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DEL Bulletin #4

Implementation of Establishment Licensing Requirements for Atypical Active Pharmaceutical Ingredients

Health Canada is notifying stakeholders of an interim approach concerning the implementation of Establishment Licensing requirements for certain Active Pharmaceutical Ingredients (APIs) that are of lower risk and widely used outside of the pharmaceutical industry, as communicated to stakeholders in the August 4, 2016 DEL Bulletin #2. Health Canada considers the listed APIs, which are currently used as pharmaceutical excipients, or as ingredients in natural health products (NHP), foods, cosmetics and that meet recognised standards other than GMPs, as atypical APIs for the purpose of this notice.

Health Canada has compiled a list of atypical APIs, which is appended to this document. The atypical API list will be consulted on shortly.

Importers of the listed atypical APIs and finished dosage form importers of products formulated using listed atypical APIs, who are not able to obtain appropriate GMP evidence, can complete the *Table A: Foreign Buildings Conducting API-Related Licensable Activities* (Table A) on the *Drug Establishment Licence Application: Forms and Instructions* (FRM-0033) in accordance with the following instructions:

1. Column L - Indicate 'Exception' and include the standard that the API is manufactured against (e.g. **'Exception - ISO'** or **'Exception - HACCP'**).
2. Columns M, N, O and P can be indicated as "Exception".
3. All other columns should be filled out as per regular Table A instructions.

It is important to note that each lot or batch of the atypical API shall, prior to its availability for sale, be tested against and comply with the specifications for that API. Importers continue to be responsible for having written agreements with foreign buildings and evidence of the foreign building's compliance to the quality standard indicated. Furthermore, the finished dosage form fabricator and the DIN-holder are responsible to assure the safety of the drug by meeting all of Part C, Division 2 of the *Food and Drug Regulations*, including Raw Material Testing sections C.02.009 and C.02.010. Should a risk to health be identified, Health Canada will take appropriate compliance and enforcement action proportional to the risk.

This approach will remain in place until Health Canada notifies stakeholders otherwise.

Atypical Active Pharmaceutical Ingredient List / Liste des ingrédients pharmaceutiques actifs atypiques

<i>(English)</i>	<i>(Français)</i>
4-Aminobenzoic Acid	Acide 4-aminobenzoïque
Acetic Acid	Acide acétique
Alkyl Benzoate	Benzoate d'alkyle
Allantoin	Allantoïne
Almond Oil	Huile d'amande
Aluminum Hydroxide	Hydroxyde d'aluminium
Ammonium Chloride	Chlorure d'ammonium
Anyhdrous Alcohol (Alcohol Anhydrous)	Alcool anhydre
Ascorbic Acid	Acide ascorbique
Avobenzene	Avobenzene
Benzalkonium Chloride	Chlorure de benzalkonium
Benzethonium Chloride	Chlorure de benzéthonium
Benzoic Acid	Acide benzoïque
Benzophenone	Benzophénone
Benzyl Alcohol	Alcool benzylique
Bisdisulizole Disodium	Bisdisulizole disodium
Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (as Bemotrizinol)	Bis-éthylhexyloxyphénol Méthoxyphényltriazine (comme le bémotrizinol)
Calamine	Calamine
Calcium Carbonate	Carbonate de calcium
Calcium Chloride	Chlorure de calcium
Calcium Undecylenate	Undécénoate de calcium
Camphor	Camphre
Carboxymethylcellulose	Carboxyméthylcellulose
Cellulose (as Methylcellulose) and Derivatives	Cellulose (comme le méthylcellulose) et ses dérivés
Cetylpyridinium Chloride	Chlorure de cetylpyridinium
Charcoal (Activated Charcoal)	Charbon de bois (charbon de bois activé)
Chlorhexidine Digluconate	Digluconate de chlorhexidine
Chlorobutanol	Chlorobutanol
Chloroxylenol	Chloroxylénol
Chlorphenesin	Chlorphénésine
Chlorpheniramine	Chlorphéniramine
Cinoxate	Cinoxate
Citric Acid	Acide citrique
Coal Tar	Goudron de houille
Cod Liver Oil	Huile de foie de morue
Colloidal Oatmeal	Avoine colloïdale
Copper Undecylenate	Undécylénate de cuivre
D&C Red No. 28	D et C rouge numéro 28
Dequalinium Chloride	Chlorure de déqualinium
Diethanolamine Methoxycinnamate	Méthoxycinnamate de diéthanolamine
Dimethicone	Diméthicone
Dioxybenzone	Dioxybenzone
Disodium Edetate	Éthylènediaminetétraacétate de disodium

Proposed / Proposée

Domiphen Bromide	Bromure de domiphène
Drometrizole Trisiloxane (as Silatrizole or Ecamsule)	Drométrizole trisiloxane (comme le silatrizole ou l'ecamsule)
Dyclonine	Dyclonine
Egg Yolk Phospholipids	Phospholipides du jaune d'œuf
Ensulizole	Ensulizole
Enzacamene	Enzacamène
Ethanol (Ethyl Alcohol)	Éthanol (alcool éthylique)
Ethyl Hexyl Methoxy Cinnamate	Méthoxycinnamate d'éthylhexyle
Ethylhexyl Salicylate	Salicylate d'éthylhexyle
Ferric Oxide	Oxyde de fer
Fish Oil	Huile de poisson
Fluorescein Sodium	Fluorescéine sodique
Fluoride (as Sodium Fluoride)	Fluorure (comme le fluorure de sodium)
Gelatin	Gélatine
Glucose (as D-Glucose or Dextrose)	Glucose (comme le D-glucose ou le dextrose)
Glycerin (as Glycerine)	Glycérine
Glycerol	Glycérol
Glycine	Glycine
Glycol	Glycol
Haloprogin	Haloprogine
Hexylresorcinol	Hexylrésorcinol
Homomenthyl Salicylate	Salicylate d'homomenthyle
Homosalate	Homosalate
Hydrochloric Acid	Acide chlorhydrique
Hydroquinone	Hydroquinone
Iron III Hydroxide	Hydroxyde de fer(III)
Isopropanol (Isopropyl Alcohol)	Isopropanol (alcool isopropylique)
Lactose	Lactose
L-Alanine	L-alanine
L-Alanyl-L-Glutamine	L-alanyl-L-glutamine (comme l'alanylglutamine)
Lanolin	Lanoline
L-Arginine	L-arginine
L-Aspartic Acid	Acide aspartique-L
L-Cysteine	L-cystéine
L-Glutamic Acid	Acide glutamique-L
L-Glutathione	L-glutathion
L-Histidine	L-histidine
L-Isoleucine	L-isoleucine
L-Leucine	L-leucine
L-Lysine Acetate	Acétate de L-lysine
L-Methionine	L-méthionine
L-Phenylalanine	L-phénylalanine
L-Proline	L-proline
L-Serine	L-sérine
L-Threonine	L-thréonine
L-Tyrosine	L-tyrosine
L-Valine	L-valine
Magnesium Carbonate	Carbonate de magnésium
Magnesium Chloride	Chlorure de magnésium

Proposed / Proposée

Magnesium Hydroxide	Hydroxyde de magnésium
Magnesium Oxide	Oxyde de magnésium
Medium Chain Triglycerides	Triglycérides à chaîne moyenne
Menthol	Menthol
Meradimate	Méradimate
Methylene Blue	Bleu de méthylène
Mineral Oil	Huile minérale
Nitrofurazone	Nitrofurazone
Oat Fibre	Fibres d'avoine
Octinoxate	Octinoxate
Octisalate	Octisalate
Octocrylene	Octocrylène
Octyl Dimethyl	Octyl diméthyl
Octyl Methoxycinnamate	Méthoxycinnamate d'octyle
Octyl Salicylate	Salicylate d'octyle
Olive Oil	Huile d'olive
Oxybenzone (Benzophenone-3)	Oxybenzone (benzophénone-3)
Padimate A	Padimate A
Padimate O	Padimate O
Patent Blue Sodium	Bleu patenté sodique
Peanut Oil	Huile d'arachide
Pectin	Pectine
Petrolatum (Petroleum Jelly)	Pétrolatum (gelée de pétrole)
Phenol	Phénol
Phenylbenzimidazole Sulfonic Acid	Acide phénylbenzimidazolesulfonique
Phosphoric Acid	Acide phosphorique
Piroctone (as Piroctone Olamine or Piroctone Ethanolamine)	Piroctone (comme la piroctone olamine ou la piroctone éthanolamine)
Polycarbophil Calcium	Polycarbophile de calcium
Polyethylene Glycol	Polyéthylèneglycol
Polyhexanide	Polyhexanide
Polyvinyl Alcohol	Alcool polyvinylique
Potassium Chloride	Chlorure de potassium
Potassium Phosphate	Phosphate de potassium
Povidone	Povidone
Pramoxine	Pramoxine
Pyrithione Disulfide	Disulfure de pyrithione
Pyrithione Zinc	Pyrithione de zinc
Resorcinol	Résorcinol
Salicyl Alcohol	Alcool salicylique
Selenium Sulfide	Sulfure de sélénium
Silica Gel	Gel de silice
Silicon Dioxide	Dioxyde de silicium
Silicone	Silicone
Sodium Acetate	Acétate de sodium
Sodium Ascorbate	Ascorbate de sodium
Sodium Bicarbonate	Bicarbonate de sodium
Sodium Chloride	Chlorure de sodium
Sodium Glycerophosphate	Glycérophosphate de sodium
Sodium Hydroxide	Hydroxyde de sodium

Proposed / Proposée

Sodium Phosphate	Phosphate de sodium
Sodium Sulfadimethoxine	Sulfadiméthoxine de sodium
Soya-Bean Oil (Soybean Oil)	Huile de soja
Sulfur	Soufre
Sulisobenzone	Sulisobenzone
Terephthalidene Dicamphor Sulfonic Acid	Acide téréphtalidènedicamphosulfonique
Thymol	Thymol
Titanium Dioxide	Dioxyde de titane
Tolnaftate	Tolnaftate
Triclosan	Triclosan
Triclocarban	Triclocarban
Triethanolamine Salicylate	Salicylate de triéthanolamine
Trolamine Salicylate	Salicylate de trolamine
Trypan Blue	Bleu trypan
Tryptophan	Tryptophane
Undecylenic Acid	Acide undécylénique
Urea	Urée
Zinc Acetate	Acétate de zinc
Zinc Carbonate	Carbonate de zinc
Zinc Chloride	Chlorure de zinc
Zinc Citrate	Citrate de zinc
Zinc Gluconate	Gluconate de zinc
Zinc Omadine	Omadine de zinc
Zinc Oxide	Oxyde de zinc
Zinc Pyrithione	Pyrithione de zinc
Zinc Sulfate	Sulfate de zinc
Zinc Undecylenate	Undécylénate de zinc