NEW DIETARY INGREDIENT (NDI)
SAFETY INFORMATION

Instructions

- In this template, which supplements the data entry screens in the NDI notification electronic submission portal, you will describe the scientific information on which you base your conclusion that the dietary supplement containing the NDI will reasonably be expected to be safe. Safety information includes, among other things, (1) information showing that the NDI is identical or related to substances documented as having a history of use as food; (2) information showing that the NDI is identical or related to test articles used in safety studies:
(3) information showing that a substance or product has a history of use as food; and (4) safety data, including the results of genetic toxicology studies, pharmacokinetic studies, animal toxicology studies and human clinical studies. This template asks for details about the identity of the NDI, verification of that identity, information about history of use as food, and any other evidence relevant to the safety of the NDI under its proposed conditions of use in the dietary supplement. After filling in the template, you will upload the completed template as an attachment to your online NDI notification and attach files containing the scientific publications cited in your notification.

- For a notification that concerns the use of an NDI in a dietary supplement that contains no other ingredients, the safety of the NDI and the dietary supplement would be synonymous.
In other situations, however, that may not be the case. For example, when an NDI is used in a dietary supplement with one or more other NDIs, the safety of the dietary supplement may not be the sum of the safety of the individual NDIs. In such circumstances, you should document your basis for concluding that the dietary supplement will reasonably be expected to be safe and explain why that conclusion is reasonable. For example, if two botanical extracts have separate histories of use in traditional medicine, but no history of being used together, the safety of the combination may not be clear from the safety information pertaining to the individual NDIs. On the other hand, if an extract of a medicinal herb is combined with an extract of a material that has a long history of safe use as food, then it may be reasonable to conclude that the combination is safe based on information about the safety of the individual NDIs. If you wish to submit a notification for the use of an NDI in a dietary supplement with other NDIs, the FDA recommends that you confer with a member of the New Dietary Ingredient Review Team in FDA's Division of Dietary Supplement Programs about how to proceed. If you have any questions concerning this matter, please contact the New Dietary Ingredients Review Team by email at NDITEAM@fda.hhs.gov.

- If a section or subsection is not applicable to your notification, mark "N/A" in your response.

- Sections marked as "Required" in the template's section headings must have complete responses in all subsections for which you have data. If you leave a "Required" section blank or respond "N/A," FDA will consider your notification incomplete for failure to

comply with 21 CFR 190.6(b). An incomplete notification does not satisfy the requirement to submit an NDI notification. You may not introduce your NDI or a dietary supplement containing the NDI into interstate commerce or deliver the NDI or dietary supplement for introduction into interstate commerce, until at least 75 days after you have submitted a complete notification to FDA.

- Please include full citations for all published and unpublished sources cited or relied on in your notification in the Reference List (Section 5). You will be prompted to attach e- copies of these sources when you return to the electronic submission portal after filling in this template.

- The template includes some sections identified as "Recommended." These sections solicit information that FDA considers helpful in evaluating NDI notifications. You are encouraged but not required to respond to template sections that are identified as "Recommended." However, if you leave a "Recommended" section blank or respond "N/A" and FDA determines that the information is needed to establish safety, your notification may be considered inadequate to conclude that the NDI will reasonably be expected to be safe under its proposed conditions of use in the dietary supplement.

Table of Contents

1. New Dietary Ingredient Identity Information (Recommended)

1.1 Description of the identity of the NDI

(b) (4)

1.2 Description of the evidence verifying the identity of the NDI

Identity of NDI was verified by (b) (4)


(b) (4)

1.3 NDI manufacture

***Please note**: In a typical NDI notification, the description of the NDI's manufacture contains trade secrets (TS) and/or confidential commercial information (CCI). You may indicate to FDA your designation of information as TS or CCI in Section 2 of the NDI portal. You also may indicate in that section whether you are attaching a redacted copy of some or all of the notification. If you provide a redacted copy of the notification or a list of information that you believe to be TS or CCI, you should upload and attach it in Section 5 of the NDI portal.*

1.3.1 Raw materials

(b) (4)

1.3.2 Formulation ingredients

(b) (4)

1.3.3 Manufacturing process

PMF powder is manufactured using the following process:

(b) (4)

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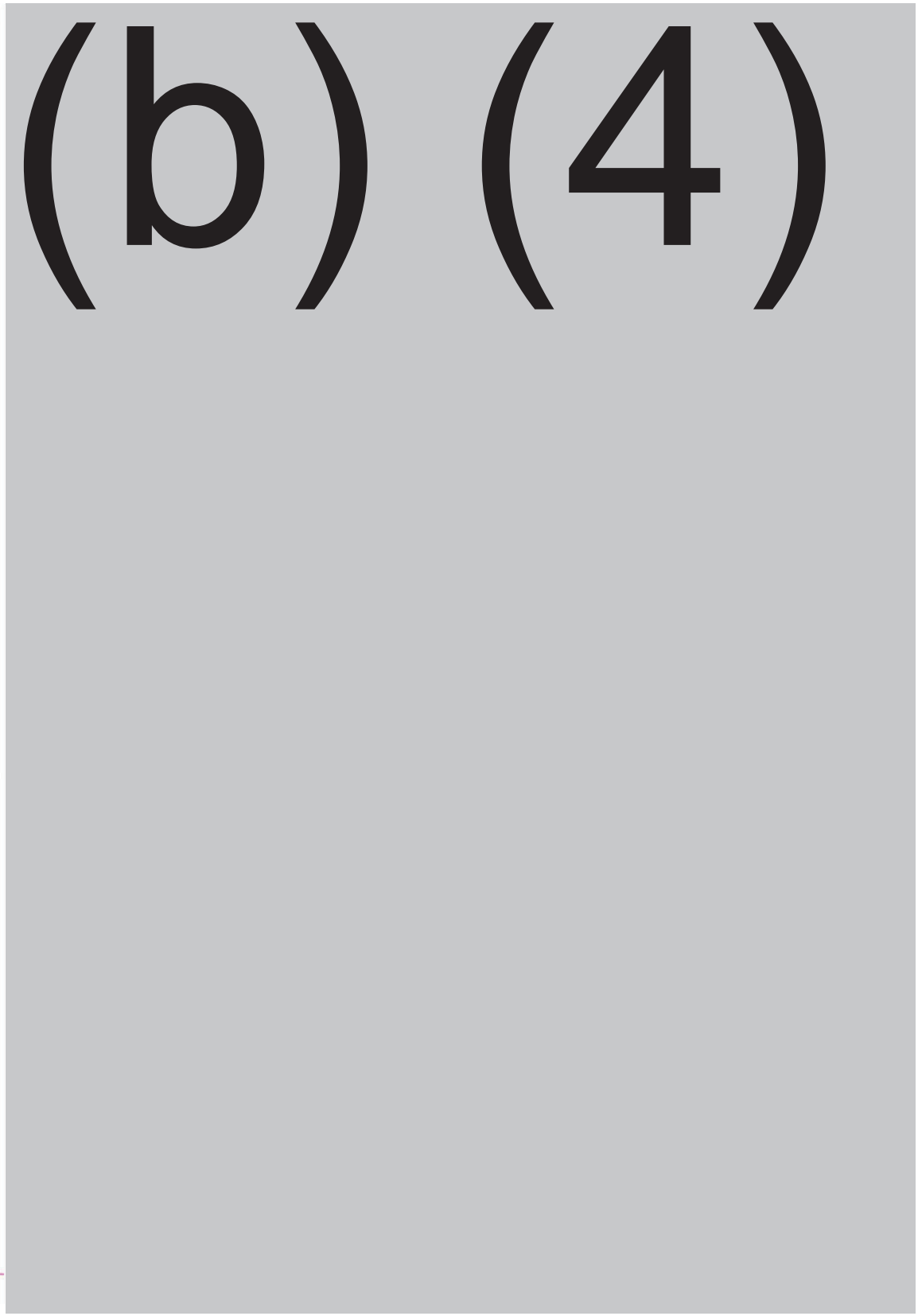
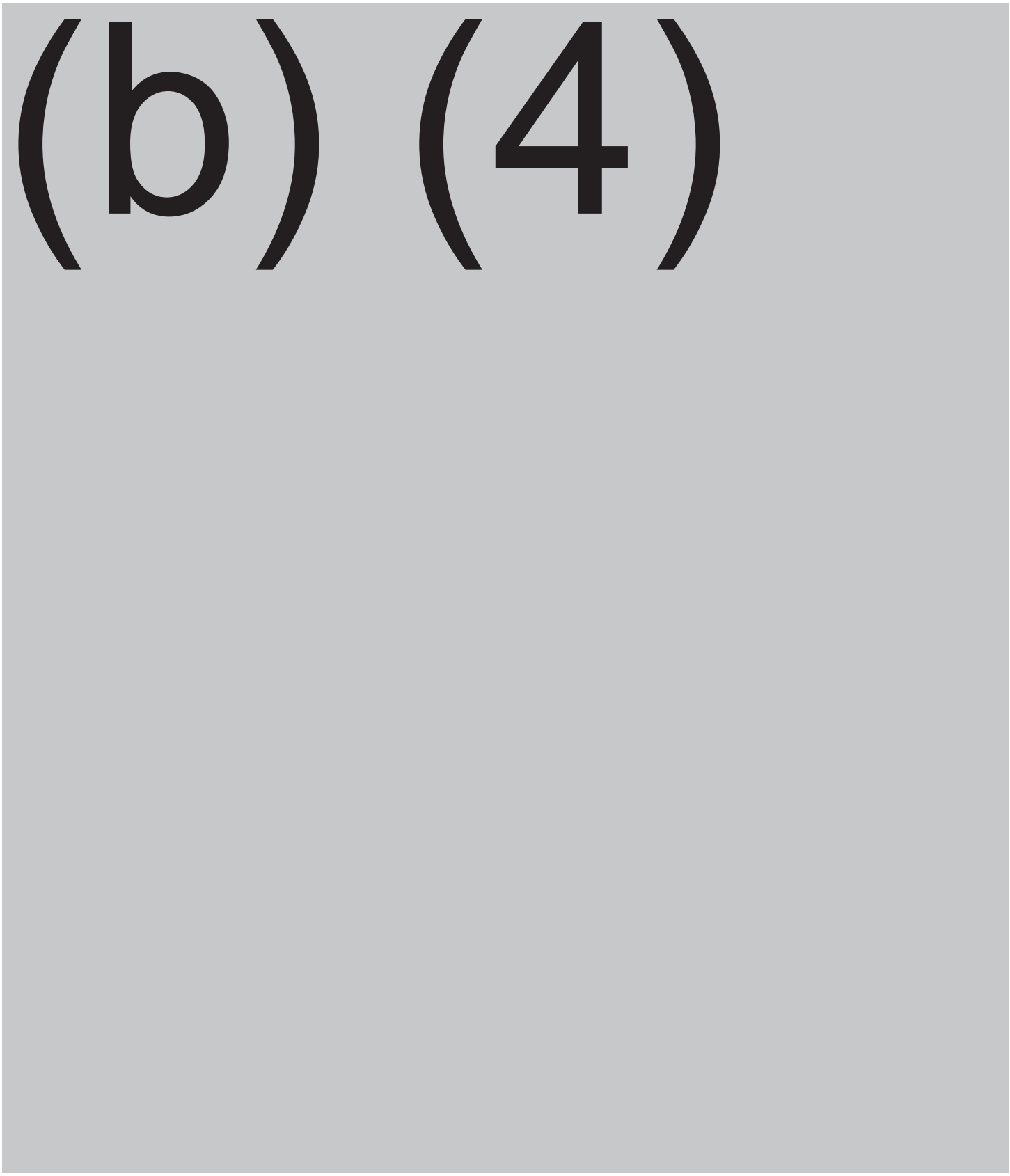
1.3.4 NDI specifications

(b) (4)

CERTIFICATE OF ANALYSIS

(b) (4)


(b) (4)


(b) (4)

1.3.5 Methods of analysis

Samples were analyzed by (b) (4)
[redacted]
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1.3.6 Analysis of potentially toxic processes

To the best of our knowledge and experience, this material does not pose any hazard to humans or environment. No potentially toxic processes were used during manufacture. Product is biodegradable.
Classification under EEC directives: Not a dangerous material.

1.3.7 Disintegration and dissolution profile

PMF powder is soluble in water and methanol. The preparation is stable under conditions of use. No hazardous processes known.

1.3.8 Shelf-life and conditions of storage

The shelf life of the finished product is 24 months. It was determined by doing stability test of the chemical compound (see Section 2.8 for details)

(b) (4)

2. Dietary Supplement Manufacture (Recommended)

2.1. Raw materials

(b) (4)

2.2. Formulation ingredients other than the NDI

All chemicals were food grade purchased from (b) (4)

Formulation ingredients in the standardized powder include;.

(b) (4)

2.3. Manufacturing process

(b) (4)

(b) (4)

(b) (4)

2.4. Product specifications

(see above)

2.5. Methods of analysis

Samples were analyzed by (b) (4)

2.6. Analysis of potentially toxic processes

To the best of our knowledge and experience, this material does not pose any hazard to humans or environment. No potentially toxic processes were used during manufacture. Product is biodegradable.

Classification under EEC directives: Not a dangerous material.

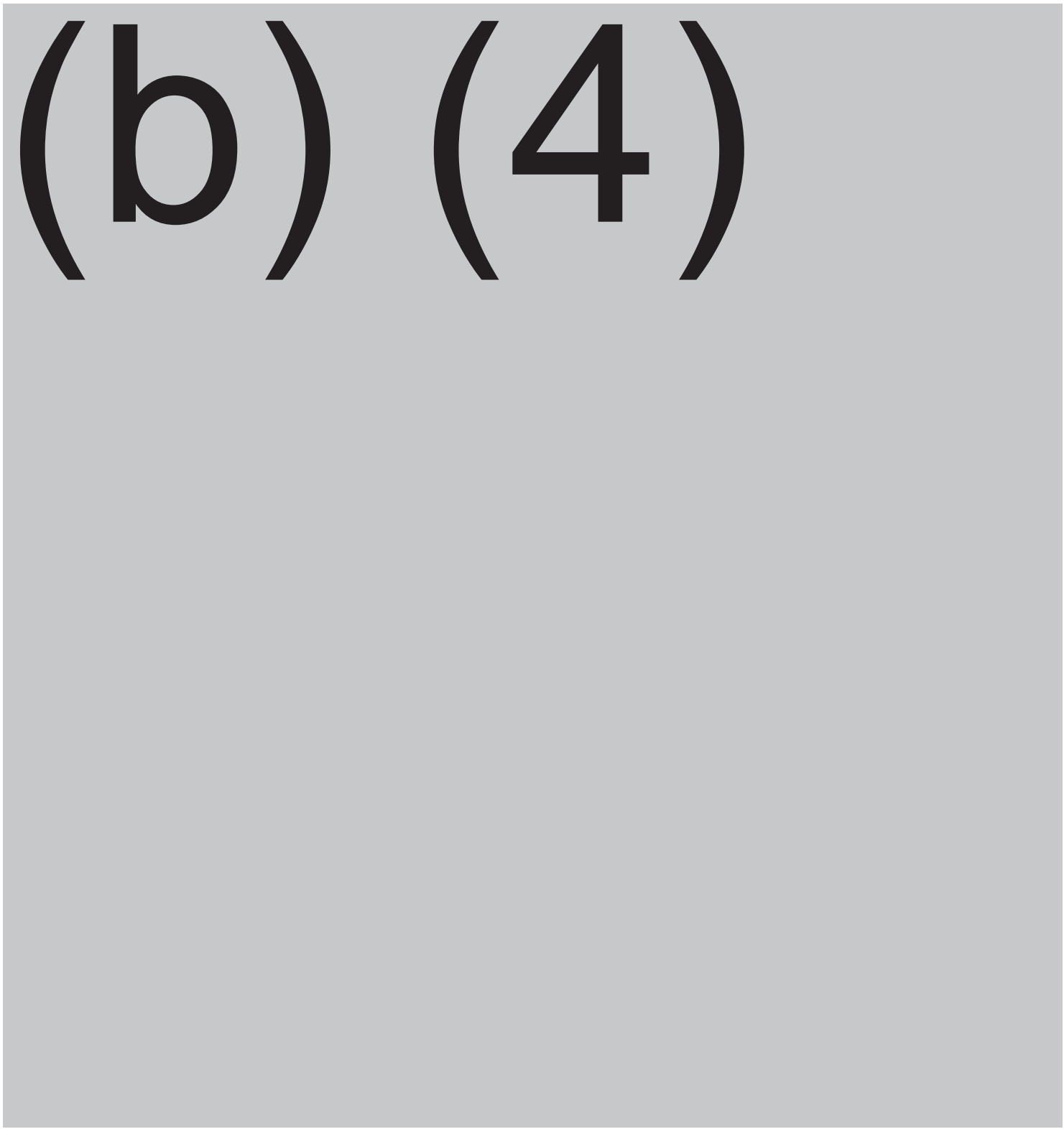
2.7. Disintegration and dissolution profile

PMF powder is soluble in water and methanol. The preparation is stable under conditions of use. No hazardous processes known.

2.8. Shelf-life and conditions of storage

The proposed shelf-life of the finished product is 24 months. (b) (4)

(b) (4)


(b) (4)

3. History Of Use Or Other Evidence Of Safety (Required)

3.1 History of use

3.1.1 Description of the relationship between the historically consumed material and the NDI or dietary supplement containing the NDI

Camel urine, a rich source of natural products with medicinal properties, has been used traditionally for thousands of years for the treatment of various diseases in the Middle East and Africa. However, the NDI, made (b) (4)

3.1.2 Describe identity information verifying the relationship between the historically consumed material and the NDI or dietary supplement containing the NDI

Historically raw camel milk or urine has been consumed. This NDI is a (b) (4) .

3.1.3 Historical conditions of use and cumulative exposure estimate for the historically consumed material

Camel urine, has been used traditionally in the treatment of many diseases in Arabic countries for thousands of years. It is used both externally and internally as a medicine. Today, camel's urine is still used in folklore and modern medicine. In Eastern Sudan, the Bedouin tribes used camel urine in the treatment of many diseases where it found that 72% of tribes were using camel urine as a treatment for internal problems, while 52%, 32%, 20% and 32% were using it for malaria, ascetic, dental problems.

For desert dwellers in Asia and Africa, the camel continues to be vital to daily life as a source of food and just as importantly, its milk and urine have been used as medicines for diverse ailments since ancient times [A]. However, beginning in the early 1980s, more mainstream publications began identifying specific diseases and medical conditions that have been treated by camel milk or urine, including chronic hepatitis [B], hepatitis C infection, cancer, and peptic ulcers [C].

The religious aspect of using camel urine stems from the fact that there has been convincing evidence that the Prophet Mohamed advised its use in the treatment of a wide range of diseases [C]. Camel's milk and urine are used for the treatment of various diseases, such as cancer, ulcers, skin problems, chronic hepatitis, hepatitis C, stomach infections, a weakened immune system, infectious diseases and certain cardiovascular conditions [D].

A. El Agamy EI, Ruppanner R, Ismail A, et al. Antibacterial and antiviral activity of camel milk protective proteins. J Dairy Res 1992; 59: 169e175. https://pubmed.ncbi.nlm.nih.gov/1319434/

B. Hamers-Casterman C, Atarhouch T, Muyldermans S, Robinson G, Hamers C, Songa EB, Bendahman N, Hamers R. Naturally occurring antibodies devoid of light chains. Nature. 1993; 363(6428): 446e448. https://pubmed.ncbi.nlm.nih.gov/8502296/

C. Abdel Galil M. Abdel Gader, PhD, and Abdulqader A. Alhaider, PhD. The unique medicinal properties of camel products: A review of the scientific evidence. Journal of Taibah University Medical Sciences. Volume 11, Issue 2, April 2016, Pages 98-10. https://www.sciencedirect.com/science/article/pii/S1658361216000238?via%3Dihub

D. Mohamad RH, Zekry ZK, Al-Mehdar HA, Salama O, El- Shaieb SE, et al. Camel milk as an adjuvant therapy for the treatment of type 1 diabetes: verification of a traditional ethnomedical practice. J Med Food 2009; 12(2): 461e465.
https://www.researchgate.net/publication/24443919_Camel_Milk_as_an_Adjuvant_Therapy_for_the_Treatment_of_Type_1_Diabetes_Verification_of_a_Traditional_Ethnomedical_Practice

3.1.4 Adverse events associated with historically consumed material

None, see section 3.1.3. NDI is a (b) (4) .

3.1.5 Alternative rationale for reasonable expectation of safety based on history of use

See section 3.1.3.

3.2 Other evidence of safety

3.2.1 Safety study type

A. Dose escalation human clinical study
B. Animal Study (mice)
C. Animal toxicity: Determination of LD50 (physiological & histological tests via oral route) in rodents
D. Evaluating hepatotoxicity and nephrotoxicity in mice.
E. Acute Study on Mice (oral: different doses). Biochemical & Histopathology studies

3.2.2 Safety study title, if any

A. J F. Khorshid, H. Alshazly, A. Al Jefery and Abdel-Moneim M. Osman. Dose Escalation Phase I Study in Healthy Volunteers to Evaluate the Safety of a Natural Product PM701. Journal of Pharmacology and Toxicology 5(3):91-97, 2010. https://scialert.net/fulltext/?doi=jpt.2010.91.97

B. Samar O Rabah, Faten A Khorshid, Huda Aboarik, Nahid H Hajrah; Jamal S Sabir and Roop S Bora. Safety Profile of PMF a Fraction Derived from Camel Urine on Mice (Acute Study). Proceedings of the International Conference on Energy, Environment and Material Science (EEMAS 2015). Chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.inase.org/library/2015/crete/EEMAS.pdf

C. F. Khorshid, 2008. Preclinical evaluation of PM701 in experimental animals. International Journal of Pharmacology, 4: 443-451. https://scialert.net/fulltext/?doi=ijp.2008.443.451.

D. Soad Al Jaouni. Using novel experimental PM 701 in refractory Hodgkin's Disease Combined with conventional Therapy. Blood. Volume 112, Issue 11, 16 November 2008, Page 4677. https://ashpublications.org/blood/article/112/11/4677/62361/Using-Noval-Experimental-PM-701-in-Refractory

E. AlAttas S, A Case-Report Highlighting Effects of PMF and Camel Milk on a Multiple Sclerosis Patient. Ann Clin Med Case Rep. 2024; V13(2): 1-4. ISSN 2639-8109. chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://acmcasereport.org/wp-content/uploads/2024/02/ACMCR-v13-2126.pdf

F. (b) (4)

G. Haifa Jannah, Ahmed Shaker Ali, Mona Mohamed Efat and Faten Khorshid: An Ointment contains PMF showed promising results for treatment of PSORIASIS in human, Int. journal of Medical and Applied Science, Vol 2 Issue 2, 2013.
file:///C:/Users/Brad/Downloads/PSORIASIS-ijmas_124%20(1).pdf

H. Khorshid FA, Rabah SO, Abuaraki H A, Ali AS, Noor SO and Alkabkaby H: Safety of Oral Administration of PMF a Fraction Derived From Camel Urine: Acute Study on Mice. International Journal of Emerging Technology & Advanced Engineering (ISSN 2250-2459, ISO 9001:2008 Certified Journal), Volume 5, Issue 6, June, 2015.
file:///C:/Users/Brad/Downloads/IJETAE_0615_62-safety%20(1).pdf

I. Samah O. Noor, Manal S. Alenini: Effects of Oral Administration of Camel Milk and Urine on Gut Microbiota: Biochemical and Microbiological Profiling in Rats. American Journal of Molecular Biology, 2017.
file:///C:/Users/Brad/Downloads/Effects_of_Oral_Administration_of_Camel_Milk_and_U.pdf

J. Sana Alattas, Fatin Khorshid, Ahmed Ali, Soad Ali; Musab Alyasin and Abeer A. Alnajjar. Assessment of Safety of Inhaled PMF Isolated from Camel Urine with Potential Activity against COVID-19. Egyptian Academic Journal of Biological Sciences. C. Physiology & Molecular Biology. SSN 2090-0767. Egypt. Acad. J. Biolog. Sci., 14(2):81-88 (2022), DOI: 10.21608/EAJBSC.2022.281089.
https://journals.ekb.eg/article_281089_1ddbfd7589b1f1c40609920b63f0234b.pdf

3.3 Citation for the safety study (either public or non-public), if any

See Section 3.2.2.

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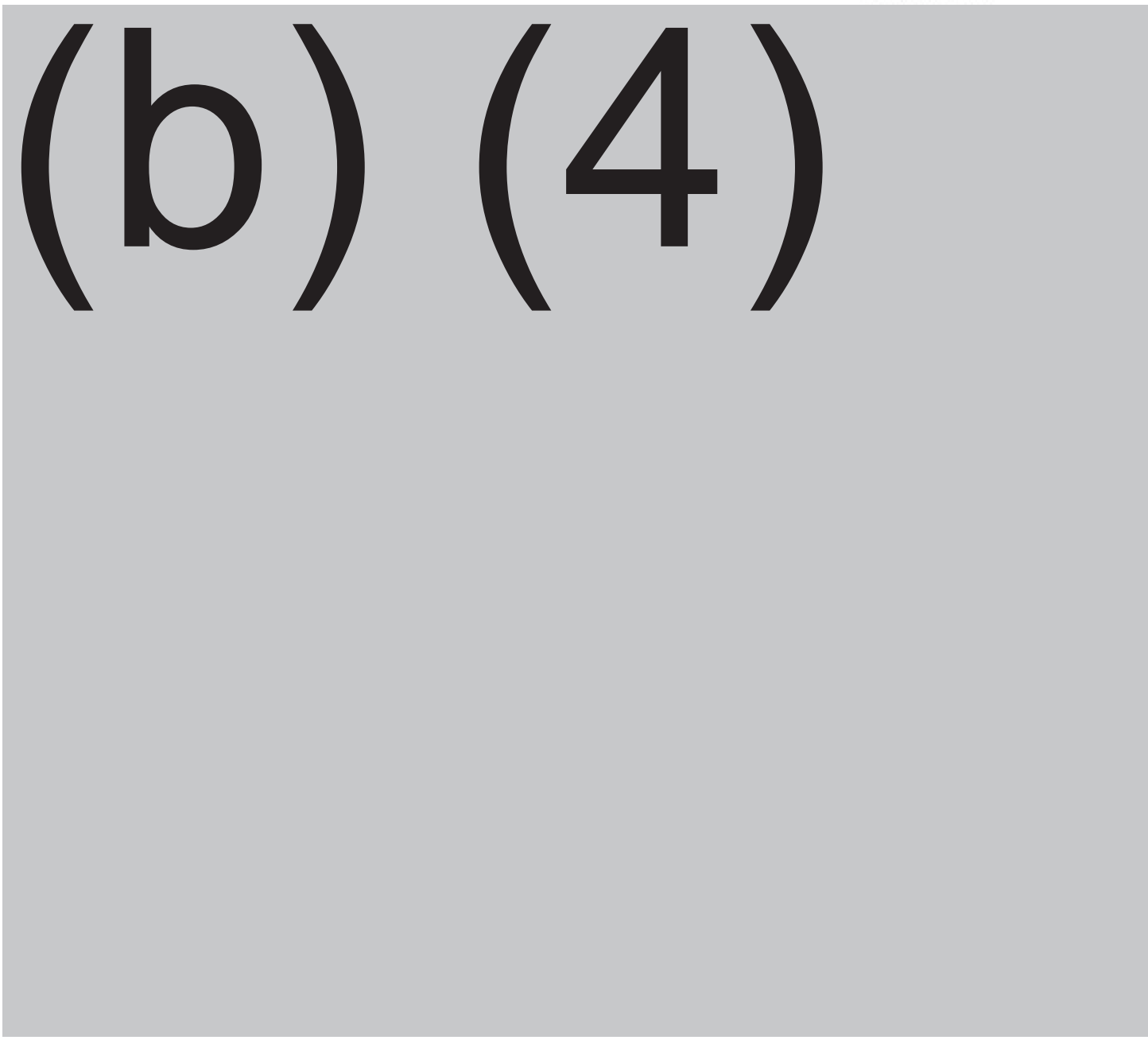
3.4 Identity information verifying the relationship between the test article and the NDI or the dietary supplement

(b) (4)


(b) (4)

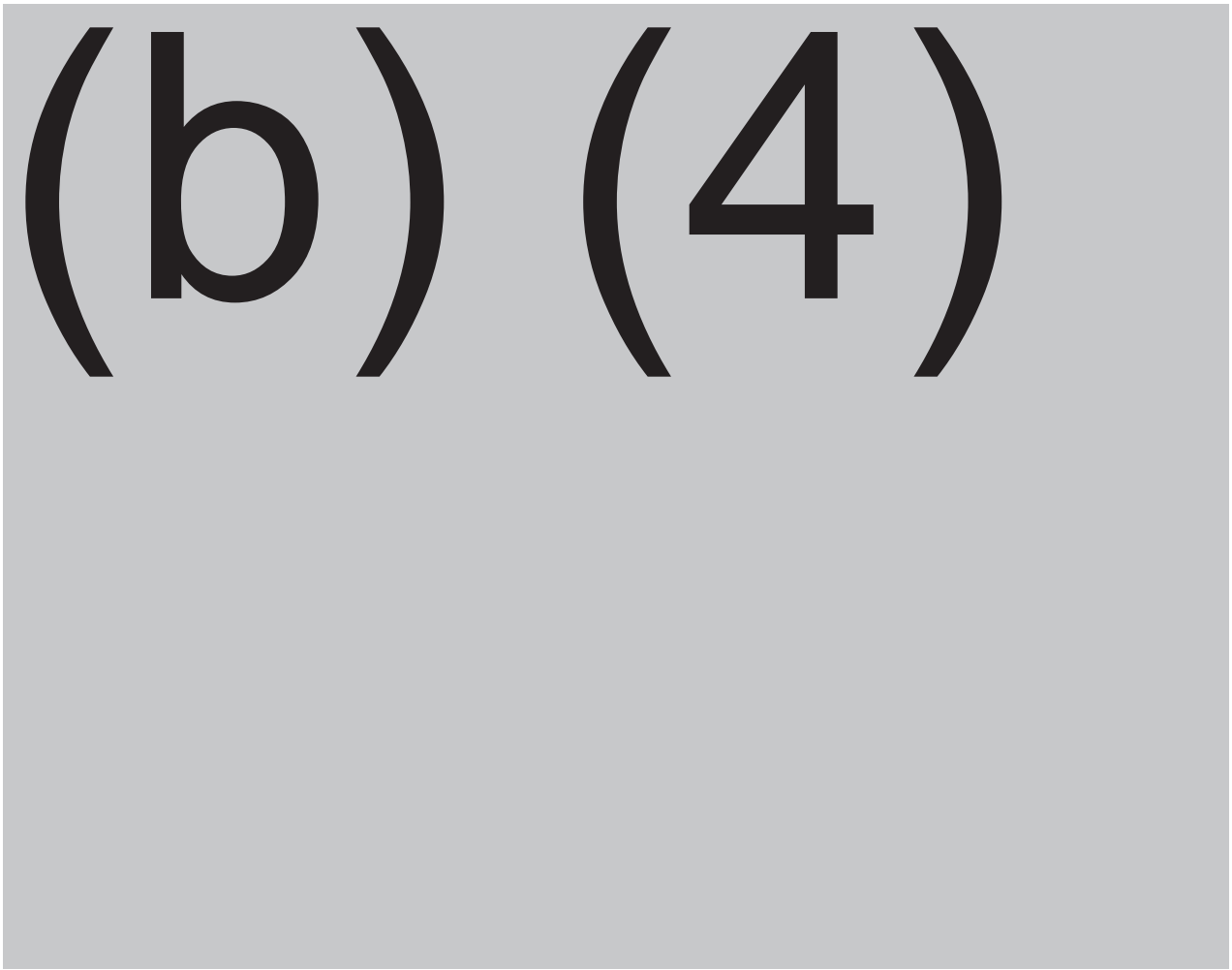
3.4.1 Route of administration, serving size, frequency of use, interval between servings, and duration of use of the test article

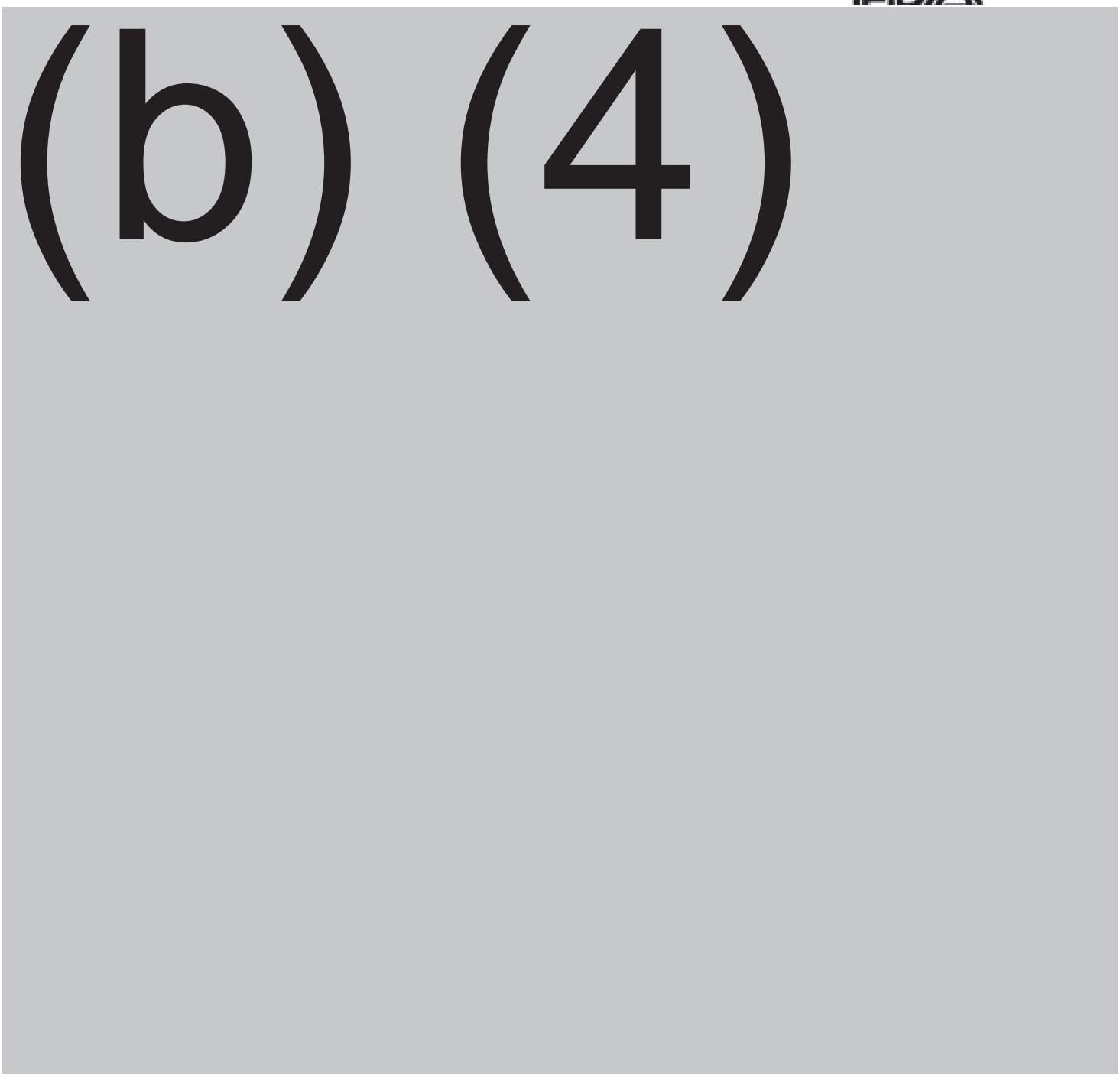
Oral. 250mg and 500mg tablets
FOR CHILDREN under 6 Years of Age; One capsule (250mg)/ once daily. FOR CHILDREN over 6 Years of Age; One capsule (250mg)/ twice daily. FOR ADULTS AND ELDERLY; One capsule (250mg)/ three times daily (separated throughout the day) or one capsule (500mg)/ once daily. Maximum daily intake is 750mg. There is no limitation on duration of use. Consultation with a health care professional is advised.

3.4.2 Study design and safety metrics

See Section 3.2.2

3.4.3 Discussion of toxicity and conclusion




(b) (4)

(b) (4)

3.4.4 Alternative rationale for reasonable expectation of safety based on other evidence of safety

4. Basis For Concluding That the New Dietary Ingredient Will Reasonably Be Expected To Be Safe For Use in the Dietary Supplement (Required)

(You must either provide the information requested in Subsections 4.1 to 4.6, when applicable, or explain in Subsection 4.7 your alternative rationale for concluding, based on the totality of the scientific evidence, that the NDI will reasonably be expected to be safe under its proposed conditions of use in the dietary supplement.)

4.1 Determination of the No-Observed-Adverse-Effect-Level (NOAEL) or Lowest-Observed Adverse Effect Level (LOAEL)

Khorshid, H. Alshazly, A. Al Jefery and Abdel-Moneim M. Osman, 2010. Dose Escalation Phase I Study in Healthy Volunteers to Evaluate the Safety of a Natural Product PM701. Journal of Pharmacology and Toxicology, 5: 91-97. https://scialert.net/fulltext/?doi=jpt.2010.91.97.

Khorshid FA. Preclinical evaluation of PM 701 in Experimental animals. International Journal of Pharmacology, 4(6): 443-451, 2008. ISSN 1811-7775. https://scialert.net/fulltext/?doi=ijp.2008.443.451.

4.2 Determination of safety factor

PM 701 at a dose of 0.35 g kg-1 (6.25-10 times human dose according to the method of Freireich et al., 1966), was injected i.p. into male albino rats for 1, 2 and 4 weeks. No significant adverse effects were observed.
Khorshid, 2008. Preclinical Evaluation of PM 701 in Experimental Animals. International Journal of Pharmacology, 4: 443-451. https://scialert.net/fulltext/?doi=ijp.2008.443.451.

4.3 Determination of the Acceptable Daily Intake (ADI)

Determined by studying safety (LD50) and efficacy profile in rodent models (see 3.2.7). Toxicological effect of PM 701 was evaluated. Results showed that there was no mortality recorded to doses up to 10 g kg-1 body weights during the 4 weeks of observation. PM 701 at a dose of 0.35 g kg-1 (6.25-10 times human dose according to the method of Freireich et al., 1966), was injected i.p. into male albino rats for 1, 2 and 4 weeks. No significant adverse effects were observed.

Khorshid, 2008. Preclinical Evaluation of PM 701 in Experimental Animals. International Journal of Pharmacology, 4: 443-451. https://scialert.net/fulltext/?doi=ijp.2008.443.451.
Khorshid, H. Alshazly, A. Al Jefery and Abdel-Moneim M. Osman, 2010. Dose Escalation Phase I Study in Healthy Volunteers to Evaluate the Safety of a Natural Product PM701. Journal of Pharmacology and Toxicology, 5: 91-97. https://scialert.net/fulltext/?doi=jpt.2010.91.97.

4.4 Determination of Estimated Daily Intake (EDI) and the EDI/ADI Ratio

Khorshid, H. Alshazly, A. Al Jefery and Abdel-Moneim M. Osman, 2010. Dose Escalation Phase I Study in Healthy Volunteers to Evaluate the Safety of a Natural Product PM701. Journal of Pharmacology and Toxicology, 5: 91-97. https://scialert.net/fulltext/?doi=jpt.2010.91.97.

4.5 Determination of margin of safety

6.25-10x based on rat data (see Section 4.2)

4.6 Safety narrative and conclusion

(see 3.2.7)

4.7 Alternative basis for reasonable expectation of safety

(see safety studies described in journal articles in Section 3.2.3)

5. Reference List (Required)

A. J F. Khorshid, H. Alshazly, A. Al Jefery and Abdel-Moneim M. Osman. Dose Escalation Phase I Study in Healthy Volunteers to Evaluate the Safety of a Natural Product PM701. Journal of Pharmacology and Toxicology 5(3):91-97, 2010. https://scialert.net/fulltext/?doi=jpt.2010.91.97

B. Samar O Rabah, Faten A Khorshid, Huda Aboarik, Nahid H Hajrah; Jamal S Sabir and Roop S Bora. Safety Profile of PMF a Fraction Derived from Camel Urine on Mice: Acute Study. International Journal of Emerging Technology and Advanced Engineering. Volume 5, Issue 6, June 2015. Chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.inase.org/library/2015/crete/EEMAS.pdf

C. F. Khorshid, 2008. Preclinical Evaluation of PM 701 in Experimental Animals. International Journal of Pharmacology, 4: 443-451. https://scialert.net/fulltext/?doi=ijp.2008.443.451.

D. Soad Al Jaouni. Using novel experimental PM 701 in refractory Hodgkin's Disease Combined with conventional Therapy. Blood: Volume 112, Issue 11, 16 November 2008, Page 4677. https://ashpublications.org/blood/article/112/11/4677/62361/Using-Noval-Experimental-PM-701-in-Refractory

E. Khorshid FA, Rabah SO, Abuaraki H A, Ali AS, Noor SO and Alkabkaby H: Safety of Oral Administration of PMF a Fraction Derived From Camel Urine: Acute Study on Mice. International Journal of Emerging Technology & Advanced Engineering (ISSN 2250-2459, ISO 9001:2008 Certified Journal), Volume 5, Issue 6, June, 2015. file:///C:/Users/Brad/Downloads/IJETAE_0615_62-safety%20(1).pdf

G. (b) (4)

H. AlAttas S, A Case-Report Highlighting Effects of PMF and Camel Milk on a Multiple Sclerosis Patient. Ann Clin Med Case Rep. 2024; V13(2): 1-4. chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://acmcasereport.org/wp-content/uploads/2024/02/ACMCR-v13-2126.pdf

14. Mal G, Pathak KM. Camel milk and milk products. Report by National Research Centre on Camel. 2010. https://www.yumpu.com/en/document/view/54367170/camel-milk-and-milk-products

15. TSh S, Zhangabylov AK, Zhaksylykova RD. Mechanism of the therapeutic action of whole mare's and camel's milk in chronic hepatitis. Voprosy pitaniia. 1982; 1(1): 17-23. https://pubmed.ncbi.nlm.nih.gov/7072173/

16. Redwan ER, Tabll A. Camel lactoferrin markedly inhibits hepatitis C virus genotype 4 infection of human peripheral blood leukocytes. Journal of immunoassay & immunochemistry. 2007; 28(3): 267-77.

https://www.tandfonline.com/doi/full/10.1080/15321810701454839?needAccess=true

17. Ikeda M, Nozaki A, Sugiyama K, Tanaka T, Naganuma A, Tanaka K, et al. Characterization of antiviral activity of lactoferrin against hepatitis C virus infection in human cultured cells. Virus research. 2000; 66(1): 51-63. https://www.researchgate.net/publication/12660714_Characterization_of_antiviral_activity_of_lactoferrin_against_hepatitis_C_virus_infection_in_human_cultured_cells

18. TSh S, RKh K, Salkhanov BA. Effectiveness of peptic ulcer diet therapy using rations containing whole mare's and camel's milk. Voprosy Pitaniia. 1981; 1(3): 10-4. https://pubmed.ncbi.nlm.nih.gov/7269439/

19. Galil AM, Gader AG, Alhaider AA. The unique medicinal properties of camel products: A review of the scientific evidence. Journal of taibah university medical sciences. 2016; 11(2): 98-103. file:///C:/Users/Brad/Downloads/TTheunique..Finalpublisheddatedversion%20(1).pdf

20. Haifa Jannah, Ahmed Shaker Ali, Mona Mohamed Efat and Faten Khorshid: An Ointment contains PMF showed promising results for treatment of PSORIASIS in human, Int. journal of Medical and Applied Science, Vol 2 Issue 2, 2013. file:///C:/Users/Brad/Downloads/PSORIASIS-ijmas_124%20(1).pdf

21. Samah O. Noor, Manal S. Alenini: Effects of Oral Administration of Camel Milk and Urine on Gut Microbiota: Biochemical and Microbiological Profiling in Rats. American Journal of Molecular Biology, 2017. file:///C:/Users/Brad/Downloads/Effects_of_Oral_Administration_of_Camel_Milk_and_U.pdf

22. Sana Alattas, Fatin Khorshid, Ahmed Ali, Soad Ali; Musab Alyasin and Abeer A. Alnajjar. Assessment of Safety of Inhaled PMF Isolated from Camel Urine with Potential Activity against COVID-19. Egyptian Academic Journal of Biological Sciences. C. Physiology & Molecular Biology. SSN 2090-0767. Egypt. Acad. J. Biolog. Sci., 14(2):81-88 (2022), DOI: 10.21608/EAJBSC.2022.281089. https://journals.ekb.eg/article_281089_1ddbfd7589b1f1c40609920b63f0234b.pdf

Comments

(You have the option to provide any additional information about the NDI or the dietary supplement that you believe will assist FDA in processing your notification.)