Summary Report

Sodium Selenite Pentahydrate

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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

Sodium selenite pentahydrate (UNII code: HIW548RQ3W) was nominated for inclusion on the 503B Bulks List by the Outsourcing Facilities Association (OFA) and Olympia Compounding Pharmacy for selenium supplementation as an intramuscular and intravenous injections with doses ranging from 4-200mcg/mL.

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

- There are no FDA-approved products containing this substance.
- A patient may need a prescribed dosage form or strength that is not commercially available.
- Commercially available products may contain excipients such as fillers and preservatives that cannot be tolerated due to patient sensitivities or allergies.
- Manufacturer backorder.

METHODOLOGY

Background information

The national medicine registers of 13 countries and regions were searched to establish the availability of sodium selenite pentahydrate 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 sodium selenite pentahydrate; name variations of sodium selenite pentahydrate 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; 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 sodium selenite pentahydrate. 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 February 28, 2019. The search included a combination of ("sodium selenite pentahydrate"[TIAB] OR "sodium biselenite"[Title/Abstract] OR "disodium selenite"[TIAB] OR "selenite sodium"[TIAB] OR "sodium selenite"[TIAB] OR "selenous acid"[TIAB]) AND (treat*[TIAB] OR therap*[TIAB] OR clinical[TIAB] OR supplement*[TIAB] OR nutrition*[TIAB] OR antiox*[TIAB] OR "trace

element*"[TIAB] OR deficienc*[TIAB]) 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 sodium selenite pentahydrate or the implementation of sodium selenite pentahydrate 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.

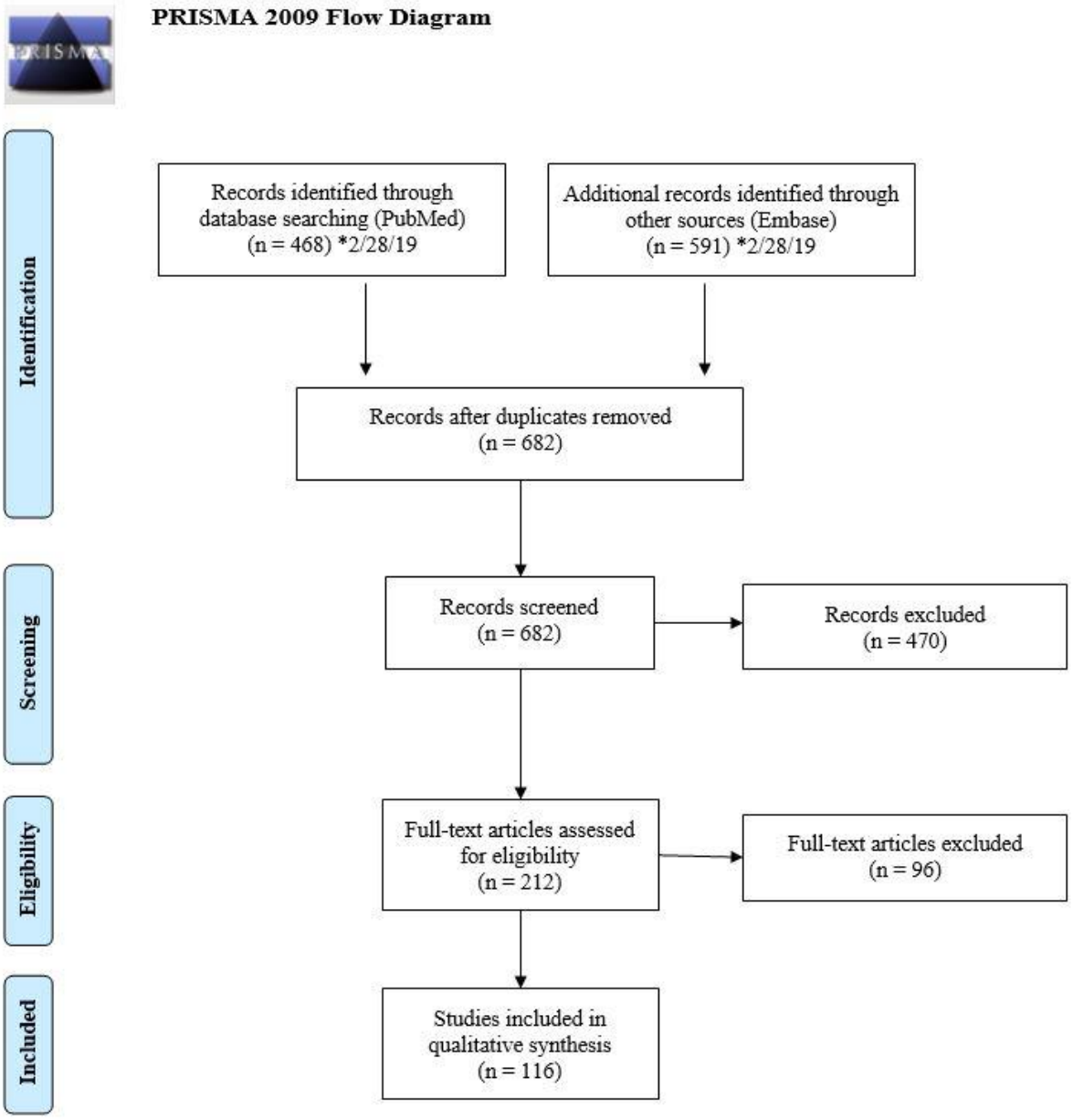
Data extraction

A standard data extraction form was used to collect study authors; article title; year published; journal title; country; indication for sodium selenite pentahydrate 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 sodium selenite pentahydrate 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). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Outreach to medical specialists and specialty organizations

Using the indication from the nomination and the results of the literature review, 10 medical specialties that would potentially use sodium selenite pentahydrate were identified: allergy, cardiology, gastroenterology, hepatology, immunology, naturopathy, oncology, pediatrics, primary care, and surgery. To determine if a formal interview was warranted, medical experts in gastroenterology, hepatology, and oncology were provided the list of substances pertinent to their specialty via email. The gastroenterologist and hepatologists replied that they do not utilize any of the substances listed. The oncologist failed to respond to the interview request. No interviews were conducted.

Survey

General professional medical associations and specialty associations for allergy, cardiology, gastroenterology, hepatology, immunology, naturopathy, oncology, pediatrics, primary care, and surgery, identified from the nomination and literature review, 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 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
Allergy/Immunology	American Academy of Allergy, Asthma and Immunology (AAAAI)
Naturopathy	American Association of Naturopathic Physicians (AANP)
Pediatrics	American Academy of Pediatrics (AAP)
Primary Care	American Academy of Environmental Medicine (AAEM)

Table 2. Associations that declined participation

Specialty	Association	Reasons for Declining
Gastroenterology	American Gastroenterological Association (AGA)	Failed to respond
Hepatology	American Association for the Study of Liver Diseases (AASLD)	Failed to respond
Oncology	American Society of Clinical Oncology (ASCO)	Declined
Medicine	American Medical Association (AMA)	Failed to respond
	American Osteopathic Association (AOA)	Failed to respond
Primary Care	American Academy of Family Physicians (AAFP)	Failed to respond
	American College of Physicians (ACP)	Failed to respond
Surgery	American College of Surgeons (ACS)	Failed to respond

CURRENT AND HISTORIC USE

Summary of background information

- Sodium selenite pentahydrate is not available as an FDA-approved product. However, selenious acid is FDA-approved as a 60mcg base/mL intravenous solution as of April 30, 2019. Selenious acid is also available as a solution for injection in combination with other trace elements as an unapproved drug in the US. These products are available under the trade names Multitrace-5 (32.7mcg/mL) and Multitrace-5 Concentrate (98mcg/mL).
- Sodium selenite pentahydrate is available as an oral OTC product in the US. Additional salt forms are also available.
- There is no current United States Pharmacopeia (USP) monograph for sodium selenite pentahydrate. There is a reagent monograph for sodium selenite.
- Sodium selenite is available in Abu Dhabi, Belgium, Hong Kong, and the UK (see Table 4).

Table 3. Currently approved products – US

No approved products in the US

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

Active Ingredient	Concentration	Dosage Form	ROA	Approved For Use		
				Country	Status	Approval Date[b]
Sodium selenite	21.9mcg/mL	Solution	Intravenous	Belgium	Medical prescription	12/01/2013
		Concentrate for solution	Infusion	UK	Prescription only medicine	06/25/2018
	40mcg/mL	Solution	–	Abu Dhabi	Active	–
	50mcg/mL	Solution	Injection	Hong Kong	Prescription only medicine	07/20/2015

Abbreviations: "–", not mentioned; ROA, route of administration.

[a]Medicine registers of national regulatory agencies were searched if they met the following criteria: freely accessible; able to search and retrieve results in English language; and desired information (product trade name, active ingredient, strength, form, ROA and approval status) provided in a useable format. Information was recorded only for products with strengths, forms and/or ROA similar to those requested in the nominations. See Methodology for full explanation.

[b]If multiple approval dates and/or multiple strengths, then earliest date provided.

Summary of literature review

- Total number of studies included: 116 studies (11 descriptive and 105 experimental studies).
- Most of the studies were from the Germany (37).
- The most common indication for the use of sodium selenite pentahydrate in the US was selenium supplementation. The most common indications from the non-US studies were selenium supplementation, sepsis/septic shock, systemic inflammatory response syndrome (SIRS), and autoimmune thyroiditis.
- Compounded products were identified from both US and non-US studies. However, neither reflected the nominated dosage forms or ROA, only the nominated indication for selenium supplementation.

Table 5. Types of studies

Types of Studies	Number of Studies
Descriptive[1-11]	11
Experimental[12-116]	105
Observational	0

Table 6. Number of studies by country

Country	Number of Studies
Austria[60,63,64,68]	4
Brazil[15]	5
China[14,43,74,113,114]	5
Czech Republic[55,56]	2
Denmark[93,94]	2
Egypt[19-21,98]	4
Finland[13,90,110,111]	4
France[47,76,91,95,97]	5
Germany[8,11,16-18,26-30,33-39,45,48,49,58,69,70,72,77-80,82-86,89,92,105,116]	37
Greece[7]	1
Hungary[112]	1
Iran[41,62,75]	3

Italy[1,25,51,87]	4
Japan[4,5,10,12,59,109]	6
The Netherlands[9]	1
New Zealand[96,106,107]	3
Nigeria[61]	1
Poland[73]	1
Scotland[6]	1
Serbia[42]	1
Slovak Republic[54,67]	2
Sweden[22-24,52,57,99,100]	7
Switzerland[102]	1
Turkey[115]	1
Ukraine[46,66]	2
UK[31,32,44,53,71,81,88,101]	8
US[2,40,50,65,103,108]	6
Multiple Countries • Canada, US, Belgium, Switzerland, Germany[104] • Germany, Switzerland, UK, Italy[3]	
	Total US[a]: 7 Total Non-US Countries[a]: 110

[a]Study 104 counted in both US and non-US total.

Table 7. Number of studies by combinations

No combination products were nominated

Table 8. Dosage by indication – US

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Selenium supplementation[2,40,108]	240µg/day	–	Solution	Intravenous	3-4 months
	200-600µg/day	–	Capsule, Tablet	Oral	3-4 months
Cardiac surgery[104]	2000µg bolus twice, 1000µg/day	–	Solution	Intravenous	Up to 10 days
Immune benefit[65]	200µg/day	–	Tablet	Oral	8 weeks
Phagocytic function of polymorphonuclear leukocytes (PMNs)[50]	400µg/day	–	–	Oral	2 weeks
Selenium supplementation in preterm infants[103]	4.75-5µg/kg/day	34.8ng/mL	Solution	Oral	3 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
Selenium supplementation [5,31,32,57,59,74,86,90,93,100,106,107,113]	1000-1400µg/week	–	Solution	Intravenous	4 months
	50-300µg/day	–	Tablet, Capsule, Yeast/wheat	Oral	14 days-5 years
Sepsis, Septic shock, and Severe inflammatory response syndrome (SIRS)[16-18,29,41,47,54,67,81,98,112]	35-3000µg/day	–	Solution	Intravenous	5-21 days
Autoimmune thyroiditis[9,30,42,45,48,49,60,62,87]	80-200µg/day	–	Tablet	Oral	3 months-1 year
Radioprotection[35-38,77,79,82-85]	500-1000µg/day	–	–	Intravenous	3 weeks
	300-1000µg/day	–	Solution, Tablet	Oral	5 weeks-6 years
	350µg/m^2	–	–	–	2 weeks

Lymphedema[34,39,64,78,116]	1000µg/day	–	Solution	Intravenous	3 weeks
	500-1000µg/day	–	Solution, Tablet	Oral	3-8 weeks
	2000µg/day	–	–	–	–
Muscular dystrophy[13,22-24,53]	1000µg/day	–	–	Oral	2 months-2 years
Parenteral nutrition[4,6,76,94,109]	15-200,000µg/day	–	Solution	Intravenous	2 weeks-1 year
	100µg/day	–	–	Oral	–
Cardiac surgery[102,104,105]	1000-4000µg/day	–	Solution	Intravenous	10-16 days
Hemodialysis[68,95,97]	350-1,200,000µg/week	–	Solution	Intravenous	8-20 weeks
	200-500µg/day	–	Solution	Oral	6 months
Non-Hodgkin's lymphoma[19-21]	200µg/kg/day		Solution	Oral	5-30 days
Oxidative stress[75,101,115]	1000-4000µg/day	–	Solution	Intravenous	10 days
	200µg/day	–	Tablet	Oral	45 days
Reduce hormone therapy side effects[26-28]	300µg/day	–	–	Oral	4 weeks-50 days
Cancer prevention[3,114]	–	15ppm	Table salt	Oral	5 years
Chronic renal failure[25] and increasing renal glomerular filtration rate[51]	10µg/kg/day	–	–	Oral	10 weeks
	100-700µg/day	–	–		
Graves' hyperthyroidism[58] and Graves' ophthalmopathy[1]	200-300µg/day	–	Tablet	Oral	24 weeks
Oxidative stress post-cardiac arrest[55,56]	2000µg/day	–	–	Intravenous	5 days

Anxiety and depression[71]	1000μg/day	–	Capsule	Oral	2 years
Atopic dermatitis[92]	7.5-15μg/kg/day	–	Solution	Oral	6 weeks
Brain tumor[89]	1000μg/day	–	Solution	Intravenous	4-8 weeks
Blood fluidity[12]	200μg/day	–	–	–	2 weeks
Chagasic cardiomyopathy[15]	100μg/day	–	Capsule	Oral	1 year
Chronic pancreatitis[46]	200-300μg/day	–	–	–	30 days
Cystic fibrosis[91]	2.8μg/kg/day	–	–	–	5 months
Down's syndrome[110]	15-25μg/kg/day	–	–	Oral	0.3-1.5 years
Enteral nutrition[10]	100μg/day	–	Solution	Intravenous	10 days
	60μg/day	–	–	Oral	30-60 days
Erysipelas prophylaxis in secondary lymphedema[63]	100,000-200,000μg/day	–	–	Oral	3 months
Fibromuscular rheumatism[96]	90-500μg/day	–	Capsule, Solution	Oral	20 days-4 weeks
HIV infection[72]	500μg/day	–	Solution	Oral	24 weeks
Hypertension[80]	500μg/day	–	Tablet	Oral	5-6 weeks
Hypothyroidism[8]	10μg/kg/day	–	Solution	Oral	4 weeks
Intrinsic asthma[52]	100μg/day	–	Tablet	Oral	14 weeks
Kashin-Beck disease[43]	200μg/day	–	–	Oral	12 weeks
Keshan disease[14]	100μg/day	–	Tablet	Oral	12 weeks
Lyell's syndrome[11]	500-1000μg/day	–	Solution	Intravenous	19 days

Lymphocyte gene expression[88]	100µg/day	–	Tablet	Oral	6 weeks
Multiple sclerosis[111]	20-40µg/kg/day	–	Tablet	Oral	10 months
Peripartum cardiomyopathy[61]	200µg/day	–	Tablet	Oral	3 months
Peripheral arterial occlusive disease[70]	500µg once	–	Solution	Intravenous	Once
Phototherapy[44]	400µg/day	–	–	Oral	4 weeks
Radioactive iodine therapy[7]	300µg	–	Tablet	Oral	10 days
Short bowel syndrome[99]	50µg/day	–	Tablet	Oral	27-54 weeks
Subclinical hypothyroid dysfunction[66]	200,000µg/day	–	Tablet	Oral	6 months

Abbreviations: "–", not mentioned; ROA, route of administration.

Table 10. Compounded products – US

Indication	Publication Year	Compounding Method	Dosage Form	Final Strength
Selenium supplementation[40]	2006	• Sodium selenite with Fast-Flo Edible Lactose	Capsule	200-600µg/capsule

Table 11. Compounded products – non-US countries

Indication	Compounding Method	Dosage Form	Final Strength
Selenium supplementation[74]	• Sodium selenite with lactose and starch	Tablet	150µg/tablet

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

No interviews were conducted.

Table 12. Overview of interviewees

No interviews were conduced

Summary of survey results

Table 13. Characteristics of survey respondents [31 people responded to the survey.[a]]

Board Certification	MD	ND	PharmD	PhD	No Response
Allergy and Immunology	1	0	0	0	0
Anesthesiology	7	0	0	0	0
Cardiovascular Disease	0	0	0	0	1
Clinical Pharmacology	1	0	0	0	0
Critical Care Medicine	3	0	0	0	0
Gastroenterology	1	0	0	0	0
Hospice and Palliative Medicine	1	0	0	0	0
Naturopathic Doctor	0	5	0	0	0
Naturopathic Physician	0	4	0	0	0
Pediatric Anesthesiology	3	0	0	0	0
Pediatrics	5	0	0	0	0
No Board Certification	0	0	1	1	0
No Response	0	0	0	0	11

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

[a]Some respondents reported more than one terminal clinical degree or board certification.

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

Types of Products	Respondents, n (N=2[a])
Compounded	0
FDA-approved	0
Over-the-counter	0
Dietary	1
Unsure	0
No Response	1

[a]Out of 31 respondents, two (2) reported using, prescribing, or recommending sodium selenite pentahydrate products.

Table 15. Compounded use of sodium selenite pentahydrate in practice

No survey respondents provided this information

Table 16. Indications for which sodium selenite pentahydrate is considered a standard therapy[a]

Indication	Standard Therapy		
	Compounded, n (N=0)	Non-compounded, n (N=1)	No Response, n (N=1)
Dandruff	0	1	0
Topical Fungal Infection	0	1	0
No Response	0	0	1

[a]Some respondents reported more than one (1) indication.

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

No survey respondents provided this information

Table 18. Change in frequency of compounded sodium selenite pentahydrate usage over the past 5 years

No survey respondents provided this information

Table 19. Do you stock non-patient specific compounded sodium selenite pentahydrate in your practice?

No survey respondents provided this information

Table 20. Questions related to stocking non-patient specific compounded sodium selenite pentahydrate

No survey respondents provided this information

CONCLUSION

Sodium selenite pentahydrate (UNII code: HIW548RQ3W) was nominated for inclusion on the 503B Bulks List for selenium supplementation as an intramuscular and intravenous injections with doses ranging from 4-200mcg/mL. Sodium selenite pentahydrate is not available as an FDA-approved product, but selenious acid was recently approved as a 60mcg base/mL intravenous solution as a source of selenium for parenteral nutrition. Sodium selenite pentahydrate is available as an oral OTC product in the US; there is no USP monograph for this substance. Sodium selenite pentahydrate is available in Abu Dhabi, Belgium, Hong Kong, and the UK.

From the literature review, the most common indication in the US was selenium supplementation. The most common indications from the non-US studies were selenium supplementation, sepsis/septic shock, SIRS, and autoimmune thyroiditis. Compounded products were identified from both US and non-US studies for the nominated indication, but not as intramuscular or intravenous injections.

No interviews were conducted.

Out of 31 survey respondents, only two (2) reported using, prescribing, or recommending sodium selenite pentahydrate. None reported using compounded product, but one (1) reported using dietary supplements and considering sodium selenite pentahydrate standard therapy for dandruff and topical fungal infections.

APPENDICES

Appendix 1. References

1. Bartalena L. Prevention of Graves' ophthalmopathy. *Best Practice and Research: Clinical Endocrinology and Metabolism.* 2012;26(3):371-379.
2. Cohen HJ, Chovaniec ME, Mistretta D, Baker SS. Selenium repletion and glutathione peroxidase - Differential effects on plasma and red blood cell enzyme activity. *American Journal of Clinical Nutrition.* 1985;41(4):735-747.
3. Dennert G, Zwahlen M, Zeegers M, Vinceti M. Selenium for prevention and treatment of cancer. *Onkologie.* 2010;33(6):87.
4. Ishida T, Himeno K, Torigoe Y, et al. Selenium deficiency in a patient with Crohn's disease receiving long-term total parenteral nutrition. *Internal Medicine.* 2003;42(2):154-157.
5. Kanekura T, Yotsumoto S, Maeno N, et al. Selenium deficiency: Report of a case. *Clinical and Experimental Dermatology.* 2005;30(4):346-348.
6. Kelly DA, Coe AW, Shenkin A, Lake BD, Walker-Smith JA. Symptomatic selenium deficiency in a child on home parenteral nutrition. *Journal of Pediatric Gastroenterology and Nutrition.* 1988;7(5):783-786.
7. Mazokopakis E. Differentiated thyroid cancer and selenium supplements for protection of salivary glands from 131I treatment. *Hellenic journal of nuclear medicine.* 21(1):83-84.
8. Pizzulli A, Ranjbar A. Selenium deficiency and hypothyroidism: A new etiology in the differential diagnosis of hypothyroidism in children. *Biological Trace Element Research.* 2000;77(3):199-208.
9. van Zuuren EJ, Albusta AY, Fedorowicz Z, Carter B, Pijl H. Selenium supplementation for Hashimoto's thyroiditis. *The Cochrane database of systematic reviews.* 2013;6((Albusta A.Y.; Fedorowicz Z.; Carter B.; Pijl H.)):CD010223.
10. Yagi M, Tani T, Hashimoto T, et al. Four cases of selenium deficiency in postoperative long-term enteral nutrition. *Nutrition.* 1996;12(1):40-44.
11. Zimmermann T, Schubert W, Albrecht S, et al. Lyell's syndrome: Treatment with centoxin and selenium. *Pediatric Surgery International.* 1994;9(4):297-300.
12. Abdulah R, Katsuya Y, Kobayashi K, et al. Effect of sodium selenite supplementation on the levels of prostacyclin I(2) and thromboxane A(2) in human. *Thrombosis research.* 2007;119(3):305-310.
13. Airenne AL, Westermarck T. Systolic time intervals in patients with progressive muscular dystrophy treated with sodium selenite and vitamin E. *Medical Biology.* 1984;62(2):154.
14. Alfthan G, Xu GL, Tan WH, et al. Selenium supplementation of children in a selenium-deficient area in China: Blood selenium levels and glutathione peroxidase activities. *Biological Trace Element Research.* 2000;73(2):113-125.
15. Alvarenga Americano do Brasil PE, Pereira de Souza A, Hasslocher-Moreno AM, et al. Selenium Treatment and Chagasic Cardiopathy (STCC): Study protocol for a double-blind randomized controlled trial. *Trials.* 2014;15(1).

16. Angstwurm MWA, Engelmann L, Zimmermann T, et al. Selenium in Intensive Care (SIC): Results of a prospective randomized, placebo-controlled, multiple-center study in patients with severe systemic inflammatory response syndrome, sepsis, and septic shock. *Critical Care Medicine.* 2007;35(1):118-126.

17. Angstwurm MWA, Schopohl J, Gaertner R. Selenium substitution has no direct effect on thyroid hormone metabolism in critically ill patients. *European Journal of Endocrinology.* 2004;151(1):47-54.

18. Angstwurm MWA, Schottdorf J, Schopohl J, Gaertner R. Selenium replacement in patients with severe systemic inflammatory response syndrome improves clinical outcome. *Critical Care Medicine.* 1999;27(9):1807-1813.

19. Asfour IA, El Shazly S, Fayek MH, Hegab HM, Raouf S, Moussa MAR. Effect of high-dose sodium selenite therapy on polymorphonuclear leukocyte apoptosis in non-Hodgkin's lymphoma patients. *Biological Trace Element Research.* 2006;110(1):19-32.

20. Asfour IA, El-Tehewi MM, Ahmed MH, et al. High-dose sodium selenite can induce apoptosis of lymphoma cells in adult patients with non-Hodgkin's lymphoma. *Biological Trace Element Research.* 2009;127(3):200-210.

21. Asfour IA, Fayek M, Raouf S, et al. The impact of high-dose sodium selenite therapy on Bcl-2 expression in adult non-Nodgkin's lymphoma patients: Correlation with response and survival. *Biological Trace Element Research.* 2007;120(1-3):1-10.

22. Backman E, Henriksson KG. Effect of sodium selenite and vitamin E treatment in myotonic dystrophy. *Journal of Internal Medicine.* 1990;228(6):577-581.

23. Bäckman E, Henriksson KG. Treatment of congenital myotonia with sodium selenite and vitamin E. *Journal of internal medicine.* 1992;232(4):376-377.

24. Backman E, Nylander E, Johansson I, Henriksson KG, Tagesson C. Selenium and vitamin E treatment of Duchenne muscular dystrophy: No effect on muscle function. *Acta Neurologica Scandinavica.* 1988;78(5):429-435.

25. Bellisola G, Perona G, Galassini S, Moschini G, Guidi GC. Plasma selenium and glutathione peroxidase activities in individuals living in the Veneto region of Italy. *Journal of Trace Elements and Electrolytes in Health and Disease.* 1993;7(4):242-244.

26. Beuth J, Schneider B, R VANL, Uhlenbruck G. Large-scale Survey of the Impact of Complementary Medicine on Side-effects of Adjuvant Hormone Therapy in Patients with Breast Cancer. *In vivo (Athens, Greece).* 2016;30(1):73-75.

27. Beuth J, Van Leendert R, Pempelfort K, Schneider B, Grund C, Engelmann U. Complementary medicine down-regulates side-effects of hormone therapy in prostate cancer patients. *In Vivo.* 2014;28(5):979-982.

28. Beuth J, Van Leendert R, Schneider B, Uhlenbruck G. Complementary medicine on side-effects of adjuvant hormone therapy in patients with breast cancer. *In Vivo.* 2013;27(6):869-871.

29. Bloos F, Trips E, Nierhaus A, et al. Effect of sodium selenite administration and procalcitonin-guided therapy on mortality in patients with severe sepsis or septic shock:A randomized clinical trial. *JAMA Internal Medicine.* 2016;176(9):1266-1276.

30. Bonfig W, Gärtner R, Schmidt H. Selenium supplementation does not decrease thyroid peroxidase antibody concentration in children and adolescents with autoimmune thyroiditis. *TheScientificWorldJournal.* 2010;10((Gärtner R.) Internal Medicine, Medical Department - Innenstadt, Ludwig Maximilians University, Munich, Germany):990-996.

31. Broome CS, McArdle F, Kyle JAM, et al. An increase in selenium intake improves immune function and poliovirus handling in adults with marginal selenium status. *American Journal of Clinical Nutrition.* 2004;80(1):154-162.

32. Brown KM, Pickard K, Nicol F, Beckett GJ, Duthie GG, Arthur JR. Effects of organic and inorganic selenium supplementation on selenoenzyme activity in blood lymphoctyes, granulocytes, platelets and erythrocytes. *Clinical Science.* 2000;98(5):593-599.

33. Bruns F, Büntzel J, Mücke R, Schönekaes K, Kisters K, Micke O. Selenium in the treatment of head and neck lymphedema. *Medical Principles and Practice.* 2004;13(4):185-190.

34. Büntzel J, Gäbert J, Mücke R, et al. Selenium substitution in head and neck surgery. *Trace Elements and Electrolytes.* 2011;28(3):185.

35. Büntzel J, Glatzel M, Kisters K, et al. Selenium as radioprotector in head and neck cancer patients - First clinical results. *Trace Elements and Electrolytes.* 2006;23(3):178-180.

36. Büntzel J, Micke O, Glatzel M, et al. Selenium substitution during radiotherapy in head and neck cancer. *Trace Elements and Electrolytes.* 2010;27(4):235-239.

37. Büntzel J, Micke O, Mücke R, et al. Amifostine and selenium during simultaneous radiochemotherapy in head and neck cancer - Redox status data. *Trace Elements and Electrolytes.* 2005;22(3):211-215.

38. Büntzel J, Riesenbeck D, Glatzel M, et al. Limited effects of selenium substitution in the prevention of radiation-associated toxicities. Results of a randomized study in head and neck cancer patients. *Anticancer Research.* 2010;30(5):1829-1832.

39. Büntzel J, Weinaug R, Glatzel M, et al. Sodium selenite in the treatment of interstitial post-irradiation edema of the head and neck area. *Trace Elements and Electrocytes.* 2002;19(1):33-37.

40. Burk RF, Norsworthy BK, Hill KE, Motley AK, Byrne DW. Effects of chemical form of selenium on plasma biomarkers in a high-dose human supplementation trial. *Cancer Epidemiology Biomarkers and Prevention.* 2006;15(4):804-810.

41. Chelkeba L, Ahmadi A, Abdollahi M, et al. The effect of parenteral selenium on outcomes of mechanically ventilated patients following sepsis: a prospective randomized clinical trial. *Annals of Intensive Care.* 2015;5(1).

42. Ciric S. Effects of selenium supplementation on TPOAb in active autoimmune thyroiditis. *European Thyroid Journal.* 2011((Ciric S.) Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia, Belgrade, Serbia):163.

43. Dai X, Xiong Y, Chu Y, Wang Z. Effect of selenium on immune function of erythrocyte in Kashin-Beck disease. *Academic Journal of Xi'an Jiaotong University.* 2006;18(1):40-43+64.

44. Desilva B, Beckett GJ, McLean S, et al. Lack of effect of oral selenite on p53 associated gene expression during TL01 therapy of psoriasis patients. *Photodermatology Photoimmunology and Photomedicine.* 2007;23(2-3):98-100.

45. Eskes SA, Endert E, Fliers E, et al. Selenite supplementation in euthyroid subjects with thyroid peroxidase antibodies. *Clinical Endocrinology.* 2014;80(3):444-451.

46. Fadieienko G, Prosolenko K, Shalimova A. Selenium deficiency and pain in chronic pancreatitis. *Pancreatology.* 2012;12(6):529-530.

47. Forceville X, Laviolle B, Annane D, et al. Effects of high doses of selenium, as sodium selenite, in septic shock: A placebo-controlled, randomized, double-blind, phase II study. *Critical Care.* 2007;11((Soubirou J.-L., soubirou@netcourrier.com) Hôpital d'Instruction des Armées Desgenettes, 108 Boulevard Pinel, 69003 Lyon, France).

48. Gärtner R, Gasnier BCH. Selenium in the treatment of autoimmune thyroiditis. *BioFactors.* 2003;19(3-4):165-170.

49. Gärtner R, Gasnier BCH, Dietrich JW, Krebs B, Angstwurm MWA. Selenium supplementation in patients with autoimmune thyroiditis decreases thyroid peroxidase antibodies concentrations. *Journal of Clinical Endocrinology and Metabolism.* 2002;87(4):1687-1691.

50. Greenman E, Phillipich MJ, Meyer CJ, Charamella LJ, Dimitrov NV. The effect of selenium on phagocytosis in humans. *Anticancer Research.* 1988;8(4):825-828.

51. Guidi GC, Bellisola G, Bonadonna G, et al. Selenium supplementation increases renal glomerular filtration rate. *Journal of Trace Elements and Electrolytes in Health and Disease.* 1990;4(3):157-161.

52. Hasselmark L, Malmgren R, Zetterstrom O, Unge G. Selenium supplementation in intrinsic asthma. *Allergy: European Journal of Allergy and Clinical Immunology.* 1993;48(1):30-36.

53. Jackson MJ, Coakley J, Stokes M, Edwards RHT, Oster O. Selenium metabolism and supplementation in patients with muscular dystrophy. *Neurology.* 1989;39(5):655-659.

54. Janka V, Ladislav K, Jozef F, Ladislav V. Restoration of antioxidant enzymes in the therapeutic use of selenium in septic patients. *Wiener Klinische Wochenschrift.* 2013;125(11-12):316-325.

55. Janotka M, Vondráková D, Krüger A, Hladká P, Pánková J, Oštádal P. Impact of supplementation of selenium on oxidative stress in patient after cardiac arrest. *Intensive Care Medicine Experimental.* 2017;5(2).

56. Janotka M, Vondrakova D, Kruger A, Neuzil P, Ostadal P. Effect of selenium supplementation on oxidative stress in patient after cardiac arrest. *Intensive Care Medicine Experimental.* 2018;6((Kruger A.; Ostadal P.) Hospital Na Homolce, Cardiology, Prague, Czech Republic).

57. Johansson E, Westermarck T. Studies of selenium supplementation with inorganic and combined inorganic- organic Se in humans. *Journal of Trace Elements and Electrolytes in Health and Disease.* 1993;7(2):113-114.

58. Kahaly GJ, Riedl M, König J, Diana T, Schomburg L. Double-blind, placebo-controlled, randomized trial of selenium in graves hyperthyroidism. *Journal of Clinical Endocrinology and Metabolism.* 2017;102(11):4333-4341.

59. Kameo S, Hanayama T, Saito Y, et al. Effect of the selenium supplementation on plasma selenium and several biochemical indices in healthy Japanese volunteers with different exercise habits. *Journal of Trace Elements in Medicine and Biology.* 2011;26((Murakami M.) Clinical Labo. of Med., Gunma Univ, Japan):19.

60. Karanikas G, Schuetz M, Kontur S, et al. No immunological benefit of selenium in consecutive patients with autoimmune thyroiditis. *Thyroid.* 2008;18(1):7-12.

61. Karaye KM, Mohammed IY, Sa'idu H, et al. Rationale and design for the Peripartum Cardiomyopathy in Nigeria (PEACE) registry, and results for cardiac function in pregnancy sub-study. *European Journal of Heart Failure.* 2018;20((Adebayo R.A.) Obafemi Awolowo University Teaching Hospital, Ile Ife, Nigeria):135.

62. Karimi F, Omrani GR. Effects of selenium and vitamin C on the serum level of antithyroid peroxidase antibody in patients with autoimmune thyroiditis. *Journal of Endocrinological Investigation.* 2018((Karimi F., karimif2002@yahoo.com; Omrani G.R.) Department of Internal Medicine, Endocrinology and Metabolism Research Center, Namazee Hospital, Shiraz University, Zand Street, Namazee Square, Shiraz, Iran).

63. Kasseroller R. Sodium selenite as prophylaxis against erysipelas in secondary lymphedema. *Anticancer Research.* 1998;18(3 C):2227-2230.

64. Kasseroller RG, Schrauzer GN. Treatment of secondary lymphedema of the arm with physical decongestive therapy and sodium selenite: a review. *American journal of therapeutics.* 2000;7(4):273-279.

65. Kiremidjian-Schumacher L, Roy M, Glickman R, et al. Selenium and immunocompetence in patients with head and neck cancer. *Biological Trace Element Research.* 2000;73(2):97-111.

66. Knyazeva AK, Komarova EB, Kuvichko NN. Influence of selenium on clinical and laboratory parameters in patients with rheumatoid arthritis and subclinical hypothyroid dysfunction. *Russian Open Medical Journal.* 2016;5(4).

67. Kočan L, Vašková J, Vaško L, Šimonová J, Šimon R, Firment J. Selenium adjuvant therapy in septic patients selected according to Carrico index. *Clinical Biochemistry.* 2014;47(15):44-50.

68. Koenig JS, Fischer M, Bulant E, Tiran B, Elmadfa I, Druml W. Antioxidant status in patients on chronic hemodialysis therapy: Impact of parenteral selenium supplementation. *Wiener Klinische Wochenschrift.* 1997;109(1):13-19.

69. Kuklinski B, Weissenbacher E, Fähnrich A. Coenzyme Q10 and antioxidants in acute myocardial infarction. *Molecular aspects of medicine.* 1994;15 Suppl:s143-147.

70. Leithäuser B, Jung F, Park JW. Influence of selenium on postischemic brachial artery dilation in patients with peripheral arterial occlusive disease and selenium deficiency: A monocentric prospective controlled open pilot study. *Applied Cardiopulmonary Pathophysiology.* 2010;14(4):203-211.

71. Leng GC, Lee AJL, Fowkes FGR, Deary IJ, Horrobin DD. Impact of antioxidant therapy on symptoms of anxiety and depression. A randomized controlled trial in patients with peripheral arterial disease. *Journal of Nutritional and Environmental Medicine.* 1998;8(4):321-328.

72. Look MP, Rockstroh JK, Rao GS, et al. Sodium selenite and N-acetylcysteine in antiretroviralnaive HIV-1- infected patients: A randomized, controlled pilot study. *European Journal of Clinical Investigation.* 1998;28(5):389-397.

73. Lubinski J. SELINA-clinical trial on lowering the risk of malignancies by optimizing selenium levels in females from families with hereditary breast cancer. *Hereditary Cancer in Clinical Practice.* 2019;17((Lubinski J.) Read-Gene SA, Grzepnica, Poland).

74. Luo X, Wei H, Yang C. Bioavailability of selenium to residents in a low-selenium area of China. *American Journal of Clinical Nutrition.* 1985;42(3):439-448.

75. Mahmoodpoor A, Hamishehkar H, Shadvar K, et al. The Effect of Intravenous Selenium on Oxidative Stress in Critically Ill Patients with Acute Respiratory Distress Syndrome. *Immunological Investigations.* 2019;48(2):147-159.

76. Messing B, Man F, Therond P, Hanh T, Thuillier F, Rambaud JC. Selenium status prior to and during one month total parenteral nutrition in gastroenterological patients: A randomised study of two dosages of Se supplementation. *Clinical Nutrition.* 1990;9(5):281-288.

77. Micke O, Bruns F, Mücke R, Büntzel J, Schäfer U. Selenium in supportive treatment for glioblastoma multiforme treated with concomitant radiotherapy and temozolomide. *Trace Elements and Electrolytes.* 2011;28(3):183.

78. Micke O, Bruns F, Mücke R, et al. Selenium in the treatment of radiation-associated secondary lymphedema. *International Journal of Radiation Oncology Biology Physics.* 2003;56(1):40-49.

79. Micke O, Schomburg L, Buentzel J, Kisters K, Muecke R. Selenium in radiation oncology - An update. *Trace Elements and Electrolytes.* 2010;27(3):162.

80. Micke O, Schomburg L, Buentzel J, Muecke R, Kisters K. Selenium and hypertension: What is the correlation? *Trace Elements and Electrolytes.* 2017;34(4):181.

81. Mishra V, Baines M, Elizabeth Perry S, et al. Effect of selenium supplementation on biochemical markers and outcome in critically ill patients. *Clinical Nutrition.* 2007;26(1):41-50.

82. Mücke R, Glatzel M, Reichl B, et al. Sodium selenite in gynecologic radiation oncology: Results of a prospective randomized observation study. *Trace Elements and Electrolytes.* 2006;23(3):173-177.

83. Mücke R, Glatzel M, Riesenbeck D, et al. Sodium selenite in gynecologic radiation oncology - First results of a phase III study. *Trace Elements and Electrolytes.* 2004;21(2):78-82.

84. Muecke R, Micke O, Schomburg L, et al. Long-term survival following supplementation of sodium selenite during adjuvant radiotherapy (RT) in patients with gynecological cancer. *Supportive Care in Cancer.* 2012;20((Buentzel J.) Otolaryngology, Südharz Hospital, Nordhausen, Germany):S27-S28.

85. Muecke R, Schomburg L, Glatzel M, et al. Multicenter, phase 3 trial comparing selenium supplementation with observation in gynecologic radiation oncology. *International Journal of Radiation Oncology Biology Physics.* 2010;78(3):828-835.

86. Muecke R, Waldschock K, Schomburg L, et al. Whole Blood Selenium Levels and Selenium Supplementation in Patients Treated in a Family Doctor Practice in Golßen (State of Brandenburg, Germany): A Laboratory Study. *Integrative Cancer Therapies.* 2018;17(4):1132-1136.

87. Nacamulli D, Mian C, Petricca D, et al. Influence of physiological dietary selenium supplementation on the natural course of autoimmune thyroiditis. *Clinical Endocrinology.* 2010;73(4):535-539.

88. Pagmantidis V, Méplan C, Van Schothorst EM, Keijer J, Hesketh JE. Supplementation of healthy volunteers with nutritionally relevant amounts of selenium increases the expression of

lymphocyte protein biosynthesis genes. *American Journal of Clinical Nutrition.* 2008;87(1):181-189.

89. Pakdaman A. Symptomatic treatment of brain tumor patients with sodium selenite, oxygen and other supportive measures. *Biological Trace Element Research.* 1998;62(1-2):1-6.

90. Persson-Moschos M, Alfthan G, Åkesson B. Plasma selenoprotein P levels of healthy males in different selenium status after oral supplementation with different forms of selenium. *European Journal of Clinical Nutrition.* 1998;52(5):363-367.

91. Portal B, Richard MJ, Coudray C, Arnaud J, Favier A. Effect of double-blind cross-over selenium supplementation on lipid peroxidation markers in cystic fibrosis patients. *Clinica Chimica Acta.* 1995;234(1-2):137-146.

92. Ranjbar A, Pizzulli A. Systemic treatment with sodium selenite, a new therapeutical concept for the treatment of atopic dermatitis in children. *International Pediatrics.* 2001;16(2):96-104.

93. Rannem T, Ladefoged K, Hylander E, et al. The effect of selenium supplementation on skeletal and cardiac muscle in selenium-depleted patients. *Journal of Parenteral and Enteral Nutrition.* 1995;19(5):351-355.

94. Rannem T, Ladefoged K, Hylander E, Hegnhøj J, Jarnum S. Selenium depletion in patients on home parenteral nutrition. The effect of selenium supplementation. *Biological trace element research.* 1993;39(1):81-90.

95. Richard MJ, Ducros V, Foret M, et al. Reversal of selenium and zinc deficiencies in chronic hemodialysis patients by intravenous sodium selenite and zinc gluconate supplementation: Time-course of glutathione peroxidase repletion and lipid peroxidation decrease. *Biological Trace Element Research.* 1993;39(2-3):149-159.

96. Robinson MF, Campbell DR, Stewart RD, et al. Effect of daily supplements of selenium on patients with muscular complaints in Otago and Canterbury. *The New Zealand medical journal.* 1981;93(683):289-292.

97. Saint-Georges MD, Bonnefont DJ, Bourely BA, et al. Correction of selenium deficiency in hemodialyzed patients. *Kidney International.* 1989;36(SUPPL. 27):S274-S277.

98. Sakr Y, Maia VPL, Santos C, et al. Adjuvant selenium supplementation in the form of sodium selenite in postoperative critically ill patients with severe sepsis. *Critical Care.* 2014;18(2).

99. Sandstrom B, Davidsson L, Bosaeus I, Eriksson B, Alpsten M. Selenium status and absorption of zinc (65Zn), selenium (75Se) and manganese (54Mn) in patients with short bowel syndrome. *European Journal of Clinical Nutrition.* 1990;44(10):697-703.

100. Sandström B, Davidsson L, Eriksson R, Alpsten M, Bogentoft C. Retention of selenium (75Se), Zinc (65Zn) and manganese (54Mn) in humans after intake of a labelled vitamin and mineral supplement. *Journal of trace elements and electrolytes in health and disease.* 1987;1(1):33-38.

101. Savory LA, Kerr CJ, Whiting P, Finer N, McEneny J, Ashton T. Selenium supplementation and exercise: Effect on oxidant stress in overweight adults. *Obesity.* 2012;20(4):794-801.

102. Schmidt T, Pargger H, Seeberger E, Eckhart F, von Felten S, Haberthür C. Effect of high-dose sodium selenite in cardiac surgery patients: A randomized controlled bi-center trial. *Clinical Nutrition.* 2018;37(4):1172-1180.

103. Smith AM, Chan GM, Moyer-Mileur LJ, Johnson CE, Gardner BR. Selenium status of preterm infants fed human milk, preterm formula, or selenium-supplemented preterm formula. *Journal of Pediatrics.* 1991;119(3):429-433.

104. Stoppe C, McDonald B, Rex S, et al. SodiUm SeleniTe Adminstration IN Cardiac Surgery (SUSTAIN CSX-trial): Study design of an international multicenter randomized double-blinded controlled trial of high dose sodium-selenite administration in high-risk cardiac surgical patients. *Trials.* 2014;15(1):1-10.

105. Stoppe C, Spillner J, Rossaint R, et al. Selenium blood concentrations in patients undergoing elective cardiac surgery and receiving perioperative sodium selenite. *Nutrition.* 2013;29(1):158-165.

106. Thomson CD, Robinson MF, Campbell DR, Rea HM. Effect of prolonged supplementation with daily supplements of selenomethionine and sodium selenite on glutathione peroxidase activity in blood of New Zealand residents. *American Journal of Clinical Nutrition.* 1982;36(1):24-31.

107. Thomson CD, Steven SM, Van Rij AM, Wade CR, Robinson MF. Selenium and vitamin E supplementation: Activities of glutathione peroxidase in human tissues. *American Journal of Clinical Nutrition.* 1988;48(2):316-323.

108. Trafikowska U, Sobkowiak E, Butler JA, Whanger PD, Zachara BA. Organic and inorganic selenium supplementation to lactating mothers increase the blood and milk Se concentrations and Se intake by breast-fed infants. *Journal of Trace Elements in Medicine and Biology.* 1998;12(2):77-85.

109. Uehara S, Soh H, Wasa M, et al. Effects of the venous administration of selenium in patients receiving home parenteral nutrition. *Clinical Nutrition.* 2013;32((Oishi M.) Pharmacy, Osaka University, Graduate School of Medicine, Osaka, Japan):S219.

110. Westermarck T, Antila E, Johansson E, Lindh U, Nordberg UR. Selenium supplementation and trace element alterations in Down's syndrome. *Journal of Trace Elements and Electrolytes in Health and Disease.* 1993;7(2):125-126.

111. Westermarck T, Salmi A, Lakomaa EL, Pohja P. Selenium level in milk during long-term supplementation with sodium selenite to a patient with multiple sclerosis. *Nutrition Research.* 1985;5(SUPPL. 1):S-232.

112. Woth G, Nagy B, Merei A, et al. The effect of sodium selenite substitution on oxidative stress markers and antioxidants in severe sepsis. *Infection, Supplement.* 2013;41(1):S57.

113. Xia Y, Hill KE, Burk RF. Biochemical studies of a selenium-deficient population in China: Measurement of selenium, glutathione peroxidase and other oxidant defense indices in blood. *Journal of Nutrition.* 1989;119(9):1318-1326.

114. Yu SY, Zhu YJ, Li WG, et al. A preliminary report on the intervention trials of primary liver cancer in high-risk populations with nutritional supplementation of selenium in China. *Biological trace element research.* 1991;29(3):289-294.

115. Yürekli VA, Naziroğlu M. Selenium and topiramate attenuates blood oxidative toxicity in patients with epilepsy: A clinical pilot study. *Biological Trace Element Research.* 2013;152(2):180-186.

116. Zimmermann T, Leonhardt H, Kersting S, Albrecht S, Range U, Eckelt U. Reduction of postoperative lymphedema after oral tumor surgery with sodium selenite. *Biological Trace Element Research.* 2005;106(3):193-203.

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 **sodium selenite**. 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. If you have questions about your rights as a research subject, please contact HRPO at 410-760-5037 or hrpo@umaryland.edu.

End of Block: Welcome Page

Start of Block: Sodium selenite

Q1. What type(s) of product(s) do you use, prescribe, or recommend for **sodium selenite**? 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: Q13. If What type(s) of product(s) do you use, prescribe, or recommend for sodium selenite?... != Compounded drug product Is Not Selected

Skip To: Q2. If What type(s) of product(s) do you use, prescribe, or recommend for sodium selenite?... = Compounded drug product Is Selected

Display This Question:

If What type(s) of product(s) do you use, prescribe, or recommend for sodium selenite?... = Compounded drug product

Q2. Please list any conditions or diseases for which you use compounded **sodium selenite** 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 **sodium selenite** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- ☐ Single
- ☐ Combination

Skip To: Q5. If Do you use compounded sodium selenite as a single agent active ingredient, or as on... != Combination Is Not Selected

Display This Question:

If Loop current: Do you use compounded sodium selenite as a single agent active ingredient, or as on... = Combination Is Selected

Q4. Please list all combination products in which you use compounded **sodium selenite**.

_____

Q5. For which, if any, diseases or conditions do you consider compounded **sodium selenite** standard therapy?

_____

Q6. Does your specialty describe the use of compounded **sodium selenite** in medical practice guidelines or other resources?

_____

Q7. Over the past 5 years, has the frequency in which you have used compounded **sodium selenite** 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 **sodium selenite** instead of any FDA-approved drug product?

_____

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

- Yes
- No

Skip To: End of Block If Do you stock non-patient-specific compounded sodium selenite in your practice locat... = No

Display This Question:

If Do you stock non-patient-specific compounded sodium selenite in your practice locat... = Yes

Q10. In what practice location(s) do you stock non-patient-specific compounded **sodium selenite**? 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 **sodium selenite**? 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 **sodium selenite**? 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 sodium selenite? Please... = Convenience

Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded sodium selenite? Please... = Emergencies

Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded sodium selenite? Please... = Other (please describe)

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

_____

Q14. Does your specialty describe the use of **sodium selenite** in medical practice guidelines or other resources? _____

End of Block: Sodium selenite

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