

Residue profiles and therapeutic applications of unapproved anti-inflammatory drugs in cattle

by

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Chapter 1 – Residue pharmacology of extra-label anti-inflammatory drugs in cattle

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Primary search

((((((((((((((((cattle) OR (bos)) OR (cow)) OR (cows)) OR (steer)) OR (steers)) OR (heifer)) OR
(heifers)) OR (bull)) OR (bulls)) OR (dairy)) OR (feedlot)) OR (beef)) AND
(((anti-inflammatory agents, non steroidal) OR
(anti-inflammatory agents, non-sterodial)) OR (NSAIDs)) OR (Analgesics)) OR (Analgesic)) OR
(aspirin)) OR (agent)) OR (steroid*)) OR (anti-inflammatory)) OR (meloxicam)) OR
(carprofen)) OR (firocoxib)) OR (phenylbutazone)) OR (acetaminophen)) OR (acetaminophen))
OR (Tylenol)) OR ("acetylsalicylic acid")) OR ("salicylic acid")) OR ("sodium salicylate")) OR
(APAP)) OR (Paracetamol)) OR ("Meclofenamic acid")) OR ("Tolfenamic acid")) OR
(etodolac)) OR (vedaprofen)) OR (deracoxib)) OR (robenacoxib)) OR (mavacoxib)) OR
(grapiprant)) OR (dipyron)) OR (metamizole)) OR (ibuprofen)) OR (motrin)) OR (advil)) OR
(naproxen)) OR (aleve)) OR (piroxicam)) OR (indomethacin)) OR (celecoxib)) OR (celebrex))
OR (valdecoxib)) OR (tepoxalin)) OR (prednisone)) OR (dehydrocortisone)) OR (prednisolone))
OR (fludrocortisone)) OR (flumetasone)) OR (fluorodexametasone)) OR (fluoro
dexametasone)) OR (triamcinolone)) OR (betametasone)) OR (methylprednisolone)) OR
(depo-medrol)) OR (medrol)) OR (histamine*)) OR (antihistamine*)) OR (diphenhydramine))
OR (benadryl)) OR (cannabinoid*)) OR (cannab*)) OR ("industrial hemp")) OR (hemp*)) OR
(sativa))) AND (((((((((((((((((unapproved) OR (non-authorized)) OR (nonauthorized)) OR (non
authorized)) OR ("non authorized")) OR (non-approved)) OR ("non approved")) OR ("not
approved")) OR ("emergency use")) OR ("emergency use authorization")) OR ("non-FDA")) OR
(EUA)) OR (extralabel)) OR ("extra label")) OR (extra-label)) OR (AMDUCA))) AND
((((((((((((((((((milk*) OR (liver*)) OR (kidney*)) OR (muscle*)) OR ("muscle tissue*")) OR

(adipose*)) OR ("fat tissue")) OR ("fat tissues")) OR ("fatty tissue")) OR ("fatty tissues")) OR ("body fat")) OR (tissue*)) OR (residue*)) OR ("residue profile*")). This search returned 1,264 results in PubMed, 24 results in Web of Science, 384 results in CABI Digital Library, and 68 results in Agricola.

Secondary search including ketoprofen

((((((((((((((((cattle) OR (bos)) OR (cow)) OR (cows)) OR (steer)) OR (steers)) OR (heifer)) OR (heifers)) OR (bull)) OR (bulls)) OR (dairy)) OR (beef)) OR (feedlot)) AND
(((anti-inflammatory agents, non steroidal) OR (anti-inflammatory agents, non-steroidal)) OR (NSAIDs)) OR (analgesic)) OR (analgesics)) OR (agent)) OR (steroid*)) OR (anti-inflammatory)) OR (aspirin)) OR ("acetylsalicylic acid")) OR ("salicylic acid")) OR ("sodium salicylate")) OR (meloxicam)) OR (carprofen)) OR (ketoprofen)) OR (firocoxib)) OR (phenylbutazone)) OR (acetaminophen)) OR (Tylenol)) OR (APAP)) OR (paracetamol)) OR ("meclofenamic acid")) OR ("tolfenamic acid")) OR (etodolac)) OR (vedaprofen)) OR (deracoxib)) OR (robenacoxib)) OR (mavacoxib)) OR (grapiprant)) OR (dipyrrone)) OR (metamizole)) OR (ibuprofen)) OR (motrin)) OR (advil)) OR (naproxen)) OR (aleve)) OR (piroxicam)) OR (indomethacin)) OR (celecoxib)) OR (celebrex)) OR (valdecoxib)) OR (tepoxalin)) OR (prednisone)) OR (dehydrocortisone)) OR (prednisolone)) OR (fludrocortisone)) OR (flumetasone)) OR (fluorodexametasone)) OR (fluoro dexametasone)) OR (triamcinolone)) OR (betametasone)) OR (methylprednisolone)) OR (depo-medrol)) OR (medrol)) OR (histamine*)) OR (antihistamine*)) OR (diphenhydramine)) OR (benadryl)) OR (cannabinoid*)) OR (cannab*)) OR ("industrial hemp")) OR (hemp*)) OR (sativa))) AND
(((unapproved) OR (non-authorized)) OR (nonauthorized)) OR ("non authorized")) OR ("non approved")) OR (non-approved)) OR ("not approved")) OR ("emergency use")) OR

("emergency use authorization")) OR (EUA)) OR ("non-FDA")) OR (extralabel)) OR (extra-label)) OR ("extra-label")) OR (AMDUCA))) AND ((((((((((((((milk*) OR (liver*) OR (kidney*) OR (muscle*) OR ("muscle tissue*")) OR (adipose*)) OR ("fat tissue")) OR ("fat tissues")) OR ("fatty tissue")) OR ("fatty tissues")) OR ("body fat")) OR (tissue*)) OR (residue*)) OR ("residue profile*")))). This search returned 58 results in PubMed, 21 results in Web of Science, 384 results in CABI Digital Library, and 68 results in Agricola.

((((((((((((((cattle) OR (bos)) OR (cow)) OR (cows)) OR (steer)) OR (steers)) OR (heifer)) OR (heifers)) OR (bull)) OR (bulls)) OR (dairy)) OR (beef)) OR (feedlot)) AND
 (((aspirin) OR ("acetylsalicylic acid")) OR ("salicylic acid")) OR ("sodium salicylate")) OR (meloxicam)) OR (piroxicam)) OR (tenoxicam)) OR (carprofen)) OR (ketoprofen)) OR (vedaprofen)) OR (ibuprofen)) OR (motrin)) OR (advil)) OR (naproxen)) OR (aleve)) OR (firocoxib)) OR (deracoxib)) OR (robenacoxib)) OR (cimicoxib)) OR (mavacoxib)) OR (celecoxib)) OR (celebrex)) OR (valdecoxib)) OR (parecoxib)) OR (tepoxalin)) OR (grapiprant)) OR (acetaminophen)) OR (tylenol)) OR (APAP)) OR (paracetamol)) OR (phenylbutazone)) OR (ramifenazone)) OR (dipyrrone)) OR (metamizole)) OR ("meclofenamic acid")) OR ("tolfenamic acid")) OR (diclofenac)) OR (etodolac)) OR (eltenac)) OR (indomethacin)) OR (flunixin)) OR (cinchophen))) AND (((((((((((((((milk*) OR (liver*)) OR (kidney*)) OR (muscle*)) OR ("muscle tissue*")) OR (adipose*)) OR ("fat tissue")) OR ("fat tissues")) OR ("fatty tissue")) OR ("fatty tissues")) OR ("body fat")) OR (tissue*)) OR (residue*)) OR ("residue profile*")). This search returned 1,265 results in PubMed, 630 results in Web of Science, 807 results in CABI Digital Library, and 340 results in Agricola.

((((((((((((((cattle) OR (bos)) OR (cow)) OR (cows)) OR (steer)) OR (steers)) OR (heifer)) OR (heifers)) OR (bull)) OR (bulls)) OR (dairy)) OR (beef)) OR (feedlot)) AND
 (((((((((((((((prednisone) OR (dehydrocortisone)) OR (prednisolone)) OR (fludrocortisone)) OR (flumethasone)) OR (fluorodexamethasone)) OR (fluoro dexamethasone)) OR (triamcinolone)) OR (betamethasone)) OR (dexamethasone)) OR (methylprednisolone)) OR (depo-medrol)) OR (medrol)) OR (histamine*)) OR (antihistamine*)) OR (diphenhydramine)) OR (benadryl))) AND
 (((((((((((((((milk*) OR (liver*)) OR (kidney*)) OR (muscle*)) OR ("muscle tissue*")) OR (adipose*)) OR ("fat tissue")) OR ("fat tissues")) OR ("fatty tissue")) OR ("fatty tissues")) OR ("body fat")) OR (tissue*)) OR (residue*)) OR ("residue profile*")). This search returned 1,872 results in PubMed, 914 results in Web of Science, 1,164 results in CABI Digital Library, and 390 results in Agricola.

Secondary hemp search

((((((((((((((cattle) OR (bos)) OR (cow)) OR (cows)) OR (steer)) OR (steers)) OR (heifer)) OR (heifers)) OR (bull)) OR (bulls)) OR (dairy)) OR (beef)) OR (feedlot)) AND (((cannabinoid*) OR (cannab*)) OR ("industrial hemp")) OR (hemp*)) OR (sativa))) AND (((((((((((((((milk*) OR (liver*)) OR (kidney*)) OR (muscle*)) OR ("muscle tissue*")) OR (adipose*)) OR ("fat tissue")) OR ("fat tissues")) OR ("fatty tissue")) OR ("fatty tissues")) OR ("body fat")) OR (tissue*)) OR (residue*)) OR ("residue profile*")). This search returned 967 results in PubMed, 634 results in Web of Science, and 716 results in Agricola. The search in CABI returned 8,403 results, which was impractical to screen for the purposes of this review. When the results were refined by research article or review, 0 results remained.

Chapter 3 – Tissue residue depletion of cannabinoids in cattle administered industrial hemp inflorescence

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Supplementary Table S1. Cannabinoid concentrations in liver and muscle tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. ND: not detected, 8-THC: Δ^8 -tetrahydrocannabinol, 9-THC: Δ^9 -tetrahydrocannabinol, THCA: Δ^9 -tetrahydrocannabinolic acid A, THCP: tetrahydrocannabiphorol, THCV: tetrahydrocannabivarin, THC-11-OH: ($\pm$)-11-Hydroxy- Δ^9 -tetrahydrocannabinol, THC-acid: ($-$)-11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol

			Concentration ng/g						
Tissue	ID	Time (d)	8-THC	9-THC	THCA	THCP	THCV	THC-11-OH	THC-acid
Liver	5602	1	ND	3.02	55.95	ND	ND	ND	ND
Liver	5638	1	ND	2.31	45.74	ND	ND	ND	ND
Liver	5657	1	ND	5.54	98.83	ND	ND	ND	ND
Liver	5660	1	ND	2.12	44.22	ND	ND	ND	ND
Liver	5611	2	ND	2.63	22.14	ND	ND	ND	ND
Liver	5643	2	ND	3.12	40.44	ND	ND	ND	ND
Liver	5644	2	ND	ND	14.65	ND	ND	ND	ND
Liver	5659	2	ND	4.89	26.72	ND	ND	ND	ND
Liver	172	3	ND	ND	7.71	ND	ND	ND	ND
Liver	5603	3	ND	ND	11.67	ND	ND	ND	ND
Liver	5623	3	ND	ND	ND	ND	ND	ND	ND
Liver	5651	3	ND	ND	10.92	ND	ND	ND	ND
Liver	5619	5	ND	1.63	12.56	ND	ND	ND	ND
Liver	5621	5	ND	ND	2.1	ND	ND	ND	ND
Liver	5649	5	ND	ND	4.78	ND	ND	ND	ND
Liver	16392	5	ND	ND	1.51	ND	ND	ND	ND
Liver	5604	8	ND	ND	0.48	ND	ND	ND	ND
Liver	5615	8	ND	ND	1.46	ND	ND	ND	ND
Liver	5625	8	ND	ND	ND	ND	ND	ND	ND
Liver	5640	8	ND	ND	ND	ND	ND	ND	ND
Muscle	5602	1	ND	ND	ND	ND	ND	ND	1.19
Muscle	5638	1	ND	ND	ND	ND	ND	ND	1.3
Muscle	5657	1	ND	ND	ND	ND	ND	ND	1.92
Muscle	5660	1	ND	ND	ND	ND	ND	ND	1.53
Muscle	5611	2	ND	ND	ND	ND	ND	ND	ND
Muscle	5643	2	ND	ND	ND	ND	ND	ND	6.67
Muscle	5644	2	ND	ND	ND	ND	ND	ND	5.18
Muscle	5659	2	ND	ND	ND	ND	ND	ND	3.02
Muscle	172	3	ND	ND	ND	ND	ND	ND	2.46
Muscle	5603	3	ND	ND	ND	ND	ND	ND	1.61
Muscle	5623	3	ND	ND	ND	ND	ND	ND	3.74
Muscle	5651	3	ND	ND	ND	ND	ND	ND	3.82
Muscle	5619	5	ND	ND	ND	ND	ND	ND	2.29
Muscle	5621	5	ND	ND	ND	ND	ND	ND	5.57
Muscle	5649	5	ND	ND	ND	ND	ND	ND	ND
Muscle	16392	5	ND	ND	ND	ND	ND	ND	ND
Muscle	5604	8	ND	ND	ND	ND	ND	ND	1.4
Muscle	5615	8	ND	ND	ND	ND	ND	ND	ND
Muscle	5625	8	ND	ND	ND	ND	ND	ND	2.15
Muscle	5640	8	ND	ND	ND	ND	ND	ND	ND

Supplementary Table S2. Cannabinoid concentrations in kidney and adipose tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. ND: not detected, 8-THC: Δ^8 -tetrahydrocannabinol, 9-THC: Δ^9 -tetrahydrocannabinol, THCA: Δ^9 -tetrahydrocannabinolic acid A, THCP: tetrahydrocannabiphorol, THCV: tetrahydrocannabivarin, THC-11-OH: ($\pm$)-11-Hydroxy- Δ^9 -tetrahydrocannabinol, THC-acid: ($-$)-11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol

Tissue	ID	Time (d)	Concentration ng/g						
			8-THC	9-THC	THCA	THCP	THCV	THC-11-OH	THC-acid
Kidney	5602	1	5.22	8.42	5.25	ND	ND	ND	32.07
Kidney	5638	1	3.82	4.74	6.76	ND	ND	ND	ND
Kidney	5657	1	5.33	7.99	10.74	ND	ND	ND	28.42
Kidney	5660	1	6.01	9.45	8.46	ND	ND	ND	22.81
Kidney	5611	2	3.9	4.13	4	ND	ND	ND	24.04
Kidney	5643	2	7.01	14.79	6.67	ND	ND	ND	27.73
Kidney	5644	2	2.51	4.02	2.99	ND	ND	ND	43.22
Kidney	5659	2	ND	5.16	3.88	ND	ND	ND	19.22
Kidney	172	3	ND	1.23	ND	ND	ND	ND	17.82
Kidney	5603	3	ND	7.89	1.26	ND	ND	ND	15.11
Kidney	5623	3	4.2	7.96	1.52	ND	ND	ND	35.04
Kidney	5651	3	1.19	1.6	1.66	ND	ND	ND	14.96
Kidney	5619	5	ND	1.08	ND	ND	ND	ND	ND
Kidney	5621	5	ND	ND	ND	ND	ND	ND	20.72
Kidney	5649	5	ND	1.55	ND	ND	ND	ND	ND
Kidney	16392	5	ND	ND	ND	ND	ND	ND	ND
Kidney	5604	8	ND	ND	ND	ND	ND	ND	ND
Kidney	5615	8	ND	2.04	ND	ND	ND	ND	ND
Kidney	5625	8	ND	2.41	ND	ND	ND	ND	ND
Kidney	5640	8	ND	2.31	ND	ND	ND	ND	ND
Adipose	5602	1	ND	47.38	ND	ND	ND	ND	ND
Adipose	5638	1	ND	52.59	ND	ND	ND	ND	ND
Adipose	5657	1	ND	50.55	ND	ND	ND	ND	ND
Adipose	5660	1	ND	36.51	ND	ND	ND	ND	ND
Adipose	5611	2	ND	43.7	ND	ND	ND	ND	ND
Adipose	5643	2	ND	63.38	ND	ND	ND	ND	ND
Adipose	5644	2	ND	72.84	ND	ND	ND	ND	ND
Adipose	5659	2	ND	56.42	ND	ND	ND	ND	ND
Adipose	172	3	ND	42.89	ND	ND	ND	ND	ND
Adipose	5603	3	ND	38.28	ND	ND	ND	ND	ND
Adipose	5623	3	ND	56.24	ND	ND	ND	ND	ND
Adipose	5651	3	ND	37.76	ND	ND	ND	ND	ND
Adipose	5619	5	ND	39.21	ND	ND	ND	ND	ND
Adipose	5621	5	ND	55.02	ND	ND	ND	ND	ND
Adipose	5649	5	ND	37.13	ND	ND	ND	ND	ND
Adipose	16392	5	ND	43.62	ND	ND	ND	ND	ND
Adipose	5604	8	ND	23.45	ND	ND	ND	ND	ND
Adipose	5615	8	ND	38.24	ND	ND	ND	ND	ND
Adipose	5625	8	ND	13.58	ND	ND	ND	ND	ND
Adipose	5640	8	ND	36.97	ND	ND	ND	ND	ND

Supplementary Table S3. Cannabinoid concentrations in liver and muscle tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. ND: not detected, THC-acid-glu: (+)-11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol glucuronide, THC-glu: Δ^9 -tetrahydrocannabinol glucuronide, CBC: cannabichromene, CBCA: cannabichromenic acid, CBD: cannabidiol, CBDA: cannabidiolic acid, CBDV: cannabidivarin

			Concentration ng/g						
Tissue	ID	Time (d)	THC-acid-glu	THC-glu	CBC	CBCA	CBD	CBDA	CBDV
Liver	5602	1	ND	11.64	ND	ND	16.2	15173.19	ND
Liver	5638	1	ND	8.82	ND	ND	15.89	14169.44	ND
Liver	5657	1	1.94	18.46	ND	ND	41.6	8586.48	ND
Liver	5660	1	ND	5.86	ND	ND	18.34	111430.34	ND
Liver	5611	2	ND	6.94	ND	ND	13.51	3492.89	ND
Liver	5643	2	ND	5.25	ND	ND	16.21	10162	ND
Liver	5644	2	ND	3.75	ND	ND	7.84	2350.37	ND
Liver	5659	2	ND	ND	ND	ND	28.12	1502.7	ND
Liver	172	3	ND	ND	ND	ND	1.79	534.58	ND
Liver	5603	3	5.51	2.57	ND	ND	1.71	1143.32	ND
Liver	5623	3	ND	ND	ND	ND	0	8.81	ND
Liver	5651	3	8.47	2.08	ND	ND	3.51	2177.6	ND
Liver	5619	5	ND	3.43	ND	ND	6.89	4391.56	ND
Liver	5621	5	ND	ND	ND	ND	0	9.46	ND
Liver	5649	5	2.58	ND	ND	ND	2.38	75.95	ND
Liver	16392	5	ND	ND	ND	ND	0	48.23	ND
Liver	5604	8	ND	ND	ND	ND	0	3.43	ND
Liver	5615	8	ND	ND	ND	ND	1.48	32.77	ND
Liver	5625	8	ND	ND	ND	ND	0	3.98	ND
Liver	5640	8	9.1	ND	ND	ND	0	4.95	ND
Muscle	5602	1	ND	ND	ND	ND	0	5.67	ND
Muscle	5638	1	ND	ND	ND	ND	2.22	35.75	ND
Muscle	5657	1	ND	ND	ND	ND	2.09	19.86	ND
Muscle	5660	1	ND	ND	ND	ND	1.35	13.89	ND
Muscle	5611	2	ND	ND	ND	ND	2	1.85	ND
Muscle	5643	2	ND	ND	ND	ND	2.02	7.2	ND
Muscle	5644	2	ND	ND	ND	ND	3.1	12.45	ND
Muscle	5659	2	ND	ND	ND	ND	1.33	10.36	ND
Muscle	172	3	ND	ND	ND	ND	0	0	ND
Muscle	5603	3	ND	ND	ND	ND	0	0	ND
Muscle	5623	3	ND	ND	ND	ND	3.22	2.66	ND
Muscle	5651	3	ND	ND	ND	ND	2.86	9.21	ND
Muscle	5619	5	ND	ND	ND	ND	0	0	ND
Muscle	5621	5	ND	ND	ND	ND	0	0	ND
Muscle	5649	5	ND	ND	ND	ND	0	0	ND
Muscle	16392	5	ND	ND	ND	ND	0	0	ND
Muscle	5604	8	ND	ND	ND	ND	0	1.38	ND
Muscle	5615	8	ND	ND	ND	ND	0	0	ND
Muscle	5625	8	ND	ND	ND	ND	0	0	ND
Muscle	5640	8	ND	ND	ND	ND	7	0	ND

Supplementary Table S4. Cannabinoid concentrations in kidney and adipose tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. ND: not detected, THC-acid-glu: (+)-11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol glucuronide, THC-glu: Δ^9 -tetrahydrocannabinol glucuronide, CBC: cannabichromene, CBCA: cannabichromenic acid, CBD: cannabidiol, CBDA: cannabidiolic acid, CBDV: cannabidivarin

Tissue	ID	Time (d)	Concentration ng/g						
			THC-acid-glu	THC-glu	CBC	CBCA	CBD	CBDA	CBDV
Kidney	5602	1	ND	ND	ND	ND	12.35	8.25	ND
Kidney	5638	1	ND	ND	ND	ND	3.95	12.39	ND
Kidney	5657	1	ND	ND	ND	ND	9.65	16.9	ND
Kidney	5660	1	ND	ND	ND	ND	11.12	4.69	ND
Kidney	5611	2	ND	ND	ND	ND	4.23	6.21	ND
Kidney	5643	2	ND	ND	ND	ND	24.99	5.1	ND
Kidney	5644	2	ND	ND	ND	ND	6.03	4.53	ND
Kidney	5659	2	ND	ND	ND	ND	10.95	9.34	ND
Kidney	172	3	ND	ND	ND	ND	1.82	ND	ND
Kidney	5603	3	ND	ND	ND	ND	13.9	2.28	ND
Kidney	5623	3	ND	ND	ND	ND	14	4.39	ND
Kidney	5651	3	ND	ND	ND	ND	2.12	ND	ND
Kidney	5619	5	ND	ND	ND	ND	2.45	ND	ND
Kidney	5621	5	ND	ND	ND	ND	0	ND	ND
Kidney	5649	5	ND	ND	ND	ND	3.06	ND	ND
Kidney	16392	5	ND	ND	ND	ND	1.85	ND	ND
Kidney	5604	8	ND	ND	ND	ND	ND	1.65	ND
Kidney	5615	8	ND	ND	ND	ND	3.28	ND	ND
Kidney	5625	8	ND	ND	ND	ND	4.7	ND	ND
Kidney	5640	8	ND	ND	ND	ND	4.6	ND	ND
Adipose	5602	1	ND	ND	ND	ND	193.59	10.86	ND
Adipose	5638	1	ND	ND	ND	ND	250.5	23.54	ND
Adipose	5657	1	ND	ND	ND	ND	280.69	67.19	ND
Adipose	5660	1	ND	ND	ND	ND	168.69	30.51	ND
Adipose	5611	2	ND	ND	ND	ND	202.38	ND	ND
Adipose	5643	2	ND	ND	ND	ND	277.49	11.51	ND
Adipose	5644	2	ND	ND	ND	ND	355.68	ND	ND
Adipose	5659	2	ND	ND	ND	ND	312.8	36.01	ND
Adipose	172	3	ND	ND	ND	ND	194.61	ND	ND
Adipose	5603	3	ND	ND	ND	ND	149.27	ND	ND
Adipose	5623	3	ND	ND	ND	ND	305.7	ND	ND
Adipose	5651	3	ND	ND	ND	ND	165.07	ND	ND
Adipose	5619	5	ND	ND	ND	ND	196.8	ND	ND
Adipose	5621	5	ND	ND	ND	ND	346.44	ND	ND
Adipose	5649	5	ND	ND	ND	ND	175.6	ND	ND
Adipose	16392	5	ND	ND	ND	ND	256.46	ND	ND
Adipose	5604	8	ND	ND	ND	ND	97.24	ND	ND
Adipose	5615	8	ND	ND	ND	ND	142.08	ND	ND
Adipose	5625	8	ND	ND	ND	ND	65.01	ND	ND
Adipose	5640	8	ND	ND	ND	ND	267.11	ND	ND

Supplementary Table S5. Cannabinoid concentrations in liver and muscle tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. ND: not detected, N/A: not applicable, CBDVA: cannabidivarinic acid, CBD-7-acid: (–)-7-nor-7-carboxy cannabidiol, CBG: cannabigerol, CBGA: cannabigerolic acid, CBL: cannabicyclol. CBLA: cannabicyclolic acid, CBN: cannabinol

Tissue	ID	Time (d)	Concentration ng/g						
			CBDVA	CBD-7-acid	CBG	CBGA	CBL	CBLA	CBN
Liver	5602	1	11.85	169.31	ND	ND	ND	18.92	ND
Liver	5638	1	8.73	45.89	ND	ND	ND	ND	ND
Liver	5657	1	14	188.5	ND	ND	ND	35.56	ND
Liver	5660	1	14.44	138.8	ND	ND	ND	10.5	ND
Liver	5611	2	5.11	137.56	ND	ND	ND	ND	ND
Liver	5643	2	3.4	132.99	ND	ND	ND	ND	ND
Liver	5644	2	ND	256.51	ND	ND	ND	ND	ND
Liver	5659	2	3.32	375.05	ND	ND	ND	9.37	ND
Liver	172	3	ND	101.75	ND	ND	ND	2.12	ND
Liver	5603	3	ND	129.09	ND	ND	ND	ND	ND
Liver	5623	3	ND	50.17	ND	ND	ND	ND	ND
Liver	5651	3	ND	91.55	ND	ND	ND	2.98	ND
Liver	5619	5	2.47	148.53	ND	ND	ND	ND	ND
Liver	5621	5	ND	291.84	ND	ND	ND	ND	ND
Liver	5649	5	ND	40.77	ND	ND	ND	1.3	ND
Liver	16392	5	ND	31.49	ND	ND	ND	ND	ND
Liver	5604	8	ND	34.72	ND	ND	ND	ND	ND
Liver	5615	8	ND	71.98	ND	ND	ND	ND	ND
Liver	5625	8	ND	52.02	ND	ND	ND	ND	ND
Liver	5640	8	ND	38.81	ND	ND	ND	ND	ND
Muscle	5602	1	ND	14.13	ND	ND	ND	ND	ND
Muscle	5638	1	ND	11.15	ND	ND	ND	ND	ND
Muscle	5657	1	ND	16.4	ND	ND	ND	ND	ND
Muscle	5660	1	ND	16.3	ND	ND	ND	ND	ND
Muscle	5611	2	ND	13.72	ND	ND	ND	ND	ND
Muscle	5643	2	ND	28.25	ND	ND	ND	ND	ND
Muscle	5644	2	ND	45.69	ND	ND	ND	ND	ND
Muscle	5659	2	ND	15.18	ND	ND	ND	ND	ND
Muscle	172	3	ND	22.32	ND	ND	ND	ND	ND
Muscle	5603	3	ND	14.15	ND	ND	ND	ND	ND
Muscle	5623	3	ND	31.56	ND	ND	ND	ND	ND
Muscle	5651	3	ND	17.12	ND	ND	ND	ND	ND
Muscle	5619	5	ND	14.15	ND	ND	ND	ND	ND
Muscle	5621	5	ND	24.74	ND	ND	ND	ND	ND
Muscle	5649	5	ND	7.68	ND	ND	ND	ND	ND
Muscle	16392	5	ND	9.26	ND	ND	ND	ND	ND
Muscle	5604	8	ND	6.44	ND	ND	ND	ND	ND
Muscle	5615	8	ND	7.99	ND	ND	ND	ND	ND
Muscle	5625	8	ND	12.73	ND	ND	ND	ND	ND
Muscle	5640	8	ND	8.12	ND	ND	ND	ND	ND

Supplementary Table S6. Cannabinoid concentrations in kidney and adipose tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. ND: not detected, N/A: not applicable, CBDVA: cannabidivarinic acid, CBD-7-acid: (-)-7-nor-7-carboxy cannabidiol, CBG: cannabigerol, CBGA: cannabigerolic acid, CBL: cannabicyclol, CBLA: cannabicyclic acid, CBN: cannabinol

Tissue	ID	Time (d)	Concentration ng/g						
			CBDVA	CBD-7-acid	CBG	CBGA	CBL	CBLA	CBN
Kidney	5602	1	ND	ND	ND	ND	ND	ND	ND
Kidney	5638	1	ND	ND	ND	ND	ND	ND	ND
Kidney	5657	1	ND	ND	ND	ND	ND	ND	ND
Kidney	5660	1	ND	ND	ND	ND	ND	ND	ND
Kidney	5611	2	ND	ND	ND	ND	ND	ND	ND
Kidney	5643	2	ND	ND	ND	ND	ND	ND	ND
Kidney	5644	2	ND	ND	ND	ND	ND	ND	ND
Kidney	5659	2	ND	ND	ND	ND	ND	ND	ND
Kidney	172	3	ND	ND	ND	ND	ND	ND	ND
Kidney	5603	3	ND	ND	ND	ND	ND	ND	ND
Kidney	5623	3	ND	ND	ND	ND	ND	ND	ND
Kidney	5651	3	ND	ND	ND	ND	ND	ND	ND
Kidney	5619	5	ND	ND	ND	ND	ND	ND	ND
Kidney	5621	5	ND	ND	ND	ND	ND	ND	ND
Kidney	5649	5	ND	ND	ND	ND	ND	ND	ND
Kidney	16392	5	ND	ND	ND	ND	ND	ND	ND
Kidney	5604	8	ND	ND	ND	ND	ND	ND	ND
Kidney	5615	8	ND	ND	ND	ND	ND	ND	ND
Kidney	5625	8	ND	ND	ND	ND	ND	ND	ND
Kidney	5640	8	ND	ND	ND	ND	ND	ND	ND
Adipose	5602	1	ND	39.18	ND	ND	ND	ND	ND
Adipose	5638	1	ND	28.59	ND	ND	ND	ND	ND
Adipose	5657	1	ND	142.78	ND	ND	ND	ND	ND
Adipose	5660	1	ND	106.99	ND	ND	ND	ND	ND
Adipose	5611	2	ND	33.44	ND	ND	ND	ND	ND
Adipose	5643	2	ND	80.1	ND	ND	ND	ND	ND
Adipose	5644	2	ND	88.51	ND	ND	ND	ND	ND
Adipose	5659	2	ND	259.69	ND	ND	ND	ND	ND
Adipose	172	3	ND	116.55	ND	ND	ND	ND	ND
Adipose	5603	3	ND	65.44	ND	ND	ND	ND	ND
Adipose	5623	3	ND	114.76	ND	ND	ND	ND	ND
Adipose	5651	3	ND	123.48	ND	ND	ND	ND	ND
Adipose	5619	5	ND	88.18	ND	ND	ND	ND	ND
Adipose	5621	5	ND	45.25	ND	ND	ND	ND	ND
Adipose	5649	5	ND	66.38	ND	ND	ND	ND	ND
Adipose	16392	5	ND	15.12	ND	ND	ND	ND	ND
Adipose	5604	8	ND	49.98	ND	ND	ND	ND	ND
Adipose	5615	8	ND	28.34	ND	ND	ND	ND	ND
Adipose	5625	8	ND	108.14	ND	ND	ND	ND	ND
Adipose	5640	8	ND	32.15	ND	ND	ND	ND	ND

Supplementary Table S7. Cannabinoid concentrations in liver and muscle tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. N/A: not applicable, Total cannabidiol (CBD): $\text{CBD} + (0.877 \times \text{CBDA})$; total Δ^9 -tetrahydrocannabinol (9-THC): $9\text{-THC} + [0.877 \times (\Delta^9\text{-tetrahydrocannabinolic acid})]$; total cannabinoids: sum of all cannabinoids detected in that sample

			Concentration ng/g		
Tissue	ID	Time (d)	Total cannabinoids	Total THC	Total CBD
Liver	5602	1	15487.64	52.08	13323.08
Liver	5638	1	14310.36	42.43	12442.49
Liver	5657	1	9025.2	92.21	7571.94
Liver	5660	1	111691.86	40.89	97742.75
Liver	5611	2	3688.97	22.05	3076.77
Liver	5643	2	10373.62	38.58	8928.28
Liver	5644	2	2642.15	12.85	2069.12
Liver	5659	2	1981.93	28.32	1345.99
Liver	172	3	650.16	6.77	470.61
Liver	5603	3	1293.87	10.24	1004.39
Liver	5623	3	58.98	N/A	7.72
Liver	5651	3	2299.41	9.58	1913.26
Liver	5619	5	4574.27	12.64	3858.29
Liver	5621	5	303.4	1.84	8.3
Liver	5649	5	127.75	4.19	68.98
Liver	16392	5	81.23	1.33	42.3
Liver	5604	8	38.63	0.42	3.01
Liver	5615	8	107.68	1.28	30.21
Liver	5625	8	56	N/A	3.49
Liver	5640	8	52.86	N/A	4.34
Muscle	5602	1	21	N/A	4.97
Muscle	5638	1	50.41	N/A	33.57
Muscle	5657	1	40.28	N/A	19.51
Muscle	5660	1	33.07	N/A	13.53
Muscle	5611	2	17.58	N/A	3.63
Muscle	5643	2	44.13	N/A	8.33
Muscle	5644	2	66.42	N/A	14.01
Muscle	5659	2	29.88	N/A	10.41
Muscle	172	3	24.78	N/A	N/A
Muscle	5603	3	15.75	N/A	N/A
Muscle	5623	3	41.18	N/A	5.55
Muscle	5651	3	33	N/A	10.94
Muscle	5619	5	16.44	N/A	N/A
Muscle	5621	5	30.31	N/A	N/A
Muscle	5649	5	7.68	N/A	N/A
Muscle	16392	5	9.26	N/A	N/A
Muscle	5604	8	9.21	N/A	1.21
Muscle	5615	8	7.99	N/A	N/A
Muscle	5625	8	14.88	N/A	N/A
Muscle	5640	8	15.12	N/A	7

Supplementary Table S8. Cannabinoid concentrations in kidney and adipose tissues of Holstein cattle administered industrial hemp at 4.22 mg/kg cannabidiolic acid (CBDA) per day for 14 days. N/A: not applicable, Total cannabidiol (CBD): $\text{CBD} + (0.877 \times \text{CBDA})$; total Δ^9 -tetrahydrocannabinol (9-THC): $9\text{-THC} + [0.877 \times (\Delta^9\text{-tetrahydrocannabinolic acid})]$; total cannabinoids: sum of all cannabinoids detected in that sample

			Concentration ng/g		
Tissue	ID	Time (d)	Total cannabinoids	Total THC	Total CBD
Kidney	5602	1	71.57	13.03	19.59
Kidney	5638	1	31.67	10.67	14.82
Kidney	5657	1	79.02	17.41	24.47
Kidney	5660	1	62.55	16.88	15.23
Kidney	5611	2	46.52	7.64	9.68
Kidney	5643	2	86.29	20.64	29.46
Kidney	5644	2	63.3	6.65	10
Kidney	5659	2	48.54	8.56	19.14
Kidney	172	3	20.88	1.23	1.82
Kidney	5603	3	40.44	9	15.9
Kidney	5623	3	67.11	9.3	17.85
Kidney	5651	3	21.53	3.05	2.12
Kidney	5619	5	3.53	1.08	2.45
Kidney	5621	5	20.72	0	0
Kidney	5649	5	4.61	1.55	3.06
Kidney	16392	5	1.85	0	1.85
Kidney	5604	8	1.65	0	1.44
Kidney	5615	8	5.31	2.04	3.28
Kidney	5625	8	7.11	2.41	4.7
Kidney	5640	8	6.91	2.31	4.6
Adipose	5602	1	291	47.38	203.11
Adipose	5638	1	355.22	52.59	271.14
Adipose	5657	1	541.2	50.55	339.61
Adipose	5660	1	342.7	36.51	195.45
Adipose	5611	2	279.52	43.7	202.38
Adipose	5643	2	432.48	63.38	287.58
Adipose	5644	2	517.03	72.84	355.68
Adipose	5659	2	664.91	56.42	344.38
Adipose	172	3	354.05	42.89	194.61
Adipose	5603	3	253	38.28	149.27
Adipose	5623	3	476.7	56.24	305.7
Adipose	5651	3	326.31	37.76	165.07
Adipose	5619	5	324.19	39.21	196.8
Adipose	5621	5	446.7	55.02	346.44
Adipose	5649	5	279.11	37.13	175.6
Adipose	16392	5	315.2	43.62	256.46
Adipose	5604	8	170.67	23.45	97.24
Adipose	5615	8	208.66	38.24	142.08
Adipose	5625	8	186.73	13.58	65.01
Adipose	5640	8	336.23	36.97	267.11

Supplementary Table S9. Industrial hemp dose calculations for all detected cannabinoids.

Animal ID	172	16392	T5602	T5603	T5604	T5611	T5615	T5619	T5621	T5623	T5625
Average animal weight, kg	306.879	333.771	341.136	307.729	311.821	352.786	282.336	276.307	290.007	276.236	234.386
Average IH weight, g	11.343	11.857	11.671	11.364	11.514	11.629	11.400	10.971	11.350	11.343	11.057
Amount, mg											
CBD	1239.774	1295.986	1275.687	1242.116	1258.511	1271.003	1246.020	1199.177	1240.555	1239.774	1208.546
CBG	41.969	43.871	43.184	42.048	42.603	43.026	42.180	40.594	41.995	41.969	40.911
9-THC	131.577	137.543	135.389	131.826	133.566	134.891	132.240	127.269	131.660	131.577	128.263
CBD	125.906	131.614	129.553	126.144	127.809	129.077	126.540	121.783	125.985	125.906	122.734
9-THC	11.343	11.857	11.671	11.364	11.514	11.629	11.400	10.971	11.350	11.343	11.057
CBC	14.746	15.414	15.173	14.774	14.969	15.117	14.820	14.263	14.755	14.746	14.374
THCA	26.089	27.271	26.844	26.138	26.483	26.746	26.220	25.234	26.105	26.089	25.431
Dose, mg/kg											
CBD	4.040	3.883	3.740	4.036	4.036	3.603	4.413	4.340	4.278	4.488	5.156
CBG	0.137	0.131	0.127	0.137	0.137	0.122	0.149	0.147	0.145	0.152	0.175
9-THC	0.429	0.412	0.397	0.428	0.428	0.382	0.468	0.461	0.454	0.476	0.547
CBD	0.410	0.394	0.380	0.410	0.410	0.366	0.448	0.441	0.434	0.456	0.524
9-THC	0.037	0.036	0.034	0.037	0.037	0.033	0.040	0.040	0.039	0.041	0.047
CBC	0.048	0.046	0.044	0.048	0.048	0.043	0.052	0.052	0.051	0.053	0.061
THCA	0.085	0.082	0.079	0.085	0.085	0.076	0.093	0.091	0.090	0.094	0.109

Supplementary Table S9, cont. Industrial hemp dose calculations for all detected cannabinoids.

Animal ID	T5638	T5640	T5643	T5644	T5649	T5651	T5657	T5659	T5660	
Average animal weight, kg	309.671	291.750	286.893	303.379	255.264	313.179	270.764	264.864	324.871	
Average IH weight, g	11.193	11.386	11.236	11.457	11.064	11.443	11.279	11.200	11.514	
Amount, mg										Average amount
CBDA	1223.379	1244.459	1228.064	1252.266	1209.326	1250.704	1232.748	1224.160	1258.511	1242.038
CBGA	41.414	42.127	41.572	42.391	40.938	42.339	41.731	41.440	42.603	42.045
CBG	129.837	132.074	130.334	132.903	128.346	132.737	130.831	129.920	133.566	131.817
CBD	124.241	126.381	124.716	127.174	122.814	127.016	125.192	124.320	127.809	126.136
9-THC	11.193	11.386	11.236	11.457	11.064	11.443	11.279	11.200	11.514	11.364
CBC	14.551	14.801	14.606	14.894	14.384	14.876	14.662	14.560	14.969	14.773
THCA	25.744	26.187	25.842	26.351	25.448	26.319	25.941	25.760	26.483	26.136
Dose, mg/kg										Average dose
CBDA	3.951	4.265	4.281	4.128	4.738	3.994	4.553	4.622	3.874	4.221
CBGA	0.134	0.144	0.145	0.140	0.160	0.135	0.154	0.156	0.131	0.143
CBG	0.419	0.453	0.454	0.438	0.503	0.424	0.483	0.491	0.411	0.448
CBD	0.401	0.433	0.435	0.419	0.481	0.406	0.462	0.469	0.393	0.429
9-THC	0.036	0.039	0.039	0.038	0.043	0.037	0.042	0.042	0.035	0.039
CBC	0.047	0.051	0.051	0.049	0.056	0.047	0.054	0.055	0.046	0.050
THCA	0.083	0.090	0.090	0.087	0.100	0.084	0.096	0.097	0.082	0.089

Supplemental Report R1. Withdrawal time for Δ^9 -tetrahydrocannabinolic acid (THCA) in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	THCA
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	5.88 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2023	278.1614
2	12.3283	136.2625
3	14.2655	67.7664
4	14.45	34.2896
5	12.6798	17.6562
6	10.5122	9.2338
7	8.7651	4.8898
8	7.4874	2.6138
9	6.5571	1.4069
10	5.8649	0.761
11	5.3362	0.4132
12	4.922	0.2249
13	4.5901	0.1227
14	4.319	0.067
15	4.0938	0.0367
16	3.9039	0.0201
17	3.7419	0.011
18	3.6021	0.006
19	3.4802	0.0033
20	3.3732	0.0018

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.6178
Homogeneity of Variance	Bartlett Test, test statistic	4.8213
Homogeneity of Variance	Bartlett Test, p-value	0.1854
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9348
Normality of Residuals	Shapiro-Wilk Test, p-value	0.3214

Linear Regression Results

Parameter	Value
Intercept (a)	4.6
Slope (b)	-0.6798
Residual Error (sy.x)	0.5616
p-value	<0.001
Multiple R-squared	0.7975
Adjusted R-squared	0.7819

Data Used for Analysis

Days	ng/g
1	55.9
1	45.7
1	98.8
1	44.2
2	22.1
2	40.4
2	14.6
2	26.7
3	7.7
3	11.7
3	
3	10.9
5	12.6
5	2.1
5	4.8
5	1.5
8	
8	
8	

End of Report

Supplemental Report R2. Withdrawal time for Total THC in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days. Total THC: 9-THC + (0.877*THCA).

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total THC
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	6.46 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	292.6935
2	12.22	152.2131
3	14.1987	80.3162
4	14.8277	43.0977
5	13.4806	23.5326
6	11.3749	13.0573
7	9.5208	7.3426
8	8.1159	4.1721
9	7.0786	2.3892
10	6.3031	1.3761
11	5.7101	0.796
12	5.2459	0.4619
13	4.8745	0.2687
14	4.5716	0.1566
15	4.3205	0.0914
16	4.1091	0.0534
17	3.929	0.0312
18	3.7739	0.0183
19	3.6389	0.0107
20	3.5204	0.0063

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.6211
Homogeneity of Variance	Bartlett Test, test statistic	4.9931
Homogeneity of Variance	Bartlett Test, p-value	0.288
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9763
Normality of Residuals	Shapiro-Wilk Test, p-value	0.9157

Linear Regression Results

Parameter	Value
Intercept (a)	4.3822
Slope (b)	-0.6172
Residual Error (sy.x)	0.6093
p-value	<0.001
Multiple R-squared	0.8516
Adjusted R-squared	0.8417

Data Used for Analysis

Days	ng/g
1	52.078765
1	42.428611
1	92.211033
1	40.891555
2	22.045149
2	38.577495
2	12.846296
2	28.321055
3	6.765178
3	10.236344
3	
3	9.575963
5	12.641997
5	1.839069
5	4.194691
5	1.326024
8	0.418329
8	1.283051
8	
8	

End of Report

Supplemental Report R3. Withdrawal time for Δ 9-tetrahydrocannabinol glucuronide (THC-glu) in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	THC-glu
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	2.12 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2818	23.1013
2	12.2576	10.9212
3	14.1174	5.1943
4	14.5928	2.4876
5	13.2188	1.1998
6	11.1811	0.5825
7	9.3943	0.2843
8	8.0341	0.1394
9	7.0243	0.0685
10	6.266	0.0338
11	5.684	0.0167
12	5.2272	0.0083
13	4.861	0.0041
14	4.5618	0.002
15	4.3133	0.001
16	4.104	5e-04
17	3.9255	2e-04
18	3.7716	1e-04
19	3.6376	1e-04
20	3.5199	0

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.8655
Homogeneity of Variance	Bartlett Test, test statistic	1.2434
Homogeneity of Variance	Bartlett Test, p-value	0.537
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9867
Normality of Residuals	Shapiro-Wilk Test, p-value	0.9899

Linear Regression Results

Parameter	Value
Intercept (a)	3.076
Slope (b)	-0.7345
Residual Error (sy.x)	0.3581
p-value	0.0019
Multiple R-squared	0.7695
Adjusted R-squared	0.7366

Data Used for Analysis

Days	ng/g
1	11.6
1	8.8
1	18.5
1	5.9
2	6.9
2	5.2
2	3.8
2	
3	
3	2.6
3	
3	2.1
5	
5	
5	
8	
8	
8	
8	

End of Report

Supplemental Report R4. Withdrawal time for cannabidiol (CBD) in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBD
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	2.98 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.1818	92.4696
2	12.151	29.9312
3	13.7906	9.8002
4	13.7906	3.2503
5	12.151	1.0919
6	10.1818	0.3711
7	8.5669	0.1273
8	7.3645	0.044
9	6.4772	0.0153
10	5.8109	0.0053
11	5.2986	0.0019
12	4.8954	7e-04
13	4.5712	2e-04
14	4.3057	1e-04
15	4.0847	0
16	3.8982	0
17	3.7388	0
18	3.6012	0
19	3.4811	0
20	3.3756	0

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.0953
Homogeneity of Variance	Bartlett Test, test statistic	0.0782
Homogeneity of Variance	Bartlett Test, p-value	0.9617
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.8423
Normality of Residuals	Shapiro-Wilk Test, p-value	0.047

Linear Regression Results

Parameter	Value
Intercept (a)	4.2969
Slope (b)	-1.1037
Residual Error (sy.x)	0.4876
p-value	<0.001
Multiple R-squared	0.8154
Adjusted R-squared	0.7924

Data Used for Analysis

Days	ng/g
1	16.2
1	15.9
1	41.6
1	18.3
2	13.5
2	16.2
2	7.8
3	1.8
3	1.7
3	
3	3.5
5	
5	
8	
8	
8	

End of Report

Supplemental Report R5. Withdrawal time for cannabidiolic acid (CBDA) in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBDA
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	14.46 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	4307413.8108
2	12.22	1289023.9073
3	14.1987	404131.3276
4	14.8277	133709.6699
5	13.4806	46776.3922
6	11.3749	17227.2202
7	9.5208	6622.275
8	8.1159	2631.855
9	7.0786	1072.3816
10	6.3031	445.0894
11	5.7101	187.2763
12	5.2459	79.6097
13	4.8745	34.1058
14	4.5716	14.6993
15	4.3205	6.3651
16	4.1091	2.7666
17	3.929	1.2061
18	3.7739	0.5271
19	3.6389	0.2308
20	3.5204	0.1012

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.4626
Homogeneity of Variance	Bartlett Test, test statistic	5.5775
Homogeneity of Variance	Bartlett Test, p-value	0.233
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9117
Normality of Residuals	Shapiro-Wilk Test, p-value	0.0686

Linear Regression Results

Parameter	Value
Intercept (a)	10.2347
Slope (b)	-1.0892
Residual Error (sy.x)	1.7814
p-value	<0.001
Multiple R-squared	0.719
Adjusted R-squared	0.7034

Data Used for Analysis

Days	ng/g
1	15173
1	14169
1	8586
1	111430
2	3493
2	10162
2	2350
2	1503
3	535
3	1143
3	9
3	2178
5	4392
5	9
5	76
5	48
8	3
8	33
8	4
8	5

End of Report

Supplemental Report R6. Withdrawal time for Total CBD in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days. Total CBD: $CBD + (0.877 \times CBDA)$.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total CBD
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	14.39 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	3760588.2897
2	12.22	1132051.8266
3	14.1987	357015.9081
4	14.8277	118817.4269
5	13.4806	41810.8136
6	11.3749	15488.6858
7	9.5208	5988.7768
8	8.1159	2393.9762
9	7.0786	981.1394
10	6.3031	409.5902
11	5.7101	173.3421
12	5.2459	74.1148
13	4.8745	31.9362
14	4.5716	13.8442
15	4.3205	6.0297
16	4.1091	2.636
17	3.929	1.1558
18	3.7739	0.5081
19	3.6389	0.2238
20	3.5204	0.0987

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.4533
Homogeneity of Variance	Bartlett Test, test statistic	5.6241
Homogeneity of Variance	Bartlett Test, p-value	0.229
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9092
Normality of Residuals	Shapiro-Wilk Test, p-value	0.0615

Linear Regression Results

Parameter	Value
Intercept (a)	10.095
Slope (b)	-1.0834
Residual Error (sy.x)	1.7809
p-value	<0.001
Multiple R-squared	0.7169
Adjusted R-squared	0.7012

Data Used for Analysis

Days	ng/g
1	13323.08267
1	12442.48544
1	7571.940579
1	97742.7454
2	3076.772099
2	8928.277755
2	2069.117184
2	1345.99321
3	470.6115509
3	1004.394805
3	7.724616
3	1913.263607
5	3858.290347
5	8.298174
5	68.981519
5	42.295079
8	3.010741
8	30.211659
8	3.486075
8	4.344658

End of Report

Supplemental Report R7. Withdrawal time for (–)-7-nor-7-carboxy cannabidiol (CBD-7-acid) in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBD-7-acid
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	67.89 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	1415.4696
2	12.22	1153.3722

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.3977
Homogeneity of Variance	Bartlett Test, test statistic	4.6423
Homogeneity of Variance	Bartlett Test, p-value	0.326
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9768
Normality of Residuals	Shapiro-Wilk Test, p-value	0.8869

Linear Regression Results

Parameter	Value
Intercept (a)	5.197
Slope (b)	-0.1623
Residual Error (sy.x)	0.6453
p-value	0.012
Multiple R-squared	0.3022

Parameter	Value
Adjusted R-squared	0.2634

Data Used for Analysis

Days	ng/g
1	169.3
1	45.9
1	188.5
1	138.8
2	137.6
2	133
2	256.5
2	375.1
3	101.8
3	129.1
3	50.2
3	91.6
5	148.5
5	291.8
5	40.8
5	31.5
8	34.7
8	72
8	52
8	38.8

End of Report

Supplemental Report R8. Withdrawal time for total cannabinoids (sum of all detected cannabinoids) in liver in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total cannabinoids
Tissue	Liver
Codified Tolerance	10 ng/g
Exact Withdrawal Period	18.52 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	903964.2047
2	12.22	382914.1452
3	14.1987	168037.37
4	14.8277	76818.4876
5	13.4806	36637.234
6	11.3749	18169.1413
7	9.5208	9308.3972
8	8.1159	4891.0196
9	7.0786	2619.0931
10	6.3031	1422.2835
11	5.7101	780.4244
12	5.2459	431.5721
13	4.8745	240.0723
14	4.5716	134.1561
15	4.3205	75.2367
16	4.1091	42.3137
17	3.929	23.8521
18	3.7739	13.4704
19	3.6389	7.6191
20	3.5204	4.315

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.1521
Homogeneity of Variance	Bartlett Test, test statistic	5.8426
Homogeneity of Variance	Bartlett Test, p-value	0.2112
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9412
Normality of Residuals	Shapiro-Wilk Test, p-value	0.2529

Linear Regression Results

Parameter	Value
Intercept (a)	9.8287
Slope (b)	-0.77
Residual Error (sy.x)	1.3529
p-value	<0.001
Multiple R-squared	0.6891
Adjusted R-squared	0.6719

Data Used for Analysis

Days	ng/g
1	15487.6
1	14310.4
1	9025.2
1	111691.9
2	3689
2	10373.6
2	2642.1
2	1981.9
3	650.2
3	1293.9
3	59
3	2299.4
5	4574.3
5	303.4
5	127.8
5	81.2
8	38.6
8	107.7
8	56
8	52.9

End of Report

Supplemental Report R9. Withdrawal time for Δ9-tetrahydrocannabinolic acid (THCA) in kidney in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	THCA
Tissue	Kidney
Codified Tolerance	10 ng/g
Exact Withdrawal Period	1.62 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	16.5951
2	12.22	7.3536
3	14.1987	3.2762
4	14.8277	1.4688
5	13.4806	0.6628
6	11.3749	0.3009
7	9.5208	0.1373
8	8.1159	0.0629
9	7.0786	0.0289
10	6.3031	0.0133
11	5.7101	0.0061
12	5.2459	0.0028
13	4.8745	0.0013
14	4.5716	6e-04
15	4.3205	3e-04
16	4.1091	1e-04
17	3.929	1e-04
18	3.7739	0
19	3.6389	0
20	3.5204	0

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.2433
Homogeneity of Variance	Bartlett Test, test statistic	1.4123
Homogeneity of Variance	Bartlett Test, p-value	0.4935
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9473
Normality of Residuals	Shapiro-Wilk Test, p-value	0.6097

Linear Regression Results

Parameter	Value
Intercept (a)	2.8952
Slope (b)	-0.8003
Residual Error (sy.x)	0.2935
p-value	<0.001
Multiple R-squared	0.8509
Adjusted R-squared	0.8343

Data Used for Analysis

Days	ng/g
1	5.3
1	6.8
1	10.7
1	8.5
2	4
2	6.7
2	3
2	3.9
3	
3	1.3
3	1.5
3	1.7
5	
5	
5	
5	
8	
8	
8	
8	

End of Report

Supplemental Report R10. Withdrawal time for total THC in kidney in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days. Total THC: 9-THC + (0.877*THCA).

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total THC
Tissue	Kidney
Codified Tolerance	10 ng/g
Exact Withdrawal Period	9.96 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	9.768	101.7852
2	11.7058	73.1691
3	13.7465	53.5142
4	14.6636	39.9411
5	13.5566	30.4553
6	11.4848	23.6924
7	9.5896	18.7451
8	8.1447	15.0281
9	7.081	12.168
10	6.2896	9.9245
11	5.6875	8.1386
12	5.2183	6.701
13	4.8443	5.5343
14	4.5402	4.5815
15	4.2888	3.7996
16	4.0778	3.1558
17	3.8983	2.6242
18	3.744	2.1842
19	3.6099	1.8194
20	3.4924	1.5165
21	3.3886	1.2647
22	3.2962	1.0552

Days	k-factor	Upper Tolerance Limit
23	3.2136	0.8808
24	3.1392	0.7354
25	3.0719	0.6143
26	3.0108	0.5132
27	2.955	0.4288
28	2.9038	0.3584
29	2.8567	0.2996
30	2.8133	0.2505
31	2.7731	0.2095
32	2.7358	0.1752
33	2.7011	0.1465
34	2.6687	0.1226
35	2.6385	0.1025
36	2.6101	0.0858
37	2.5834	0.0718
38	2.5584	0.0601
39	2.5347	0.0503
40	2.5124	0.0421
41	2.4913	0.0352
42	2.4714	0.0295
43	2.4524	0.0247
44	2.4344	0.0206
45	2.4173	0.0173
46	2.4011	0.0145
47	2.3855	0.0121
48	2.3707	0.0101
49	2.3566	0.0085
50	2.343	0.0071
51	2.3301	0.0059
52	2.3177	0.005
53	2.3058	0.0042
54	2.2944	0.0035
55	2.2834	0.0029
56	2.2729	0.0024
57	2.2627	0.002
58	2.253	0.0017
59	2.2436	0.0014
60	2.2345	0.0012

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.0632
Homogeneity of Variance	Bartlett Test, test statistic	8.4377
Homogeneity of Variance	Bartlett Test, p-value	0.0768
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.8911

Assumption	Test	Result
Normality of Residuals	Shapiro-Wilk Test, p-value	0.0581

Linear Regression Results

Parameter	Value
Intercept (a)	2.6234
Slope (b)	-0.283
Residual Error (sy.x)	0.7191
p-value	0.0019
Multiple R-squared	0.5095
Adjusted R-squared	0.4745

Data Used for Analysis

Days	ng/g
1	10.67252
1	17.405349
1	16.875051
2	7.636246
2	20.637344
2	6.645984
2	8.563391
3	1.234
3	8.999774
3	9.296548
3	3.054189
5	1.079
5	
5	1.551
5	
8	
8	2.035
8	2.408
8	2.309

End of Report

Supplemental Report R11. Withdrawal time for cannabidiol (CBD) in kidney in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBD
Tissue	Kidney
Codified Tolerance	10 ng/g
Exact Withdrawal Period	8.5 Day
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Day	k-factor	Upper Tolerance Limit
1	9.3641	23.2626
2	11.0464	20.317
3	12.8291	17.858
4	13.8356	15.8132
5	13.2229	14.1131
6	11.5355	12.6918
7	9.7803	11.4902
8	8.356	10.4595
9	7.2751	9.5622

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.1557
Homogeneity of Variance	Bartlett Test, test statistic	2.8996
Homogeneity of Variance	Bartlett Test, p-value	0.2346
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.8729
Normality of Residuals	Shapiro-Wilk Test, p-value	0.132

Linear Regression Results

Parameter	Value
Intercept (a)	2.3243
Slope (b)	-0.1166
Residual Error (sy.x)	0.3441
p-value	0.0163
Multiple R-squared	0.5853
Adjusted R-squared	0.5261

Data Used for Analysis

Day	ng/g
1	12.4
1	9.6
1	11.1
2	4.2
2	6
2	10.9
3	
3	
5	
5	
5	
8	
8	3.3
8	4.7
8	4.6

End of Report

Supplemental Report R12. Withdrawal time for total CBD in kidney in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days. Total CBD: $CBD + (0.877 \times CBDA)$.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total CBD
Tissue	Kidney
Codified Tolerance	10 ng/g
Exact Withdrawal Period	14.57 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	188.5876
2	12.22	137.1562
3	14.1987	101.7154
4	14.8277	77.1526
5	13.4806	59.9047
6	11.3749	47.5251
7	9.5208	38.3864
8	8.1159	31.4405
9	7.0786	26.022
10	6.3031	21.7043
11	5.7101	18.207
12	5.2459	15.3389
13	4.8745	12.9648
14	4.5716	10.9857
15	4.3205	9.3271
16	4.1091	7.9313
17	3.929	6.7529
18	3.7739	5.7555
19	3.6389	4.9096
20	3.5204	4.1909

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.1216
Homogeneity of Variance	Bartlett Test, test statistic	8.5904
Homogeneity of Variance	Bartlett Test, p-value	0.0722
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9256
Normality of Residuals	Shapiro-Wilk Test, p-value	0.144

Linear Regression Results

Parameter	Value
Intercept (a)	2.941
Slope (b)	-0.2693
Residual Error (sy.x)	0.7678
p-value	0.0012
Multiple R-squared	0.4683
Adjusted R-squared	0.437

Data Used for Analysis

Days	ng/g
1	19.588881
1	14.819907
1	24.471177
1	15.232007
2	9.682801
2	29.459454
2	9.996302
2	19.135795
3	1.821
3	15.901806
3	17.852907
3	2.123
5	2.447
5	
5	3.06
5	1.848
8	1.443542
8	3.279
8	4.704
8	4.599

End of Report

Supplemental Report R13. Withdrawal time for total cannabinoids (sum of all cannabinoids detected) in kidney in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total cannabinoids
Tissue	Kidney
Codified Tolerance	10 ng/g
Exact Withdrawal Period	12.58 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	857.622
2	12.22	531.3245
3	14.1987	335.7341
4	14.8277	217.0417
5	13.4806	143.6684
6	11.3749	97.1952
7	9.5208	66.96
8	8.1159	46.7862
9	7.0786	33.038
10	6.3031	23.5129
11	5.7101	16.8312
12	5.2459	12.1007
13	4.8745	8.7285
14	4.5716	6.312
15	4.3205	4.5737
16	4.1091	3.3194
17	3.929	2.4121
18	3.7739	1.7546
19	3.6389	1.2775
20	3.5204	0.9307

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.054
Homogeneity of Variance	Bartlett Test, test statistic	4.6858
Homogeneity of Variance	Bartlett Test, p-value	0.3211
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9235
Normality of Residuals	Shapiro-Wilk Test, p-value	0.1156

Linear Regression Results

Parameter	Value
Intercept (a)	4.5841
Slope (b)	-0.4291
Residual Error (sy.x)	0.7553
p-value	<0.001
Multiple R-squared	0.6884
Adjusted R-squared	0.6711

Data Used for Analysis

Days	ng/g
1	71.574
1	31.67
1	79.022
1	62.551
2	46.516
2	86.286
2	63.295
2	48.543
3	20.877
3	40.442
3	67.111
3	21.529
5	3.526
5	20.72
5	4.611
5	1.848
8	1.646
8	5.314
8	7.112
8	6.908

End of Report

Supplemental Report R14. Withdrawal time for (–)-11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol (THC-acid) in muscle in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	THC-acid
Tissue	Muscle
Codified Tolerance	10 ng/g
Exact Withdrawal Period	3.37 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	8.3737	14.9197
2	9.9732	12.5226
3	11.9146	10.6054
4	13.4655	9.0806
5	13.3217	7.8699
6	11.6331	6.9034
7	9.7179	6.1206
8	8.1807	5.4738
9	7.0461	4.928
10	6.2118	4.4587
11	5.5862	4.0489
12	5.1055	3.6869
13	4.7271	3.3641
14	4.4229	3.0745
15	4.1738	2.8132
16	3.9664	2.5766
17	3.7913	2.3617
18	3.6416	2.1661
19	3.5124	1.9877
20	3.3996	1.8248

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.2225
Homogeneity of Variance	Bartlett Test, test statistic	0.1386
Homogeneity of Variance	Bartlett Test, p-value	0.933
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9674
Normality of Residuals	Shapiro-Wilk Test, p-value	0.872

Linear Regression Results

Parameter	Value
Intercept (a)	1.628
Slope (b)	-0.144
Residual Error (sy.x)	0.4135
p-value	0.0474
Multiple R-squared	0.4516
Adjusted R-squared	0.3733

Data Used for Analysis

Days	ng/g
2	
2	6.7
2	5.2
2	3
3	2.5
3	1.6
3	3.7
3	3.8
5	
5	
8	1.4
8	
8	2.1
8	

End of Report

Supplemental Report R15. Withdrawal time for cannabidiolic acid (CBDA) in muscle in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBDA
Tissue	Muscle
Codified Tolerance	10 ng/g
Exact Withdrawal Period	3.44 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	9.507	62.3847
2	11.475	29.2271
3	13.5074	13.8208
4	14.2176	6.6072
5	12.8508	3.1947
6	10.7342	1.5609
7	8.924	0.7692
8	7.5842	0.3816
9	6.6107	0.1902
10	5.8908	0.0952
11	5.3445	0.0477
12	4.9192	0.024
13	4.5803	0.0121
14	4.3048	0.0061
15	4.0769	0.0031
16	3.8855	0.0015
17	3.7226	8e-04
18	3.5825	4e-04
19	3.4607	2e-04
20	3.3539	1e-04

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.8853
Homogeneity of Variance	Bartlett Test, test statistic	1.4377
Homogeneity of Variance	Bartlett Test, p-value	0.4873
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9523
Normality of Residuals	Shapiro-Wilk Test, p-value	0.7349

Linear Regression Results

Parameter	Value
Intercept (a)	3.7823
Slope (b)	-0.7343
Residual Error (sy.x)	0.477
p-value	0.0145
Multiple R-squared	0.6582
Adjusted R-squared	0.6013

Data Used for Analysis

Days	ng/g
1	35.7
1	19.9
1	13.9
2	7.2
2	12.4
2	10.4
3	
3	
3	2.7
3	9.2
5	
5	
5	
5	
8	
8	
8	

End of Report

Supplemental Report R16. Withdrawal time for total CBD in muscle in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days. Total CBD: $CBD + (0.877 \times CBDA)$.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total CBD
Tissue	Muscle
Codified Tolerance	10 ng/g
Exact Withdrawal Period	11.89 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	74.8158
2	12.22	58.3719
3	14.1987	46.1735
4	14.8277	37.1104
5	13.4806	30.3223
6	11.3749	25.1554
7	9.5208	21.1349
8	8.1159	17.9328
9	7.0786	15.3285
10	6.3031	13.174
11	5.7101	11.3683
12	5.2459	9.8398
13	4.8745	8.5364
14	4.5716	7.4189
15	4.3205	6.4566
16	4.1091	5.6253
17	3.929	4.9054
18	3.7739	4.2808
19	3.6389	3.7379
20	3.5204	3.2655

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.7996
Homogeneity of Variance	Bartlett Test, test statistic	1.0862
Homogeneity of Variance	Bartlett Test, p-value	0.7804
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9456
Normality of Residuals	Shapiro-Wilk Test, p-value	0.5737

Linear Regression Results

Parameter	Value
Intercept (a)	2.7156
Slope (b)	-0.2135
Residual Error (sy.x)	0.7068
p-value	0.0303
Multiple R-squared	0.3887
Adjusted R-squared	0.3276

Data Used for Analysis

Days	ng/g
1	4.974344
1	33.574873
1	19.509466
1	13.532161
2	3.62645
2	8.329015
2	14.013265
2	10.409966
3	
3	
3	5.550943
3	10.938801
5	
5	
5	
5	
8	1.209383
8	
8	
8	7.002

End of Report

Supplemental Report R17. Withdrawal time for (–)-7-nor-7-carboxy cannabidiol (CBD-7-acid) in muscle in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBD-7-acid
Tissue	Muscle
Codified Tolerance	10 ng/g
Exact Withdrawal Period	38.36 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	90.2186
2	12.22	78.3912
3	14.1987	68.8919
4	14.8277	61.3437
5	13.4806	55.3706
6	11.3749	50.6095
7	9.5208	46.7435
8	8.1159	43.5249
9	7.0786	40.7751
10	6.3031	38.3713
11	5.7101	36.2297
12	5.2459	34.2932
13	4.8745	32.5219
14	4.5716	30.8872
15	4.3205	29.3684
16	4.1091	27.9497
17	3.929	26.619
18	3.7739	25.3669
19	3.6389	24.1856
20	3.5204	23.0689

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.176
Homogeneity of Variance	Bartlett Test, test statistic	3.8083
Homogeneity of Variance	Bartlett Test, p-value	0.4326
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9256
Normality of Residuals	Shapiro-Wilk Test, p-value	0.1269

Linear Regression Results

Parameter	Value
Intercept (a)	3.1193
Slope (b)	-0.1119
Residual Error (sy.x)	0.4344
p-value	0.0104
Multiple R-squared	0.3125
Adjusted R-squared	0.2743

Data Used for Analysis

Days	ng/g
1	14.1
1	11.1
1	16.4
1	16.3
2	13.7
2	28.2
2	45.7
2	15.2
3	22.3
3	14.1
3	31.6
3	17.1
5	14.1
5	24.7
5	7.7
5	9.3
8	6.4
8	8
8	12.7
8	8.1

End of Report

Supplemental Report R18. Withdrawal time for total cannabinoids (sum of all detected cannabinoids) in muscle in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total cannabinoids
Tissue	Muscle
Codified Tolerance	10 ng/g
Exact Withdrawal Period	21.84 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	176.5777
2	12.22	142.7811
3	14.1987	116.841
4	14.8277	96.9442
5	13.4806	81.5956
6	11.3749	69.5893
7	9.5208	60.0059
8	8.1159	52.1865
9	7.0786	45.6776
10	6.3031	40.1702
11	5.7101	35.4511
12	5.2459	31.3688
13	4.8745	27.812
14	4.5716	24.6965
15	4.3205	21.9566
16	4.1091	19.5393
17	3.929	17.4016
18	3.7739	15.5076
19	3.6389	13.8269
20	3.5204	12.3337

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.62
Homogeneity of Variance	Bartlett Test, test statistic	1.5607
Homogeneity of Variance	Bartlett Test, p-value	0.8158
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9633
Normality of Residuals	Shapiro-Wilk Test, p-value	0.6114

Linear Regression Results

Parameter	Value
Intercept (a)	3.7824
Slope (b)	-0.1824
Residual Error (sy.x)	0.4573
p-value	<0.001
Multiple R-squared	0.5211
Adjusted R-squared	0.4945

Data Used for Analysis

Days	ng/g
1	21
1	50.4
1	40.3
1	33.1
2	17.6
2	44.1
2	66.4
2	29.9
3	24.8
3	15.8
3	41.2
3	33
5	16.4
5	30.3
5	7.7
5	9.3
8	9.2
8	8
8	14.9
8	15.1

End of Report

Supplemental Report R19. Withdrawal time for Δ 9-tetrahydrocannabinol (9-THC) in adipose in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	9-THC
Tissue	Fat
Codified Tolerance	10 ng/g
Exact Withdrawal Period	48.02 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	144.5249
2	12.22	129.2144
3	14.1987	116.3846
4	14.8277	105.7303
5	13.4806	96.9074
6	11.3749	89.55
7	9.5208	83.3171
8	8.1159	77.9298
9	7.0786	73.1806
10	6.3031	68.9228
11	5.7101	65.0541
12	5.2459	61.5027
13	4.8745	58.2171
14	4.5716	55.1597
15	4.3205	52.302
16	4.1091	49.6218
17	3.929	47.1015
18	3.7739	44.7267
19	3.6389	42.4853
20	3.5204	40.3671

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.2663
Homogeneity of Variance	Bartlett Test, test statistic	5.3495
Homogeneity of Variance	Bartlett Test, p-value	0.2533
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9372
Normality of Residuals	Shapiro-Wilk Test, p-value	0.2124

Linear Regression Results

Parameter	Value
Intercept (a)	4.0915
Slope (b)	-0.0933
Residual Error (sy.x)	0.2834
p-value	0.0018
Multiple R-squared	0.4261
Adjusted R-squared	0.3942

Data Used for Analysis

Days	ng/g
1	47.38
1	52.592
1	50.546
1	36.511
2	43.7
2	63.38
2	72.841
2	56.415
3	42.885
3	38.284
3	56.241
3	37.759
5	39.209
5	55.018
5	37.13
5	43.618
8	23.453
8	38.241
8	13.583
8	36.965

End of Report

Supplemental Report R20. Withdrawal time for total THC in adipose in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days. Total THC: 9-THC + (0.877*THCA).

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total THC
Tissue	Fat
Codified Tolerance	10 ng/g
Exact Withdrawal Period	48.02 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	144.5249
2	12.22	129.2144
3	14.1987	116.3846
4	14.8277	105.7303
5	13.4806	96.9074
6	11.3749	89.55
7	9.5208	83.3171
8	8.1159	77.9298
9	7.0786	73.1806
10	6.3031	68.9228
11	5.7101	65.0541
12	5.2459	61.5027
13	4.8745	58.2171
14	4.5716	55.1597
15	4.3205	52.302
16	4.1091	49.6218
17	3.929	47.1015
18	3.7739	44.7267
19	3.6389	42.4853
20	3.5204	40.3671
21	3.4156	38.3631
22	3.3223	36.4656

Days	k-factor	Upper Tolerance Limit
23	3.2387	34.6677
24	3.1634	32.963
25	3.0952	31.346
26	3.0332	29.8116
27	2.9765	28.3549
28	2.9246	26.9716
29	2.8768	25.6577
30	2.8326	24.4093
31	2.7918	23.2231
32	2.7538	22.0957
33	2.7185	21.024
34	2.6855	20.0051
35	2.6547	19.0364
36	2.6257	18.1152
37	2.5986	17.2391
38	2.573	16.4059
39	2.5489	15.6134
40	2.5262	14.8595
41	2.5047	14.1423
42	2.4843	13.4601
43	2.4649	12.811
44	2.4466	12.1934
45	2.4291	11.6058
46	2.4125	11.0467
47	2.3966	10.5147
48	2.3815	10.0084
49	2.367	9.5266
50	2.3532	9.0681
51	2.3399	8.6318
52	2.3272	8.2166
53	2.3151	7.8214
54	2.3034	7.4453
55	2.2922	7.0873
56	2.2814	6.7466
57	2.271	6.4224
58	2.261	6.1137
59	2.2514	5.82
60	2.2421	5.5404

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.2663
Homogeneity of Variance	Bartlett Test, test statistic	5.3495
Homogeneity of Variance	Bartlett Test, p-value	0.2533
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9372

Assumption	Test	Result
Normality of Residuals	Shapiro-Wilk Test, p-value	0.2124

Linear Regression Results

Parameter	Value
Intercept (a)	4.0915
Slope (b)	-0.0933
Residual Error (sy.x)	0.2834
p-value	0.0018
Multiple R-squared	0.4261
Adjusted R-squared	0.3942

Data Used for Analysis

Days	ng/g
1	47.38
1	52.592
1	50.546
1	36.511
2	43.7
2	63.38
2	72.841
2	56.415
3	42.885
3	38.284
3	56.241
3	37.759
5	39.209
5	55.018
5	37.13
5	43.618
8	23.453
8	38.241
8	13.583
8	36.965

End of Report

Supplemental Report R21. Withdrawal time for cannabidiol (CBD) in adipose in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBD
Tissue	Fat
Codified Tolerance	10 ng/g
Exact Withdrawal Period	153.26 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	955.8067
2	12.22	855.5431
3	14.1987	773.4193
4	14.8277	707.2321
5	13.4806	654.4291
6	11.3749	612.2275
7	9.5208	577.9909
8	8.1159	549.5487
9	7.0786	525.2863
10	6.3031	504.0692
11	5.7101	485.1181
12	5.2459	467.8979
13	4.8745	452.0365
14	4.5716	437.2709
15	4.3205	423.4109
16	4.1091	410.3163
17	3.929	397.8814
18	3.7739	386.0249
19	3.6389	374.6832
20	3.5204	363.8052

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.2618
Homogeneity of Variance	Bartlett Test, test statistic	3.6554
Homogeneity of Variance	Bartlett Test, p-value	0.4546
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9789
Normality of Residuals	Shapiro-Wilk Test, p-value	0.9198

Linear Regression Results

Parameter	Value
Intercept (a)	5.6442
Slope (b)	-0.0859
Residual Error (sy.x)	0.379
p-value	0.0216
Multiple R-squared	0.26
Adjusted R-squared	0.2189

Data Used for Analysis

Days	ng/g
1	193.586
1	250.502
1	280.689
1	168.692
2	202.379
2	277.485
2	355.677
2	312.803
3	194.613
3	149.27
3	305.704
3	165.071
5	196.803
5	346.438
5	175.598
5	256.461
8	97.243
8	142.077
8	65.012
8	267.106

End of Report

Supplemental Report R22. Withdrawal time for total CBD in adipose in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days. Total CBD: $CBD + (0.877 \times CBDA)$.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total CBD
Tissue	Fat
Codified Tolerance	10 ng/g
Exact Withdrawal Period	105.47 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	1012.9689
2	12.22	895.5653
3	14.1987	799.6084
4	14.8277	722.1138
5	13.4806	659.8739
6	11.3749	609.5947
7	9.5208	568.2756
8	8.1159	533.5042
9	7.0786	503.5115
10	6.3031	477.0638
11	5.7101	453.3151
12	5.2459	431.6833
13	4.8745	411.7612
14	4.5716	393.2579
15	4.3205	375.9599
16	4.1091	359.7072
17	3.929	344.3765
18	3.7739	329.8705
19	3.6389	316.1109
20	3.5204	303.0336
21	3.4156	290.5845
22	3.3223	278.718

Days	k-factor	Upper Tolerance Limit
23	3.2387	267.3944
24	3.1634	256.5791
25	3.0952	246.2413
26	3.0332	236.3537
27	2.9765	226.8915
28	2.9246	217.832
29	2.8768	209.1547
30	2.8326	200.8405
31	2.7918	192.8718
32	2.7538	185.2321
33	2.7185	177.9063
34	2.6855	170.8799
35	2.6547	164.1394
36	2.6257	157.6723
37	2.5986	151.4664
38	2.573	145.5104
39	2.5489	139.7937
40	2.5262	134.3059
41	2.5047	129.0375
42	2.4843	123.9793
43	2.4649	119.1224
44	2.4466	114.4585
45	2.4291	109.9797
46	2.4125	105.6784
47	2.3966	101.5472
48	2.3815	97.5793
49	2.367	93.768
50	2.3532	90.107
51	2.3399	86.5902
52	2.3272	83.2118
53	2.3151	79.9663
54	2.3034	76.8483
55	2.2922	73.8527
56	2.2814	70.9747
57	2.271	68.2095
58	2.261	65.5527
59	2.2514	63
60	2.2421	60.5472
61	2.2332	58.1904
62	2.2245	55.9257
63	2.2162	53.7496
64	2.2081	51.6586
65	2.2003	49.6492
66	2.1927	47.7183
67	2.1854	45.8627
68	2.1783	44.0796
69	2.1715	42.366

Days	k-factor	Upper Tolerance Limit
70	2.1648	40.7193
71	2.1584	39.1368
72	2.1521	37.616
73	2.146	36.1544
74	2.1401	34.7498
75	2.1344	33.3998
76	2.1288	32.1025
77	2.1234	30.8557
78	2.1181	29.6574
79	2.1129	28.5057
80	2.1079	27.3989
81	2.1031	26.3351
82	2.0983	25.3127
83	2.0937	24.3301
84	2.0892	23.3857
85	2.0848	22.478
86	2.0805	21.6056
87	2.0763	20.7671
88	2.0722	19.9613
89	2.0682	19.1867
90	2.0643	18.4422
91	2.0605	17.7267
92	2.0568	17.0389
93	2.0531	16.3779
94	2.0496	15.7426
95	2.0461	15.1319
96	2.0427	14.545
97	2.0394	13.9808
98	2.0361	13.4386
99	2.0329	12.9174
100	2.0298	12.4164
101	2.0267	11.9349
102	2.0237	11.4721
103	2.0208	11.0272
104	2.0179	10.5996
105	2.0151	10.1886
106	2.0123	9.7936
107	2.0096	9.4139
108	2.007	9.0489
109	2.0044	8.6981
110	2.0018	8.3609
111	1.9993	8.0367
112	1.9968	7.7252
113	1.9944	7.4257
114	1.992	7.1379
115	1.9897	6.8612
116	1.9874	6.5953

Days	k-factor	Upper Tolerance Limit
117	1.9852	6.3396
118	1.983	6.0939
119	1.9808	5.8577
120	1.9787	5.6307
121	1.9766	5.4125
122	1.9745	5.2027
123	1.9725	5.0011
124	1.9705	4.8073
125	1.9685	4.621
126	1.9666	4.4419
127	1.9647	4.2698
128	1.9628	4.1043
129	1.961	3.9453
130	1.9592	3.7924
131	1.9574	3.6454
132	1.9557	3.5042
133	1.9539	3.3684
134	1.9523	3.2379
135	1.9506	3.1124
136	1.9489	2.9918
137	1.9473	2.8759
138	1.9457	2.7645
139	1.9441	2.6574
140	1.9426	2.5544
141	1.9411	2.4555
142	1.9396	2.3604
143	1.9381	2.2689
144	1.9366	2.181
145	1.9352	2.0965
146	1.9338	2.0153
147	1.9324	1.9372
148	1.931	1.8622
149	1.9296	1.79
150	1.9283	1.7207
151	1.927	1.654
152	1.9257	1.59
153	1.9244	1.5284
154	1.9231	1.4692
155	1.9218	1.4123
156	1.9206	1.3576
157	1.9194	1.305
158	1.9182	1.2544
159	1.917	1.2058
160	1.9158	1.1591

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.3429
Homogeneity of Variance	Bartlett Test, test statistic	3.139
Homogeneity of Variance	Bartlett Test, p-value	0.5348
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9748
Normality of Residuals	Shapiro-Wilk Test, p-value	0.8516

Linear Regression Results

Parameter	Value
Intercept (a)	5.7215
Slope (b)	-0.0984
Residual Error (sy.x)	0.377
p-value	0.0096
Multiple R-squared	0.3179
Adjusted R-squared	0.28

Data Used for Analysis

Days	ng/g
1	203.111974
1	271.143072
1	339.611122
1	195.451024
2	202.379
2	287.57927
2	355.677
2	344.382016
3	194.613
3	149.27
3	305.704
3	165.071
5	196.803
5	346.438
5	175.598
5	256.461
8	97.243
8	142.077
8	65.012
8	267.106

End of Report

Supplemental Report R23. Withdrawal time for (–)-7-nor-7-carboxy cannabidiol (CBD-7-acid) in adipose in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	CBD-7-acid
Tissue	Fat
Codified Tolerance	10 ng/g
Exact Withdrawal Period	77.07 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	9.7594	881.5874
2	11.8123	720.7807
3	13.8514	600.5962
4	14.3648	511.6365
5	12.7906	445.8879
6	10.6202	396.6709
7	8.8258	358.8341
8	7.5111	328.7393
9	6.5577	303.97
10	5.8523	282.9628
11	5.316	264.705
12	4.8976	248.529
13	4.5637	233.9833
14	4.2917	220.7534
15	4.0664	208.6141
16	3.8769	197.399
17	3.7155	186.9823
18	3.5764	177.2661
19	3.4554	168.1726
20	3.3493	159.6387

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.6596
Homogeneity of Variance	Bartlett Test, test statistic	3.9071
Homogeneity of Variance	Bartlett Test, p-value	0.4187
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.922
Normality of Residuals	Shapiro-Wilk Test, p-value	0.14

Linear Regression Results

Parameter	Value
Intercept (a)	4.7813
Slope (b)	-0.1552
Residual Error (sy.x)	0.6091
p-value	0.0229
Multiple R-squared	0.2837
Adjusted R-squared	0.2389

Data Used for Analysis

Days	ng/g
1	39.176
1	142.776
1	106.988
2	33.437
2	80.103
2	88.511
2	259.685
3	116.553
3	65.444
3	114.759
3	123.478
5	88.176
5	45.248
5	66.378
5	15.124
8	49.977
8	28.337
8	32.154

End of Report

Supplemental Report R24. Withdrawal time for total cannabinoids (sum of all detected cannabinoids) in adipose in Holstein cattle administered industrial hemp at 4.22 mg/kg CBDA for 14 days.

FDA Withdrawal Period Application Report

Withdrawal Period Calculation Results

Parameter	Value
Species	Cattle
Active Pharmaceutical Ingredient	Industrial hemp
Marker Residue	Total cannabinoids
Tissue	Fat
Codified Tolerance	10 ng/g
Exact Withdrawal Period	103.93 Days
Percentile Coverage	99th
Confidence Level	95%
k-factor Type	non-central t

99th Percentile Upper Tolerance Limits with 95% Confidence

Days	k-factor	Upper Tolerance Limit
1	10.2084	1128.4668
2	12.22	1015.9252
3	14.1987	921.3864
4	14.8277	842.8117
5	13.4806	777.7893
6	11.3749	723.6603
7	9.5208	677.8892
8	8.1159	638.3766
9	7.0786	603.5505
10	6.3031	572.2964
11	5.7101	543.839
12	5.2459	517.6369
13	4.8745	493.3056
14	4.5716	470.5659
15	4.3205	449.2093
16	4.1091	429.0762
17	3.929	410.0412
18	3.7739	392.0033
19	3.6389	374.8794
20	3.5204	358.5994
21	3.4156	343.1037
22	3.3223	328.3404

Days	k-factor	Upper Tolerance Limit
23	3.2387	314.2637
24	3.1634	300.8328
25	3.0952	288.0112
26	3.0332	275.7654
27	2.9765	264.065
28	2.9246	252.8819
29	2.8768	242.1902
30	2.8326	231.9655
31	2.7918	222.1855
32	2.7538	212.829
33	2.7185	203.876
34	2.6855	195.308
35	2.6547	187.1073
36	2.6257	179.2572
37	2.5986	171.742
38	2.573	164.5466
39	2.5489	157.657
40	2.5262	151.0595
41	2.5047	144.7414
42	2.4843	138.6905
43	2.4649	132.8951
44	2.4466	127.3442
45	2.4291	122.0272
46	2.4125	116.934
47	2.3966	112.055
48	2.3815	107.381
49	2.367	102.9033
50	2.3532	98.6135
51	2.3399	94.5035
52	2.3272	90.5658
53	2.3151	86.793
54	2.3034	83.1782
55	2.2922	79.7146
56	2.2814	76.3958
57	2.271	73.2158
58	2.261	70.1686
59	2.2514	67.2488
60	2.2421	64.4509
61	2.2332	61.7697
62	2.2245	59.2005
63	2.2162	56.7384
64	2.2081	54.379
65	2.2003	52.118
66	2.1927	49.9512
67	2.1854	47.8747
68	2.1783	45.8848
69	2.1715	43.9778

Days	k-factor	Upper Tolerance Limit
70	2.1648	42.1501
71	2.1584	40.3986
72	2.1521	38.72
73	2.146	37.1113
74	2.1401	35.5696
75	2.1344	34.092
76	2.1288	32.6759
77	2.1234	31.3186
78	2.1181	30.0179
79	2.1129	28.7713
80	2.1079	27.5765
81	2.1031	26.4314
82	2.0983	25.3339
83	2.0937	24.282
84	2.0892	23.2738
85	2.0848	22.3076
86	2.0805	21.3815
87	2.0763	20.4939
88	2.0722	19.6432
89	2.0682	18.8278
90	2.0643	18.0463
91	2.0605	17.2973
92	2.0568	16.5794
93	2.0531	15.8913
94	2.0496	15.2318
95	2.0461	14.5997
96	2.0427	13.9939
97	2.0394	13.4132
98	2.0361	12.8566
99	2.0329	12.3231
100	2.0298	11.8118
101	2.0267	11.3217
102	2.0237	10.852
103	2.0208	10.4017
104	2.0179	9.9702
105	2.0151	9.5565
106	2.0123	9.1601
107	2.0096	8.7801
108	2.007	8.4158
109	2.0044	8.0667
110	2.0018	7.7321
111	1.9993	7.4114
112	1.9968	7.1039
113	1.9944	6.8093
114	1.992	6.5268
115	1.9897	6.2561
116	1.9874	5.9966

Days	k-factor	Upper Tolerance Limit
117	1.9852	5.7479
118	1.983	5.5095
119	1.9808	5.281
120	1.9787	5.062

Withdrawal Period Calculation Assumptions

Assumption	Test	Result
Linearity	Lack of Fit Test, p-value	0.4427
Homogeneity of Variance	Bartlett Test, test statistic	0.9926
Homogeneity of Variance	Bartlett Test, p-value	0.9109
Normality of Residuals	Shapiro-Wilk Test, W-statistic	0.9492
Normality of Residuals	Shapiro-Wilk Test, p-value	0.3556

Linear Regression Results

Parameter	Value
Intercept (a)	6.1426
Slope (b)	-0.0865
Residual Error (sy.x)	0.2826
p-value	0.0032
Multiple R-squared	0.3905
Adjusted R-squared	0.3567

Data Used for Analysis

Days	ng/g
1	291.004
1	355.217
1	541.197
1	342.703
2	279.516
2	432.478
2	517.029
2	664.911
3	354.051
3	252.998
3	476.704
3	326.308
5	324.188
5	446.704
5	279.106
5	315.203
8	170.673

Days	ng/g
8	208.655
8	186.733
8	336.225

End of Report