

Statement

Regarding: Possible Nitrosamine contamination in chromatography resins


According to the World Health Organization (WHO), nitrosamines are any compound containing a nitroso (NO) functional group. These compounds are of concern because they are potential carcinogens. Nitrosamine is formed when secondary or tertiary amines react with a nitrosating agent. The most common source of nitrosating agents is sodium nitrite.

EMA finalized a review under Article 5(3) of Regulation (EC) No 726/2004 in June 2020 to provide guidance to marketing authorization holders on how to avoid presence of nitrosamine impurities in human medicines. Assessment report EMA/369136/2020 "Nitrosamine impurities in human medicinal products" as adopted by the CHMP was published on 25 June 2020.

FDA Guidance for Industry "Control of Nitrosamine Impurities in Human Drugs" published in September 2020 recommends steps manufacturers of APIs and drug products should take to detect and prevent unacceptable levels of nitrosamine impurities in pharmaceutical products.

It is hereby stated that sodium nitrite is not used in the manufacturing process of our chromatography resins listed in the attachment. Amines can be included as part of the product or as degradation products. Raw materials used in the manufacturing process of a product and information on possible degradation products can be found in corresponding regulatory support file (RSF) at Cytiva.com/rsf. Extensive washing is performed as part of the manufacturing processes which would significantly reduce any possible impurity of nitrosamine originating from other raw materials in the final chromatography resins.

Specific analytical testing for nitrosamines is not performed.

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| Signature:  | Date: 20 October, 2022 |
| Name: Johanna Nurbo | Title: Regulatory Support Manager |

The information herein is provided to the best of our knowledge and belief, based on the information we have been given and the information available to us at the time that this document was issued. The information may change as additional facts come to light, or as the circumstances warrant. Your use hereof is hence at your own risk and does not relieve you of your own responsibility for checking the suitability of our products for your intended use.

Attachment

| Product/Part name | Product code |
|--|--|
| 6-AKS Sepharose™ 4 Fast Flow | 17310004 |
| AH Sepharose 4B | 17047003 |
| Amino Sepharose 6 Fast Flow | 17309202, 17309209 |
| ANX Sepharose 4 Fast Flow | 17128601, 17128604 |
| ANX Sepharose 4 Fast Flow (High Sub) | 17128701, 17128704, 17128705, 17128710, 17128760 |
| AVB Sepharose High Performance | 28411201, 28411202, 28411203, 28411204, 28411210 |
| Benzamidine Sepharose 4 Fast Flow (High Sub) | 17512301, 17512302, 17512303, 17512310 |
| Benzamidine Sepharose 4 Fast Flow (Low Sub) | 28410801, 28410802, 28410803, 28410810 |
| Benzamidine Sepharose 6B | 17056801, 17056802, 17056804 |
| Blue Sepharose 6 Fast Flow | 17094801, 17094802, 17094803, 17094804 |
| Butyl Sepharose 4 Fast Flow | 17098001, 17098002, 17098004, 17098005, 17098010 |
| Butyl Sepharose 4B | 17096003, 17096004, 17096098 |
| Butyl Sepharose High Performance | 17543201, 17543202, 17543203, 17543204, 17543260 |
| Butyl Sepharose High Performance (High Sub) | 17543303, 17543304 |
| Butyl-S Sepharose 6 Fast Flow | 17097802, 17097803, 17097804, 17097810 |
| Capto™ adhere | 17544401, 17544403, 17544404, 17544405, 17544410, 17544460 |
| Capto adhere ImpRes | 17371501, 17371502, 17371503, 17371504, 17371505 |
| Capto AVB | 17372201, 17372202, 17372203, 17372204 |
| Capto Blue | 17544801, 17544802, 17544804, 17544805, 17544860 |
| Capto Blue High Sub | 17545201, 17545202, 17545204, 17545205 |
| Capto Butyl | 17545901, 17545902, 17545903, 17545904, 17545905 |
| Capto Butyl ImpRes | 17371901, 17371902, 17371903, 17371904 |
| Capto Butyl-S | 17549701, 17549702, 17549703, 17549704, 17549723, 17549724 |
| Capto Chelating | 17548501, 17548502, 17548503, 17548504, 17548505 |
| Capto Core 400 | 17372401, 17372402, 17372403, 17372404 |
| Capto Core 700 | 17548101, 17548102, 17548103, 17548104 |
| Capto DEAE | 17544301, 17544303, 17544304, 17544305, 17544310, 17544360 |
| Capto DeVirS | 17546601, 17546602, 17546603, 17546604 |
| Capto Heparin | 17546201, 17546202, 17546203, 17546204 |
| Capto L | 17547801, 17547802, 17547803, 17547804, 17547805, 17547806 |
| Capto Lentil Lectin | 17548901, 17548902, 17548903, 17548904 |
| Capto MMC | 17531702, 17531703, 17531704, 17531705, 17531710, 17531760 |
| Capto MMC ImpRes | 17371601, 17371602, 17371603, 17371604, 17371605 |
| Capto Octyl | 17546501, 17546502, 17546503, 17546504 |
| Capto Phenyl High Sub | 17545101, 17545102, 17545103, 17545104, 17545105, 17545160 |
| Capto Phenyl ImpRes | 17548401, 17548402, 17548403, 17548404 |
| Capto PlasmidSelect | 17549901, 17549902, 17549903, 17549904 |
| Capto Q | 17531602, 17531603, 17531604, 17531605, 17531610, 17531660 |
| Capto Q ImpRes | 17547002, 17547003, 17547004, 17547005, 17547010 |
| Capto Q XP | 17547301, 17547302, 17547303, 17547304 |
| Capto S | 17544101, 17544103, 17544104, 17544105, 17544110, 17544160 |

| Product/Part name | Product code |
|--------------------------------------|--|
| Capto S ImpAct | 17371701, 17371702, 17371703, 17371704, 17371705 |
| Capto SP ImpRes | 17546802, 17546803, 17546804, 17546805, 17546810, 17546860 |
| Capto STI | 17549001, 17549002, 17549003, 17549004, 17549005 |
| Chelating Sepharose Big Beads | 17527203, 17527205 |
| Chelating Sepharose Fast Flow | 17057501, 17057502, 17057504 |
| CM Sephadex™ C-25 | 17021001, 17021002, 17021003, 17021007 |
| CM Sephadex C-50 | 17022001, 17022002, 17022003, 17022007 |
| CM Sepharose Fast Flow | 17071901, 17071905, 17071910, 17071960, 17071922, 17071923, 17071924 |
| CM Sepharose High Performance | 17127701, 17127703, 17127705 |
| CNBr Activated Sepharose 4 Fast Flow | 17098101, 17098103, 17098105 |
| CNBr Activated Sepharose 4B | 17043001, 17043002, 17043003 |
| Con A Sepharose 4B | 17044001, 17044002, 17044003, 17044004 |
| DEAE Sephacel™ | 17050001, 17050005 |
| DEAE Sephadex A-25 | 17017001, 17017002, 17017003, 17017007 |
| DEAE Sephadex A-50 | 17018001, 17018002, 17018003, 17018007 |
| DEAE Sephadex A-50 Special grade | 17018103 |
| DEAE Sepharose CL-6B | 17071001, 17071005 |
| DEAE Sepharose Fast Flow | 17070901, 17070905, 17070910, 17070960 |
| ECH Lysine Sepharose 4 Fast Flow | 17090202, 17090204 |
| GCSFSelect | 17548301, 17548302, 17548303, 17548304 |
| Gelatin Sepharose 4 Fast Flow | 17097603, 17097604 |
| Gelatin Sepharose 4B | 17095601, 17095603, 17095604 |
| Glutathione Sepharose 4B | 17075601, 17075604, 17075605 |
| Glutathione Sepharose 4 Fast Flow | 17513201, 17513202, 17513203 |
| Heparin Sepharose 6 Fast Flow | 17099801, 17099803, 17099804, 17099825 |
| Heparin Sepharose CL-6B | 17055202, 17055204, 17055298, 17046701, 17046709 |
| IgSelect | 28411301, 28411302, 28411303 |
| IMAC Sepharose 6 Fast Flow | 17092107, 17092108, 17092109, 17092110 |
| IXSelect | 17371401, 17371402, 17371403, 17371404 |
| KappaSelect | 17545801, 17545802, 17545803, 17545804 |
| LambdaFabSelect | 17548201, 17548202, 17548203, 17548204 |
| Lentil Lectin Sepharose 4B | 17044401, 17044403 |
| MabSelect™ PrismA | 17549801, 17549802, 17549803, 17549804, 17549805, 17549806 |
| MabSelect SuRe™ | 17543801, 17543802, 17543803, 17543804, 17543805, 17543821, 17543822, 17543823 |
| MabSelect SuRe LX | 17547401, 17547402, 17547403, 17547404, 17547405, 17547421, 17547422, 17547423 |
| MabSelect SuRe pcc | 17549101, 17549102, 17549103, 17549104, 17549105 |
| MabSelect VL | 17542001, 17542002, 17542003, 17542004, 17542005, 17542023, 17542024, 17542025 |
| MabSelect Xtra™ | 17526902, 17526903, 17526904, 17526905, 17526906, 17526907 |
| MabSelect | 17519901, 17519902, 17519903, 17519904, 17519906, 17519921, 17519922 |
| MacroCap™ Q | 17546901, 17546902, 17546904 |
| MacroCap SP | 17544001, 17544002, 17544003, 17544005, 17544010 |
| NHS-activated Sepharose 4 Fast Flow | 17090601, 17090602, 17090604, 17090607 |
| Ni Sepharose excel | 17371201, 17371202, 17371203, 17371213 |

| Product/Part name | Product code |
|---|--|
| Ni Sepharose 6 Fast Flow | 17531801, 17531802, 17531803, 17531804, 17531805, 17531806 |
| Ni Sepharose High Performance | 17526801, 17526802, 17526804 |
| nProtein A Sepharose 4 Fast Flow | 17528001, 17528002, 17528003, 17528004, 17528005, 17528006 |
| Octyl Sepharose 4 Fast Flow | 17094602, 17094603, 17094604, 17094610 |
| Octyl Sepharose 6 Fast Flow | 17372001, 17372002, 17372003, 17372004, 17372005 |
| Octyl Sepharose CL-4B | 17079001, 17079005 |
| Phenyl Sepharose 6 Fast flow (High Sub) | 17097303, 17097304, 17097305, 17097306, 17097310 |
| Phenyl Sepharose 6 Fast flow (Low Sub) | 17096503, 17096504, 17096505, 17096510 |
| Phenyl Sepharose Big Beads | 17509803, 17509805 |
| Phenyl Sepharose CL-4B | 17081001, 17081005 |
| Phenyl Sepharose High Performance | 171082-01, 17108203, 17108204, 17108260 |
| PlasmidSelect Xtra | 28402401, 28402402, 28402403, 28402404 |
| Plasminogen Removal Gel | 28410903 |
| Protein A Sepharose 6 Fast Flow | 17097002, 17097003 |
| Protein A Sepharose CL-4B | 17096302, 17096303, 17078001, 17078003, 17078004 |
| Protein G Sepharose 4 Fast Flow | 17061801, 17061802, 17061804, 17061805, 17061806 |
| Q Sepharose High Performance | 17101401, 17101403, 17101404, 17101405 |
| Q Sepharose Big Beads | 17098903, 17098905, 17098960 |
| Q Sepharose Fast Flow | 17051001, 17051004, 17051005, 17051010, 17051011, 17051060, 17051022, 17051023, 17051024 |
| Q Sepharose XL | 17507201, 17507204, 17507205, 17507260 |
| QAE Sephadex A-25 | 17019001, 17019003 |
| QAE Sephadex A-50 | 17020001, 17020003 |
| rmfProtein A Sepharose Fast Flow | 17513801, 17513802, 17513803, 17513804, 17513805 |
| rProtein A Sepharose Fast Flow | 17127901, 17127902, 17127903, 17127904, 17127905, 17127906, 17127907 |
| S Sepharose Fast Flow | 17051104, 17051105, 17051160 |
| Sephacryl™ S-100 HR | 17061201, 17061205, 17061210 |
| Sephacryl S-300 HR | 17059901, 17059905, 17059910 |
| Sephacryl S-400 HR | 17060901, 17060905, 17060910 |
| Sephacryl S-500 HR | 17061301, 17061305, 17061310 |
| Sephacryl S-200 HR | 17058401, 17058405, 17058410 |
| Sephadex G-10 | 17001001, 17001002, 17001003 |
| Sephadex G-100 | 17006001, 17006003, 17006015 |
| Sephadex G-100 SF | 17006101, 17006133 |
| Sephadex G-15 | 17002001, 17002003, 17002005, 17002007 |
| Sephadex G-25 Coarse | 17003401, 17003402, 17003403, 17003407 |
| Sephadex G-25 Fine | 17003201, 17003202, 17003203 |
| Sephadex G-25 Medium | 17003301, 17003302, 17003303, 17003307 |
| Sephadex G-25 Superfine | 17003101, 17003102, 17003103 |
| Sephadex G-50 Fine | 17004201, 17004202, 17004203 |
| Sephadex G-50 Medium | 17004301, 17004302, 17004303 |
| Sephadex G-50 Superfine | 17004101, 17004103 |
| Sephadex G-75 | 17005001, 17005003 |
| Sephadex G-75 Superfine | 17005101, 17005103 |
| Sephadex LH-20 | 17009001, 17009002, 17009003, 17009010 |
| Sepharose 4 Fast Flow | 17014901, 17014905, 17014960 |
| Sepharose 4B | 17012001, 17012005 |

| Product/Part name | Product code |
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| Sepharose 6 Fast Flow | 17015901, 17015905 |
| Sepharose 6B | 17011001, 17011005 |
| Sepharose CL-2B | 17014001, 17014005 |
| Sepharose CL-4B | 17015001, 17015005 |
| Sepharose CL-6B | 17016001, 17016005 |
| SOURCE™ 15S | 17094401, 17094402, 17094403, 17094405, 17094410 |
| SOURCE 15ISO | 17014801, 17014802, 17014804 |
| SOURCE 15PHE | 17014701, 17014702, 17014704, 17014705 |
| SOURCE 15RPC | 17072702, 17072703, 17072704, 17072705, 17072720 |
| SOURCE 30RPC | 17512002, 17512003, 17512004, 17512005, 17512020 |
| SOURCE 30Q | 17127501, 17127502, 17127503, 17127504 |
| SOURCE 30S | 17127301, 17127302, 17127303, 17127304, 17127330, 17127335, 17127340, 17127345 |
| SOURCE 15Q | 17094701, 17094702, 17094703, 17094704, 17094705, 17094720 |
| SP Sepharose Big Beads | 17065703, 17065705, 17065760 |
| SP Sepharose Fast Flow | 17072901, 17072904, 17072905, 17072910, 17072960, 17072922, 17072923, 17072924 |
| SP Sepharose High Performance | 17108701, 17108703, 17108704, 17108705, 17108708 |
| SP Sepharose XL | 17507301, 17507304, 17507305, 17507360 |
| STREAMLINE™ Chelating | 17128001, 17128002 |
| STREAMLINE DEAE | 17099401, 17099402, 17099405 |
| STREAMLINE PHENYL | 17512101, 17512102, 17512103, 17512104 |
| STREAMLINE Q XL | 17507501, 17507502, 17507505 |
| STREAMLINE SP | 17099301, 17099302, 17099305 |
| STREAMLINE SP XL | 17507601, 17507602, 17507605 |
| Superdex™ 75 Prep Grade | 17104401, 17104402, 17104404 |
| Superdex 30 Prep Grade | 17090501, 17090503, 17090504 |
| Superdex 200 Prep Grade | 17104301, 17104302, 17104304, 17104305, 17104306 |
| Superose™ 12 Prep Grade | 17053601, 17053603, 17053604 |
| Superose 6 Prep Grade | 17048901, 17048903, 17048904 |
| VIISelect | 17545001, 17545002, 17545004 |
| VIISelect | 17547701, 17547702, 17547703, 17547704 |