Summary Report

Coal Tar Solution

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

Coal tar solution (UNII code: R533ESO2EC) was nominated for inclusion on the 503B Bulks List by Sincerus Florida, LLC and Outsourcing Facilities Association (OFA). While the exact medical condition for which the compounded drug is being requested may not be known, coal tar solution is generally used to treat the itching, scaling, and flaking due to skin conditions such as psoriasis or seborrheic dermatitis. Based on the prescriber's request, various topical dosage forms and strengths may be compounded. The This includes, but is not limited to, the therapeutic dose range of 2-8%, gels, creams, ointments, solutions, and suspensions. Coal tar solution was nominated for use in combination with other active pharmaceutical ingredients (API) (see Table 7 for the nominated combination formulations).

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

- There are no FDA approved drugs containing coal tar solution
- Commercially available products may be inappropriate for the patient due to the dosage form, strength, or flavor.
- Commercially available medications may contain excipients, filler, binders, dyes, preservatives, or other materials that cannot be tolerated by the patient.
- Commercially available finished products have an inherent variance in potency creating an uncertain final concentration for the new product.
- Patients respond differently and the nominated form may be the only formulation to effectively treat the indication for which it is intended to treat.

METHODOLOGY

Background information

The national medicine registers of 13 countries and regions were searched to establish the availability of coal tar solution 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 coal tar solution; name variations of coal tar solution 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 coal tar solution. 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 December 11, 2018. The search included a combination of ("coal tar"[TIAB]) AND (treatment[TIAB] OR therapy[TIAB] OR therapeutic*[TIAB] OR clinical[TIAB] OR itch*[TIAB] OR pruritus[TIAB] OR scaling[TIAB] OR scaly[TIAB] OR psoriasis[TIAB] OR derm*[TIAB] OR skin[TIAB] OR topical[TIAB] OR solution[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 coal tar solution or the implementation of coal tar solution 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.

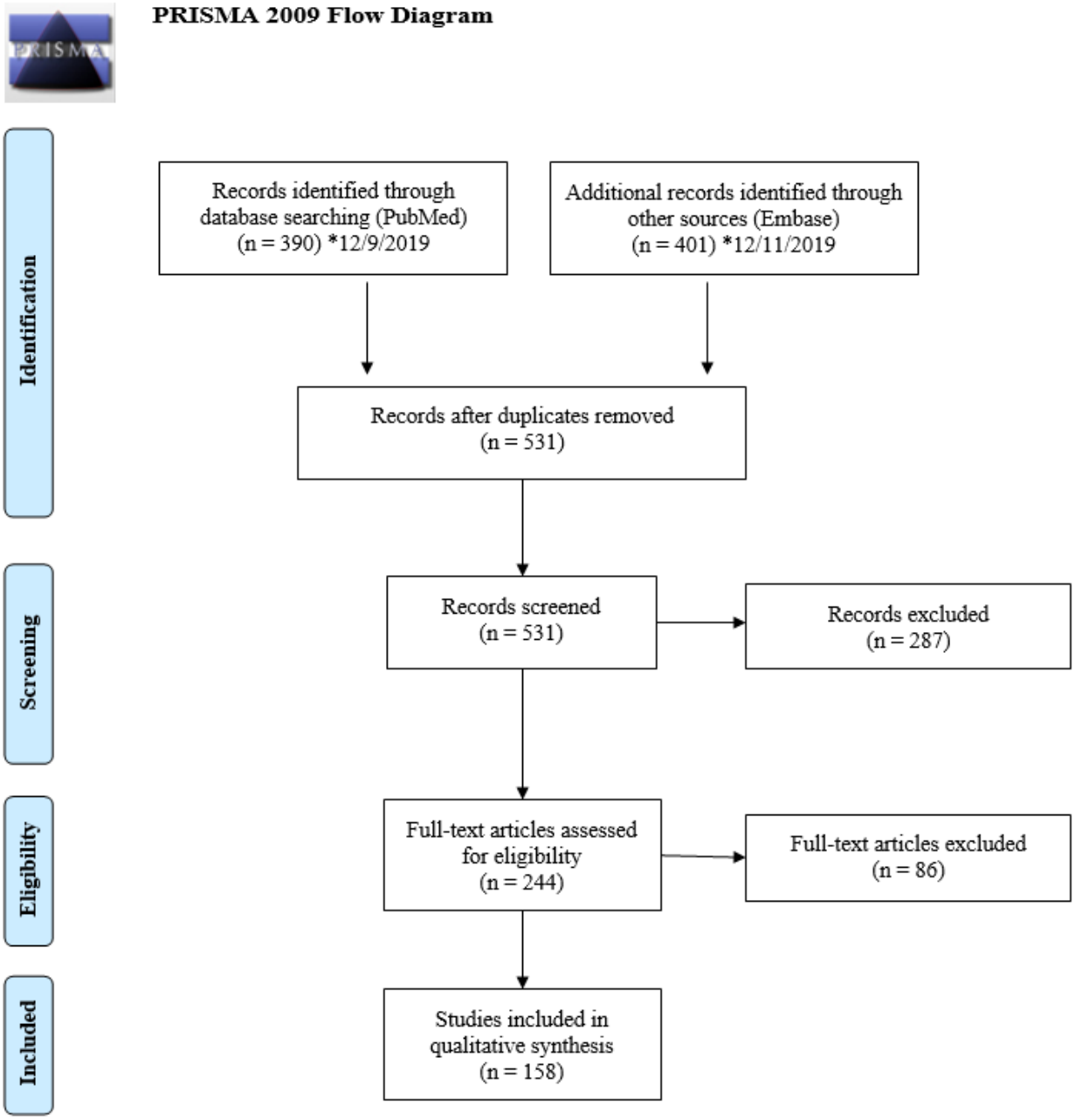
Data extraction

A standard data extraction form was used to collect study authors; article title; year published; journal title; country; indication for coal tar solution 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 coal tar solution 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 indications from the nominations and the results of the literature review, one (1) medical specialty that would potentially use coal tar solution was identified: dermatology. 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. One (1) expert was contacted, of which one (1) accepted and zero (0) declined interviews. All interviews were 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 dermatology, 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 four (4) 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
Dermatology	American Academy of Dermatology (AAD)
	American Society for Dermatologic Surgery (ASDS)

Table 2. Associations that declined participation

Specialty	Association	Reasons for Declining
Medicine	American Medical Association (AMA)	Failed to respond
	American Osteopathic Association (AOA)	Failed to respond

CURRENT AND HISTORIC USE

Summary of background information

- Coal tar solution is not available as an FDA-approved product.
- Coal tar solution is available as an OTC product in the US.
- There is a current United States Pharmacopoeia (USP) monograph for coal tar solution.
- Coal tar solution is available in the UK. Combination products that do not meet nominated formulation criteria are available in Abu Dhabi, Australia, and Hong Kong. In Australia, Canada, Hong Kong, Ireland, and New Zealand, coal tar solution products are available as OTC products.

Table 3. Currently approved products – US

No FDA-approved products

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]
Coal tar solution	5% v/w	Emulsion	Cutaneous	UK	Pharmacy[c]	11/3/1999

Abbreviation: 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, route of administration and approval status) provided in a useable format. Information was recorded only for products with strengths, forms and/or routes of administration 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.

[c]Pharmacy-only medications may only be sold in a pharmacy, and a pharmacist must make or supervise the sale.

Summary of literature review

- Total number of studies included: 158 studies (62 descriptive, 84 experimental, and 12 observational).
- Most of the studies were from the US (70 studies).
- The most common indications in both the US and non-US studies were psoriasis and eczema.
- Compounded uses were identified in both US and non-US studies, but none of the studies used the same formulation as the nominated products.

Table 5. Types of studies

Types of Studies	Number of Studies
Descriptive[1–62]	62
Experimental[63–146]	84
Observational[147–158]	12

Table 6. Number of studies by country

Country	Number of Studies
Australia[29,37]	2
Austria[136]	1
Canada[13,56,62,73]	4
Czech Republic[86,141,154,155]	4
Denmark[11,70,111]	3
Egypt[63,76]	2
Finland[100]	1
Germany[126]	1
India[1,3,38,44,47,51,85,88,90–94,96,98,112,115,125,128,131]	20
Israel[127]	1
Italy[9,31,89]	3
Kuwait[2]	1
Mexico[36,40,156]	3

The Netherlands[41,53,54,137,145,158]	6
Poland[20,99]	2
Singapore[25,134]	2
South Africa[129]	1
Spain[157]	1
Sweden[55,79–81]	4
Taiwan[148]	1
Thailand[135]	1
Turkey[65]	1
UK[7,14,18,21,22,42,49,64,66,71,72,78,83,84,87,95,110,116,124,139,143,144,153]	23
US[4–6,8,10,12,15–17,19,23,24,26–28,30,32–35,39,43,45,46,48,50,52,57–61,67–69,74,75,77,82,97,101–109,113,114,117–123,130,132,133,138,140,142,146,147,149–152]	70
Total US: 70 Total Non-US Countries: 88	

Table 7. Number of studies by combinations

	Combination Formula	Number of Studies
Nominated	Coal tar solution 2% / Clioquinol 1% / Hydrocortisone 1% / Metronidazole 2% / Salicylic acid 2%	0
	Coal tar solution 5% / Clobetasol propionate 0.05% / Salicylic acid 4% / Shark cartilage 5%	0
	Coal tar solution 8% / Clobetasol propionate 0.05% / Salicylic acid 6%	0
Others found in literature	Coal tar solution 5% / Allantoin 2%[64,68,87,130]	4
	Coal tar solution 2% / Allantoin 2% / Hexachlorophene 1%[16]	1
	Coal tar solution 5% / Allantoin 2% / Hydrocortisone 0.5%[48,124]	2
	Coal tar solution 5% / Anthralin 1-3% / Salicylic acid 2%[126]	1
	Coal tar solution 2.5% / Archis oil extract of crude coal tar 7.5% / Juniper tar 7.5% / Pine tar 7.5%[148]	1
	Coal tar solution 5% / Benzocaine / Salicylic acid 1%[48]	1
	Coal tar solution 4% / Ciclopirox olamine 1%[71]	1
	Coal tar solution 1% / Coconut oil 1% / Salicylic acid 0.5%[95]	1
	Coal tar solution / Diiodoquin / Hydrocortisone[113]	1
	Coal tar solution / Dithranol / Phenol / Salicylic acid / Urea[90]	1
	Coal tar solution 1-5.3% / Dithranol 0.11-1.15% / Salicylic acid 1.5-1.6%[87,125]	2
	Coal tar solution 5% / Fluocinonide[102]	1
	Coal tar solution 2% / Fluocinonide 0.05% / Salicylic acid 6%[48]	1
	Coal tar solution 2-5% / Hydrocortisone 0.5-1%[67,119,140,151]	4

	Coal tar solution 1.8% / Menthol 1.5%[23]	1
	Coal tar solution 5% / Pyrilamine 2%[82]	1
	Coal tar solution 1-10% / Salicylic acid 2-10%[29,30,36,44,48,65,92-94,96,112,115,128,131,133,144]	16
	Coal tar solution 5% / Salicylic acid 3% / Sulfur 4%[12]	1
	Coal tar solution 4% / Triamcinolone acetonide 0.1%[157]	1

Table 8. Dosage by indication – US

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Psoriasis[4,5,8,10,12,17,19,23,26,27,30,32,34,35,45,46,48,50,52,57-61,68,69,74,75,97,101–105,107–109,113,117,118,120–122,130,132,133,138,140,142,146,147,149–151]	–	1-25%	Ointment, cream, gel, lotion, shampoo, bath oil, soap, emulsion, solution, paste, foam	Topical	Until disease clears
Eczema[4,6,12,15,23,24,30,33,39,43,48,57,67,69,82,113,119,140,142,147,152]	–	1-20%	Ointment, emulsion, shampoo, cream, lotion, bath, paste, gel, solution	Topical	2 weeks-18 months
Lichen simplex[67,147]	–	1-10%	Ointment, cream	Topical	Up to 2 weeks
Tinea infections[12,16,43,45,113]	–	1-5%	Ointment, cream, lotion, shampoo	Topical	–
Pruritus[28,43,140]	–	2%	Cream	Topical	Up to 18 months
Lichen planus[113,140,142,147]	–	1-10%	Ointment, cream, lotion	Topical	Up to 18 months
Hyperkeratosis[106,113]	–	–	Cream, lotion	Topical	–
Alopecia[52,114]	–	5%	Shampoo	Topical	8 weeks
Dandruff[23,123]	–	0.5-1.8%	Shampoo	Topical	4 weeks
Acne[12,113]	–	5%	Ointment, cream, lotion	Topical	–

Varicose ulcer[57]	–	5%	Ointment	Topical	–
Recalcitrant pustular eruption[147]	–	1-10%	Ointment	Topical	–
Pityriasis rosea[113]	–	–	Cream, Lotion	Topical	–

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

Table 9. Dosage by indication – non-US countries

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Psoriasis[1–3,7,9,18,20–22,25,29,31,36–38,41,42,47,49,51,53,54,56,62–66,70,72,73,76,78–80,83–96,98–100,110,112,115,116,124–126,128,129,131,134–136,139,141,143–145,148,153–158]	–	0.5-80%	Stick, cream, gel, ointment, bath, foam, paste, shampoo, lotion, solution, soap	Topical	Up to 3 months
Eczema[13,14,18,25,41,71,81,111,137]	–	1.5-10%	Cream, ointment, paste, shampoo, lotion, solution	Topical	Up to 4 weeks
Acne[25]	–	5%	Solution	Topical	–
Folliculitis[25]	–	5%	Solution	Topical	2-4 weeks
Vitiligo[25]	–	5%	Cream	Topical	–
Dandruff[71]	–	4%	Shampoo	Topical	4 weeks
Keratoderma[44]	–	6%	Ointment	Topical	–
Pityriasis amiantacea[127]	–	–	Shampoo	Topical	–
Prurigo[55]	–	2-5%	Bath	Topical	Up to 5 months

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

Table 10. Compounded products – US

Indication	Publication Year	Compounding Method	Dosage Form	Final Strength
Psoriasis[10,17,30,59,60,74,101,108,147,151]	1955-2016	• 2% CCT in aquaphor with 2%-10% salicylic acid[10] • 10% LCD in hydrophilic ointment +/- 5% salicylic acid[30] • 10% LCD in petrolatum +/- 5% salicylic acid[30] • 15% LCD with betamethasone 0.025% in hydrophilic ointment [30] • 10%-20% LCD in Nivea oil[30] • 200g of coal tar, 50g of polysorbate 80, and alcohol qs ad 1000mL[30] • 2-3% CCT in 0.1% triamcinolone cream[60] • 10g of CCT with 5g of polysorbate 80 and 985g of zinc oxide paste[30,147] • 20% LCD in aquaphor[10,59], cetaphil[59], vanicream,[59] or nutraderm[10] 1%-20% CCT in Aquaphor[10,108], white petrolatum[59,74,101,151] cetaphil[59], hydrophilic ointment base[17], fatty-acid based lotion[60]	Ointment, cream, lotion, solution	1%-20%
Eczema[6,30,33,57,147,152]	1947-2017	• 3%-5% coal tar with unguentum leniens[6] • 1%-5% CCT in petrolatum, starch, and zinc oxide[30] • Coal tar solution 10mL, soft soap 50g, alcohol 95% 120mL [33] • 1%-3% coal tar solution 0.3mL-0.9mL, rose water ointment or hydrophilic petrolatum 30g[33] • Coal tar solution 15mL, salicylic acid 8mL, resorcin 4mL, zinc sulfocarbolate 15mL, glycerin 15mL, alcohol 70% qs ad 240mL[33] • 5% CCT in collodion[57] • 10%-20% CCT in water or cottonseed oil[57] • 1%-20% CCT in Aquaphor[152], white petrolatum[6] cetaphil[152], cholesterol base or unspecified ointment base[57] • 20% LCD in aquaphor, cetaphil[152]	Ointment, cream, lotion, solution	1%-20%

Abbreviations: CCT, crude coal tar; LCD, liquor carbonis detergens.

Table 11. Compounded products – non-US countries

Indication	Compounding Method	Dosage Form	Final Strength
Psoriasis [7,18,25,56,63,66,72,73,76,78,90–92,96,148,153]	• 4%-10% CCT and zinc[7] • 0.72% purified fraction in oil-in-water base[18] • 3% coal tar in oil-in-water base[18] • 0.72% purified fraction, 1% salicylic acid, 11.5% starch, 11.5% zinc oxide, white soft paraffin[18] • 3% coal tar, 1% salicylic acid, 11.5% starch, 11.5% zinc oxide, white soft paraffin[18] • 0.5 parts coal tar, 0.5 parts polysorbate 80, 1 part ammoniated mercury, 1 part salicylic acid, 25 parts water, hydrophilic ointment qs 100 parts[56] • 5 parts coal tar solution, 0.1 parts mercury bichloride, 2.5 parts resorcin monoacetate, 1.5 parts salicylic acid, 70 parts, water qs 100 parts[56] • 1g CCT in 200mL petrolatum, 5% anhydrous lanolin, 5% liquid paraffin[63] • 2%-10% CCT in zinc oxide 2 parts, starch 25 parts, soft paraffin to 100%[66] • 20% CCT in zinc oxide 20 parts, lanolin 30 parts, Vaseline 30 parts[66] • 50% coal tar oil, 5% salicylic acid, hydrophilic petrolatum[73] • 2.5% CCT in petrolatum[76] • 80% CCT in hard paraffin[78] • 10mL coal tar solution, 10g urea, 3g salicylic acid, 250g dithranol, 1mL phenol white petrolatum qs 100g[90] • 10% LCD, 3% salicylic acid, Vaseline base[91] • 2%-10% Polytar® in Vaseline[148] • 10% coal tar solution in yellow soft paraffin[153] • 10%-30% CCT in yellow soft paraffin[72,78] • 5g-6g CCT, 3g salicylic acid, white petrolatum qs 100g[92,96] • 5-10mL coal tar solution, 100g aqueous cream[72]	Ointment, paste, cream, solution	2%-80%
Eczema[18]	• 0.72% purified fraction in oil-in-water base • 3% coal tar in oil-in-water base • 0.72% purified fraction, 1% salicylic acid, 11.5% starch, 11.5% zinc oxide, white soft paraffin • 3% coal tar, 1% salicylic acid, 11.5% starch, 11.5% zinc oxide, white soft paraffin	Ointment, paste, cream, solution	2%-80%
Vitiligo[25]	• 5% coal tar solution, 0.25% Celestoderm cream • 6mL coal tar solution, Betnovate scalp application 30mL, glycerin 30mL, distilled water qs ad 120mL • 5mL-10mL coal tar solution, 1g-2g salicylic acid, 100g aqueous cream	Ointment, paste, cream, solution	2%-80%

Abbreviations: CCT, crude coal tar; LCD, liquor carbonis detergens.

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

One (1) interview was conducted.

Table 12. Overview of interviewee

Interviewee	Level of Training	Specialty	Current Practice Setting	Experience with coal tar solution	Interview Summary Response
DER_04	MD	Dermatology/ Immunology	Independent consultant	Not using currently	• Interviewee stated that there may be potential for usage in large daycare centers for psoriasis.

Abbreviation: MD, Doctor of Medicine.

Compounded use

- Historically was used as a 2% topical solution that was compounded in the pharmacy with UV light for "really horrible psoriasis" at the hospital. Coal tar was applied topically and left on for two hours; the patient would then shower and lastly receive the light therapy.
- Stopped being used in the inpatient setting due to a change in reimbursement model. Currently, prescribers generally use light therapy alone. Some people may still use coal tar in outpatient centers, phototherapy centers, or psoriasis daycares.

Concerns regarding use of coal tar

- Concerns with the carcinogenicity of the coal tars.
- Was a black ointment so would stain everything.
- Adverse events, referred to as tar smarts, which was a stinging and burning on administration. Some patients developed pustules.

Usage over FDA-approved products

- Used for patients with concomitant medical problems: patients with liver failure are not a candidate for methotrexate; patients with renal failure are not a candidate for cyclosporine; and immunocompromised patients are not candidates for biologic therapy.
- Some patients just do not want to take biologics; worried about long-term effect.

Use of coal tar

- Available in OTC products to treat dandruff.
- Used as an anti-inflammatory, keratolytic. Not ideal for acne and eczema because it will be irritating for sensitive skin.

Summary of survey results

Table 13. Characteristics of survey respondents [3 people responded to the survey.[a]]

Board Certification	MD	No response
Dermatology	3	0
Pediatric dermatology	1	0
No response	0	0

Abbreviation: MD, Doctor of Medicine.
[a]Some respondents reported more than one terminal clinical degree or one board certification.

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

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

[a]Out of three (3) respondents, two (2) reported using, prescribing, or recommending multiple types of coal tar solution product.
[b]One (1) respondent used in combinations: Coal tar solution 8% / Clobetasol propionate 0.05% / Salicylic acid 6%; "in white petrolatum; other base."

Table 15. Compounded use of coal tar solution in practice[a]

Indication	Strength	Dosing frequency	Dosage Form	ROA	Duration of Treatment	Patient Population
Eczema	1-5%	Once a day	Ointment	Topical	2-12 months	All ages and races
Psoriasis						All
Hand dermatitis, seborrheic dermatitis	–	–	–	–	–	–

Abbreviations: –", not mentioned; ROA, route of administration.
[a]One (1) respondent.

Table 16. Indications for which coal tar solution is considered a standard therapy

Indication	Standard therapy	
	Compounded, n (N=1)	Non-compounded, n (N=1)
Eczema, prurigo nodularis, seborrheic dermatitis	1	0
Psoriasis	1	1

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

Reasons
• "When the FDA approved product does not work, is insufficient"

Table 18. Change in frequency of compounded coal tar solution usage over the past 5 years

	Respondents, n (N=1)
No - use has remained consistent	0
Yes - I use it LESS often now[a]	1
Yes - I use it MORE often now	0

[a]One respondent wrote "compounded meds freq not covered by ins".

Table 19. Do you stock non-patient specific compounded coal tar solution in your practice?

	Respondents, n (N=1)
No	1
Yes	0

Table 20. Questions related to stocking non-patient specific compounded coal tar solution

No survey respondents provided this information

CONCLUSION

Coal tar solution (UNII code: R533ESO2EC) was nominated for inclusion on the 503B Bulks List by Sincerus Florida, LLC and Outsourcing Facilities Association (OFA). While the exact medical condition for which the compounded drug is being requested may not be known, coal tar solution is generally used to treat the itching, scaling, and flaking due to skin conditions such as psoriasis or seborrheic dermatitis. Based on the prescriber's request, various topical dosage forms and strengths may be compounded. The This includes, but is not limited to, the therapeutic dose range of 2-8%, gels, creams, ointments, solutions, and suspensions. Coal tar solution is approved in the UK.

From the literature review conducted, the most common indications in both the US and non-US studies were psoriasis and eczema. Compounded uses were identified in both US and non-US studies.

From the interviews, the interviewee stated that it historically was used for inpatient psoriasis treatment, but due to the change in reimbursement model, this is no longer the case. The interviewee stated that if there was a facility that might need coal tar solution to be compounded in bulk from outsourcing facilities, it would likely be large daycare centers to treat psoriasis. Compounded coal tar solution may be used over FDA-approved products for patients with concomitant medical conditions that prohibit them from using other available treatment options, such as cyclosporine, methotrexate, and biologics.

From the survey responses, two (2) out of three (3) respondents used coal tar solution. The most common indication respondents used compounded coal tar solution for were eczema, psoriasis, hand and seborrheic dermatitis. One (1) respondent reported using compounded coal tar solution if the FDA-approved product is insufficient. None of the respondents reported stocking compounded coal tar solution in the office.

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 **coal tar solution**. 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.

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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: Coal tar solution

Q1. What type(s) of product(s) do you use, prescribe, or recommend for **coal tar solution**? 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 coal tar solution? Please check all th... != Compounded drug product

Skip To: Q2 If What type(s) of product(s) do you use, prescribe, or recommend for coal tar solution? Please check all th... = Compounded drug product

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Display This Question:

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

Q2. Please list any conditions or diseases for which you use compounded **coal tar solution** 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 **coal tar solution** 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 coal tar solution as a single agent active ingredient, or as one active ingredient... != Combination

Display This Question:

If Loop current: Do you use compounded coal tar solution as a single agent active ingredient, or as one active ingredient... = Combination

Q4. In which combination(s) do you use compounded **coal tar solution**? Please check all that apply.

- ☐ Coal tar solution 2% / Clioquinol 1% / Hydrocortisone 1% / Metronidazole 2% / Salicylic acid 2%
- ☐ Coal tar solution 3% / Salicylic acid 4% / Shark cartilage 5%
- ☐ Coal tar solution 5% / Clobetasol propionate 0.05% / Salicylic acid 4% / Shark cartilage 5%
- ☐ Coal tar solution 8% / Clobetasol propionate 0.05% / Salicylic acid 6%
- ☐ Other (please describe) _____

Q5. For which, if any, diseases or conditions do you consider compounded **coal tar solution** standard therapy?

_____

Q6. Does your specialty describe the use of compounded **coal tar solution** in medical practice guidelines or other resources?

_____

Q7. Over the past 5 years, has the frequency in which you have used compounded **coal tar solution** changed?

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

Q8. Why do you use compounded **coal tar solution** instead of any FDA-approved drug product?

_____

Q9. Do you stock non-patient-specific compounded **coal tar solution** in your practice location?

- o Yes
- o No

Skip To: End of Block If Do you stock non-patient-specific compounded coal tar solution in your practice location? = No

Display This Question:

If Do you stock non-patient-specific compounded coal tar solution in your practice location? = Yes

Q10. In what practice location(s) do you stock non-patient-specific compounded **coal tar solution**? 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 **coal tar solution**? 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 **coal tar solution**? 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 coal tar solution? Please check all that apply. = Convenience

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

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

Q13. For which, if any, diseases or conditions do you consider **coal tar solution** standard therapy?

_____

Q14. Does your specialty describe the use of **coal tar solution** in medical practice guidelines or other resources?

_____

End of Block: Coal tar solution

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
