specific compounded choline chloride in your practice?

	<b>Respondents, n (N=1)</b>
No	1
Yes	0

Table 20. Questions related to stocking non-patient specific compounded choline chloride

*No survey respondents provided information for this section*

## **CONCLUSION**

Choline chloride (UNII code: 45I14D8O27) was nominated for inclusion on the 503B Bulks List for oral and intravenous use. Orally choline chloride is used in liver disease including chronic hepatitis and cirrhosis; hypercholesterolemia; depression; memory loss; Alzheimer’s disease and dementia; schizophrenia; body building; delaying fatigue in endurance sports; preventing neural tube defects; preventing cancer; Huntington's chorea; Tourette's disease; cerebellar ataxia; complex partial seizures; asthma; and as a supplement in infant formulas. Intravenously choline chloride is used for TPN-associated hepatic steatosis, choline deficiency, and fetal alcohol syndrome.

The nominated formulations include a 0.1 mg/mL injection, a 25-100mg/mL injection, and an injection in various concentrations and formulations in combination with other vitamins, supplements, and/or minerals, refer to Table 7 for the nominated combination formulas. Choline chloride will be administered via intravenous or intramuscular injection. Choline chloride was not available in any of the foreign regulatory databases searched.

From the literature review conducted, the most common indications in the US were for tardive dyskinesia followed by memory impairment in the elderly, hepatic steatosis, and Huntington’s disease. From the non-US studies, the most common indications were cerebellar and spinocerebellar ataxia. There were no combination products found identical to the nominator’s example combination. There were six (6) US studies with compounded products identified for hepatic steatosis, verbal and visual memory improvement, cystinuria, Huntington’s disease, tardive dyskinesia, manic-depressive illness, schizophrenia, and lipotropic states in cardiovascular disease. Four (4) of the studies utilized choline chloride as an intravenous or intramuscular injection and two (2) studies used and oral solution. One (1) non-US study used a 0.1% oral solution as a compounded product for Huntington’s disease.

From the interviews, the interviewee sometimes used supplements like lecithin or phosphatidylcholine that contain choline chloride. The hepatologist and psychiatrist contacted both stated that they do not use choline chloride.

From the survey responses, two (2) out of 29 respondents used choline chloride. One (1) respondent reported using compounded choline chloride in combination with inositol 50mg and L-methionine 25mg.

## APPENDICES

### Appendix 1. References

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## Appendix 2. Survey instrument

### Start of Block: Welcome Page

The University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in collaboration with the Food and Drug Administration (FDA), is conducting research regarding the use of certain bulk drug substances nominated for use in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act. In particular, we are interested in the current and historic use of these substances in clinical practice. This survey is for **choline chloride**. As a medical expert, we appreciate your input regarding the use of this substance in your clinical practice. This information will assist FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Act. All responses are anonymous.

OMB Control No. 0910-0871

Expiration date: June 30, 2022

The time required to complete this information collection is estimated to average 30 minutes, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

If you have additional questions or concerns about this research study, please email: [compounding@rx.umaryland.edu](mailto:compounding@rx.umaryland.edu). If you have questions about your rights as a research subject, please contact HRPO at 410-760-5037 or [hrpo@umaryland.edu](mailto:hrpo@umaryland.edu).

### End of Block: Welcome Page

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### Start of Block: Choline chloride

Q1. What type(s) of product(s) do you use, prescribe, or recommend for **choline chloride**? Please check all that apply.

- Compounded drug product
- FDA-approved drug product
- Over the counter drug product
- Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- Unsure

*Skip To: Q14 If What type(s) of product(s) do you use, prescribe, or recommend for choline chloride? Please check all th... != Compounded drug product*

*Skip To: Q3 If What type(s) of product(s) do you use, prescribe, or recommend for choline chloride? Please check all th... = Compounded drug product*

*Display This Question:*

*If What type(s) of product(s) do you use, prescribe, or recommend for choline chloride? Please check all th... = Compounded drug product*

Q2. Please list any conditions or diseases for which you use compounded **choline chloride** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe)						
Condition 2 (please describe)						
Condition 3 (please describe)						
Condition 4 (please describe)						
Condition 5 (please describe)						

Q3. Do you use compounded **choline chloride** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- Single
- Combination

*Skip To: Q6 If Do you use compounded choline chloride as a single agent active ingredient, or as one active ingredient... != Combination*

*Display This Question:*

*If Loop current: Do you use compounded choline chloride as a single agent active ingredient, or as one active ingredient... = Combination*

Q4. In which combination(s) do you use compounded **choline chloride**? Please check all that apply.

- Choline chloride 50mg / Inositol 50mg / L-methionine 25mg
- Other (please describe) \_\_\_\_\_

Q5. For which, if any, diseases or conditions do you consider compounded **choline chloride** standard therapy? \_\_\_\_\_

Q6. Does your specialty describe the use of compounded **choline chloride** in medical practice guidelines or other resources? \_\_\_\_\_

Q7. Over the past 5 years, has the frequency in which you have used compounded **choline chloride** changed?

- Yes - I use it **MORE** often now (briefly describe why) \_\_\_\_\_
- Yes - I use it **LESS** often now (briefly describe why) \_\_\_\_\_
- No - use has remained consistent

Q8. Why do you use compounded **choline chloride** instead of any FDA-approved drug product?

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Q9. Do you stock non-patient-specific compounded **choline chloride** in your practice location?

- Yes
- No

*Skip To: End of Block If Do you stock non-patient-specific compounded choline chloride in your practice location? = No*

*Display This Question:*

*If Do you stock non-patient-specific compounded choline chloride in your practice location? = Yes*

Q10. In what practice location(s) do you stock non-patient-specific compounded **choline chloride**? Please check all that apply.

- Physician office
- Outpatient clinic
- Emergency room
- Operating room
- Inpatient ward
- Other (please describe) \_\_\_\_\_

Q11. How do you obtain your stock of non-patient-specific compounded **choline chloride**? Please check all that apply.

- Purchase from a compounding pharmacy
- Purchase from an outsourcing facility
- Compound the product yourself
- Other (please describe) \_\_\_\_\_

Q12. Why do you keep a stock of non-patient-specific compounded **choline chloride**? Please check all that apply.

- Convenience
- Emergencies
- Other (please describe) \_\_\_\_\_

*Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded choline chloride? Please check all that apply. = Convenience*

*Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded choline chloride? Please check all that apply. = Emergencies*

*Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded choline chloride? Please check all that apply. = Other (please describe)*

Q13. For which, if any, diseases or conditions do you consider **choline chloride** standard therapy?

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Q14. Does your specialty describe the use of **choline chloride** in medical practice guidelines or other resources? \_\_\_\_\_

**End of Block: Choline chloride**

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**Start of Block: Background Information**

Q15. What is your terminal clinical degree? Please check all that apply.

- Doctor of Medicine (MD)
- Doctor of Osteopathic Medicine (DO)
- Doctor of Medicine in Dentistry (DMD/DDS)
- Naturopathic Doctor (ND)
- Nurse Practitioner (NP)
- Physician Assistant (PA)
- Other (please describe) \_\_\_\_\_

Q16. Which of the following Board certification(s) do you hold? Please check all that apply.

- No Board certification
- Allergy and Immunology
- Anesthesiology
- Cardiovascular Disease
- Critical Care Medicine
- Dermatology
- Emergency Medicine
- Endocrinology, Diabetes and Metabolism
- Family Medicine
- Gastroenterology
- Hematology
- Infectious Disease
- Internal Medicine
- Medical Toxicology
- Naturopathic Doctor
- Naturopathic Physician
- Nephrology
- Neurology
- Obstetrics and Gynecology
- Oncology
- Ophthalmology
- Otolaryngology
- Pain Medicine
- Pediatrics
- Psychiatry
- Rheumatology
- Sleep Medicine
- Surgery (please describe) \_\_\_\_\_
- Urology
- Other (please describe) \_\_\_\_\_

End of Block: Background Information