



ALDEVRON RESEARCH GRADE RNA SERVICE TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES (TSE)/ BOVINE SPONGIFORM ENCEPHALOPATHY (BSE) ASSESSMENT

The research grade RNA manufacturing process at Aldevron employs a wide variety of critical raw materials including buffer solution ingredients, enzymes, and laboratory consumables. Each material category has been assessed regarding risk of introduction of TSE/BSE into the manufacturing process workflow and final deliverable product via animal derived components (ADCs).

- For all research grade manufacturing processes, ADC-free raw materials are incorporated as appropriate and when performance is equivalent to an ADC-containing raw materials.
- Raw materials of known direct animal origin, such as porcine shoulder, bovine-derived nucleases or rabbit muscle, may be used within the research grade manufacturing process and are sourced from countries of low risk as supported by the appropriate TSE/BSE documentation from the original manufacturer.
- Raw materials with known potential contact with ADCs during their individual manufacturing process such as some plastic laboratory consumable subsets, may also be used within the research grade manufacturing process. These are sourced from countries of low risk as supported by the appropriate TSE/BSE documentation from the original manufacturer dependent on the individual product and its application within the manufacturing process.
- Raw materials with unknown potential for contact with ADCs during their individual manufacturing process, such as process-specific inorganic/ organic compounds and chemicals, are assessed for overall risk and sourced from approved vendors.

All reasonable efforts have been made to reduce or eliminate the risk of TSE/BSE transmission from critical raw materials to the final deliverable product within the research grade manufacturing environment based on known raw material manufacturing raw material manufacturing process parameters. At this service level the research grade raw materials procurement team does not institute formal change control notification agreements with raw material vendors.

Full RNA manufacturing raw materials assessment can be referenced in Appendix 1 and Appendix 2.

Aldevron

4055 41st Avenue South, Fargo, ND 58104 | www.aldevron.com

T: (701) 297-9256 | Toll-free 1 877 Pure-DNA (787-3362) | F: 1 (701) 280-1642



Appendix 1: Risk Assessment for Raw Materials with Animal origin used in RNA Research Grade manufacturing

Raw Material	Manufacturer	Item Manufactured in Country	Manufacturing Country BSE Risk	Known Animal Sourced Materials used in process	AO Source Country	AO Source Country BSE Risk	Animal Type	Risk of Animal Type
S-Adenosylmethionine (SAM)	New England Biolabs	USA	Negligible BSE Risk	AOF	Per New England Biolabs, this item is manufactured without the use or exposure to any animal derived components.			
GTP, 100mM	Roche Diagnostics Corp	Germany	Negligible BSE Risk	Porcine Shoulder	Denmark	Negligible BSE Risk	Porcine	Exempt from complying with the TSE/BSE regulation
				Rabbit Muscle	Hungary or Germany	Negligible BSE Risk		
ATP, 100mM	Roche Diagnostics Corp	Germany	Negligible BSE Risk	Porcine Shoulder	Denmark	Negligible BSE Risk	Porcine	Exempt from complying with the TSE/BSE regulation
				Rabbit Muscle	Hungary or Germany	Negligible BSE Risk		
CTP, 100mM	Roche Diagnostics Corp	Germany	Negligible BSE Risk	Porcine Shoulder	Hungary	Negligible BSE Risk	Porcine	Exempt from complying with the TSE/BSE regulation
				Rabbit Muscle	Denmark or Germany	Negligible BSE Risk		
UTP, 100mM	Roche Diagnostics Corp	Germany	Negligible BSE Risk	Porcine Shoulder	Hungary	Negligible BSE Risk	Porcine	Exempt from complying with the TSE/BSE regulation
				Rabbit Muscle	Denmark or Germany	Negligible BSE Risk		
Pyrophosphatase, 1.0mg/mL	Aldevron Madison	USA	Negligible BSE Risk	<i>See MAD AO Component # 1, 2, 3, 4 below</i>				
2-O-Methyltransferase, 1.8mg/mL				<i>See MAD AO Component # 2, 3, 4 below</i>				
T7 RNA Polymerase, 2.0mg/mL				<i>See MAD AO Component # 1, 3 below</i>				
DNase I, 2.5mg/mL				<i>See MAD AO Component # 1, 3 below</i>				
RNase Inhibitor, 1.5mg/mL				<i>See MAD AO Component # 1, 3 below</i>				
Guanylyltransferase, 2.0mg/mL				<i>See MAD AO Component # 1, 3, 4 below</i>				

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Raw Material	Manufacturer	Item Manufactured in Country	Manufacturing Country BSE Risk	Known Animal Sourced Materials used in process	AO Source Country	AO Source Country BSE Risk	Animal Type	Risk of Animal Type
N1-Methyl Pseudo UTP	Thermo Fisher Milwaukee	USA	Negligible BSE Risk	AOF	Per Thermo Fisher, this item is manufactured without the use or exposure to any animal derived components			

Note: Items S-Adenosylmethionine (SAM), 2-O-Methyltransferase, 1.8mg/mL, and Guanylyltransferase, 2.0mg/mL are utilized only in enzymatic capping reactions. Molecules utilizing a co-transcriptional cap analog do not utilize these components.

Note: RISK of TSE and BSE in Pharmaceutical Products. Risk of Transmissible Spongiform Encephalopathy (TSE) in pharmaceutical products and methods to minimize it before manufacturing the pharmaceutical products. TSE is a human disorder caused by an infectious protein known as Prion.

Note: For the classification of the countries or regions according to their BSE risk please refer to the World Organization for Animal Health (OIE) <http://www.oie.int/en/animal-health-in-the-world/official-disease-status/bse/list-of-bse-risk-status/>

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Appendix 2: Aldevron Madison Subcomponents assessment

MAD AO Subcomponent	Item Manufactured in Country	Manufacturing Country BSE Risk	Known Animal Sourced Materials used in process	AO Source Country	AO Source Country BSE Risk	Animal Type	Risk of Animal Type	Animal Body Part	Risk of type of animal body part
1 LB Broth Powder	USA	Negligible BSE Risk	Tryptone	USA or Canada or New Zealand	Negligible/ Controlled BSE Risk	Bovine	TSE/BSE Relevant species	Milk	Negligible BSE/TSE Risk
						Porcine	Exempt from complying with TSE/BSE regulation		Exempt from complying with TSE/BSE regulation
2 Terrific Broth w/ Glycerol Powder	USA	Negligible BSE Risk	Tryptone	USA or Canada or New Zealand	Negligible/ Controlled BSE Risk	Bovine	TSE/BSE Relevant species	Milk	Negligible BSE/TSE Risk
						Porcine	Exempt from complying with TSE/BSE regulation		Exempt from complying with TSE/BSE regulation

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MAD AO Subcomponent	Item Manufactured in Country	Manufacturing Country BSE Risk	Known Animal Sourced Materials used in process	AO Source Country	AO Source Country BSE Risk	Animal Type	Risk of Animal Type	Animal Body Part	Risk of type of animal body part	
3 Pierce Universal	Lithuania	Negligible BSE Risk	Heparin Sepharose	China	Controlled BSE Risk	Porcine	Exempt from complying with TSE/BSE regulation	Intestine	Exempt from complying with TSE/BSE regulation	
			Lactose ¹	Germany	Negligible BSE Risk	Bovine	TSE/BSE relevant species	Milk	The whey used in the process is obtained by application of rennet. In compliance with EMEA statement CPMP/571/02 of 27 February 2002, this process is to be considered acceptable	
			Dextran ¹	AOF						
			Skim Milk ¹	USA	Negligible BSE Risk	Bovine	TSE/BSE relevant species	Milk	Negligible BSE/TSE Risk	
			IPTG	AOF						
			Tryptone	Australia	Negligible BSE Risk	Bovine	TSE/BSE relevant species	Milk	Negligible BSE/TSE Risk	
				New Zealand	Negligible BSE Risk					
			Bacteriological Tryptone	UK	Controlled BSE Risk					
			Casein ¹	New Zealand	Negligible BSE Risk	Bovine		Milk	Negligible BSE/TSE Risk	
Pancreatic Extract ¹	USA or Canada	Negligible/ Controlled BSE Risk	Porcine	Exempt from complying with TSE/ BSE	Muscle	Exempt from complying with TSE/BSE regulation				

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MAD AO Subcomponent	Item Manufactured in Country	Manufacturing Country BSE Risk	Known Animal Sourced Materials used in process	AO Source Country	AO Source Country BSE Risk	Animal Type	Risk of Animal Type	Animal Body Part	Risk of type of animal body part
4 Pierce Protease Inhibitor Tablets	USA	Negligible BSE Risk	Lung ¹	USA	Negligible BSE Risk	Bovine	Category IB-Lower infectivity	Lung	Per manufacturer, animals that did not show signs of OIE listed diseases and were not vaccinated against OIE listed diseases

1. Items are ingredients of subcomponents.

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Note: For the classification of the countries or regions according to their BSE risk please refer to the World Organization for Animal Health (OIE) <http://www.oie.int/en/animal-health-in-the-world/official-disease-status/bse/list-of-bse-risk-status/>

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Signatures:

MHP
Matthew Howard (Apr 1, 2025 14:40 CDT)

04/01/2025

Date

Date

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TSEBSE Assessment

Final Audit Report

2025-04-01

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