RE: MPI dog testing - proposal by PR 071108.doc

Wednesday, September 19, 2012
3:36 PM

Subject	**RE: MPI dog testing - proposal by PR 071108.doc**
From	Dieterle Roland Mario CHBS
To	Dixon Monty USGR
Cc	Mewes Kersten CHBS
Sent	Wednesday, November 14, 2007 11:58 AM
Attachments	 MPI dog testing - pr...

Monty

Please listen to the voicemail I've just dropped.

We fully agree with your comments which are in line of what we've discussed recently. We also fully support the testing of a PQ product with increased emetic level, however, such a study can probably only be started next year. The only possible test we therefore see (subject to availability of the CoA and SEARC approval), is the one with G. 240 1x emetic plus adjuvant system.

I hope you and your colleagues can agree. Please call me as soon as you are back in office to further discuss.

Regards, Roland

PS: Please check the names of the authors of the doc.

From: Dixon Monty USGR
Sent: Tuesday, November 13, 2007 21:06
To: Dieterle Roland Mario CHBS; Abbott John USGR; Akins Jonathan USGR
Cc: Mewes Kersten CHBS
Subject: RE: MPI dog testing - proposal by PR 071108.doc

Dear Roland,

I am attaching my suggestions for possible next steps which are only two really. These are based upon showing a direct comparison between what is available to growers in US.....Inteon vs. Non-Inteon. In my mind, that is still the big question to answer as it deals with real world exposure potential. However, as we discussed, the question will still remain that even with differences between the two, will these be enough to cross the threshold where EPA would be compelled to grant a standard and I am aware that this option does not address what we have seen so far.....

I look forward to the follow up and our face to face meeting which I believe to be in the works. To me, such a direct meeting is critical at this stage.

Kindest Regards,

Monty

<< File: MPI dog testing - proposal by PR 071108.doc >>

From: Dieterle Roland Mario CHBS
Sent: Thursday, November 08, 2007 11:25 AM
To: Dixon Monty USGR; Abbott John USGR; Akins Jonathan USGR
Cc: Mewes Kersten CHBS
Subject: MPI dog testing - proposal by PR 071108.doc

All

As follow-up of yesterday's telecon with the request to provide proposals and rationales for further dog testings, I prepared a 1-pager outlining the critical issues we need to address from the regulatory point of view and the proposed next steps.

Please discuss the paper, make any comments and suggestions, and provide the NAFTA view where requested. We have then to agree on the proposed next MPI test. Deadline for that is next Wednesday.

Best regards,

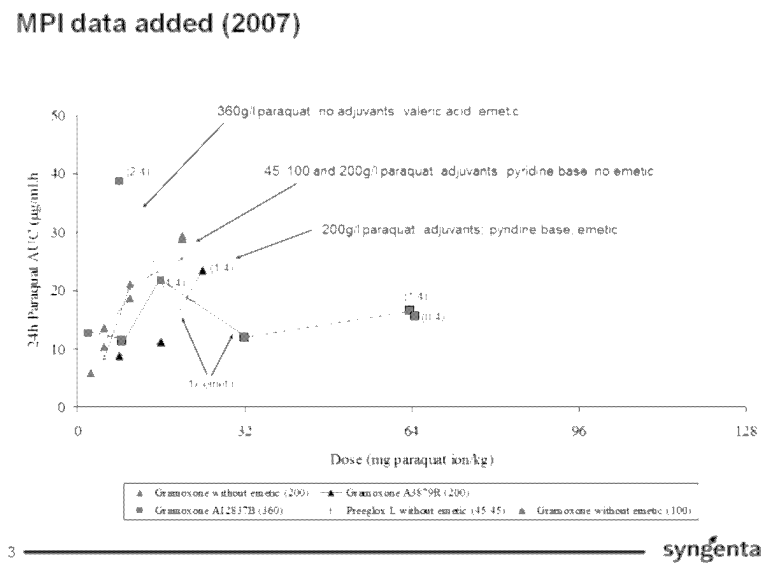
Roland

<< File: MPI dog testing - proposal by PR 071108.doc >>

Paper for discussion at telecon on Tuesday, 18 September

Wednesday, September 19, 2012
3:46 PM

Subject	**Paper for discussion at telecon on Tuesday, 18 September**
From	Phillips Alison GBAP
To	Doe John GBJH; Earl Michael SGSG; Ford Sherry USGR; Hamer Mick GBJH; Kobel Werner CHBS; Mihaliak Charles USRE; Odum Jenny GBAP; Pastoor Tim USGR; Persia Michael USRE; Phillips Alison GBAP; Puri Emilio CHBS; Stanbrook Lionel CHBS
Cc	Elliott Barry GBAP
Sent	Thursday, September 13, 2007 7:06 AM
Attachments	SAERC info on MPI pr... Request for approval o... Amended wording fo... SAERC considerat...



Dog studies required in support of the introduction of Inteon technology

Proposal for change in status for two dog studies to be undertaken at MPI

Prior to the current project at MPI, the paradigm for paraquat absorption and toxicity following oral administration was based on the studies conducted at IRI in 1988 (Slide 2). These covered paraquat strength formulations of 100 and 200g/l paraquat ion, and also a 45/45g/l paraquat/diquat mixture. None of the formulations contained added emetic. The profile of paraquat absorption measured as area under the curve (AUC) and also terminations required (or mortalities observed), was consistent, and indicated a relatively smooth curve for both endpoints over a range of ca 4x increase in dose (ca 5-20mg/kg).

As we have progressed with our work at MPI, which involves the testing of formulations with added emetic, we have seen the same initial curve for the A3879R formulation (Slide 3), and also for the two INTEON formulations tested (not shown). However, for the formulation A12837B, we have seen a more erratic profile of AUC and terminations with dose (Slide 3). An important question now is whether the erratic curve seen with the 360g/l formulation (A12837B) is isolated to this formulation, or whether in reality it is perhaps a paradigm for paraquat formulations containing emetic. The 360g/l formulation is unique amongst the others tested in the past and also concurrently in having: i) high strength paraquat, ii) valeric acid as the alerting agent and iii) no adjuvants present (Slide 3). In order to determine this, it is considered necessary to take a formulation that is more typical of the other (and majority of) paraquat formulations (lower strength etc) and evaluate it at dose levels that define most or all of the termination curve (ie up to 4/4 terminations). This will address whether for such formulations we have the IRI paradigm of response, or one more similar to that seen with A12837B (Slide 4).

The proposal is to bring forward the two 240g/l paraquat strength formulations that have already been approved for conduct (Slides 5 and 6, shown as Variation 2 & 3), and to test these, but to proceed up the dose levels to obtain the full curve up to 4/4 terminations. The studies will therefore provide the data on full dose response for the two key aspects of a lower paraquat strength formulation (but one more typical of that sold in the majority of countries worldwide), and also an increased emetic formulation, a key consideration for the USA and potentially rest of the world). Identifying the full shape of the dose response curve will allow us to be more confident on the comparison of toxicity with the new INTEON formulations. This will allow Syngenta to make the relevant comparative assessments, and then to communicate these to relevant external bodies in order to gain acceptance for the reduced toxicity INTEON formulations.

The conditions for termination will remain as present, and the intent is still to have no animal die due to toxicity, but rather to be euthanised when in a condition where it is considered not likely to survive. This proposed modification

would not therefore involve any more pain and distress for any individual animal, but would, of necessity, involve more animals reaching this point. This is considered necessary for us to be able to fully evaluate and interpret the data generated to date, and also that from the studies approved for future conduct.

We have interrogated the conduct of the studies undertaken with A12837B, including return and reanalysis of the test sample, use of gavage instead of capsule dosing, and concluded that the data are sound.

****

For reference, the initial submission and follow-up submissions for approval by SAERC are given below:

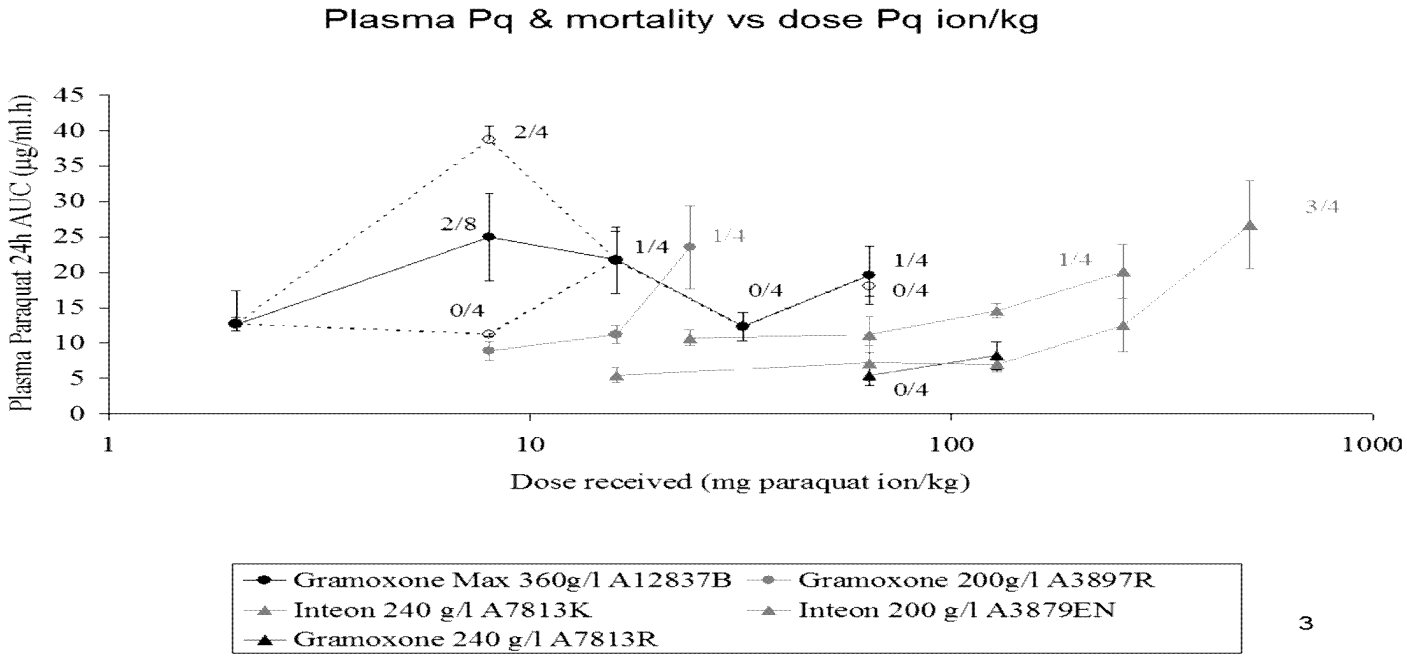
2007 formulation comparisons

Thursday, September 20, 2012
11:29 AM

Purpose of the meeting:
To review the emerging data from **64 mg paraquat ion/kg (equivalent to 0.267ml kg)** on MPI study 1390-008 (Non Inteon 240g l A7813R).

Comparison data:
Recipe for A7813R

	J4818/179		J4818/175
	"Inteon K" A7813K	**"US Variation 3 not on sale" A7813R**	**"Gramoxone" A3879R**
	g/l	**g/l**	**g/l**
PQ ion (100%, emetic free)	240.00	240.00	200.00
PP796 (100%)	1.50	0.50	0.50
Manutex RM	9.00	-	-
Mag Sulphate	61.87	-	-
Antifoam DB-100	-	-	-
Antifoam MSA	0.25	0.25	-
Silcolapse5020	-	-	0.25
Agnique PG-8105 / AI2575	10.00	10.00	-
BioSoft SDBS 30LA	-	-	86.00
Synprolam 35X15	-	-	43.00
Sulfacid blue 5J	-	-	5.00
F,D & C, blue no.1 (13%)	3.85	3.85	-
Pyridine bases H	-	-	10.00
cis-3-hexenol	2.00	2.00	-
Valeric acid	-	-	-
Acetic acid/sodium hydroxide	As required to reach pH 7.0		

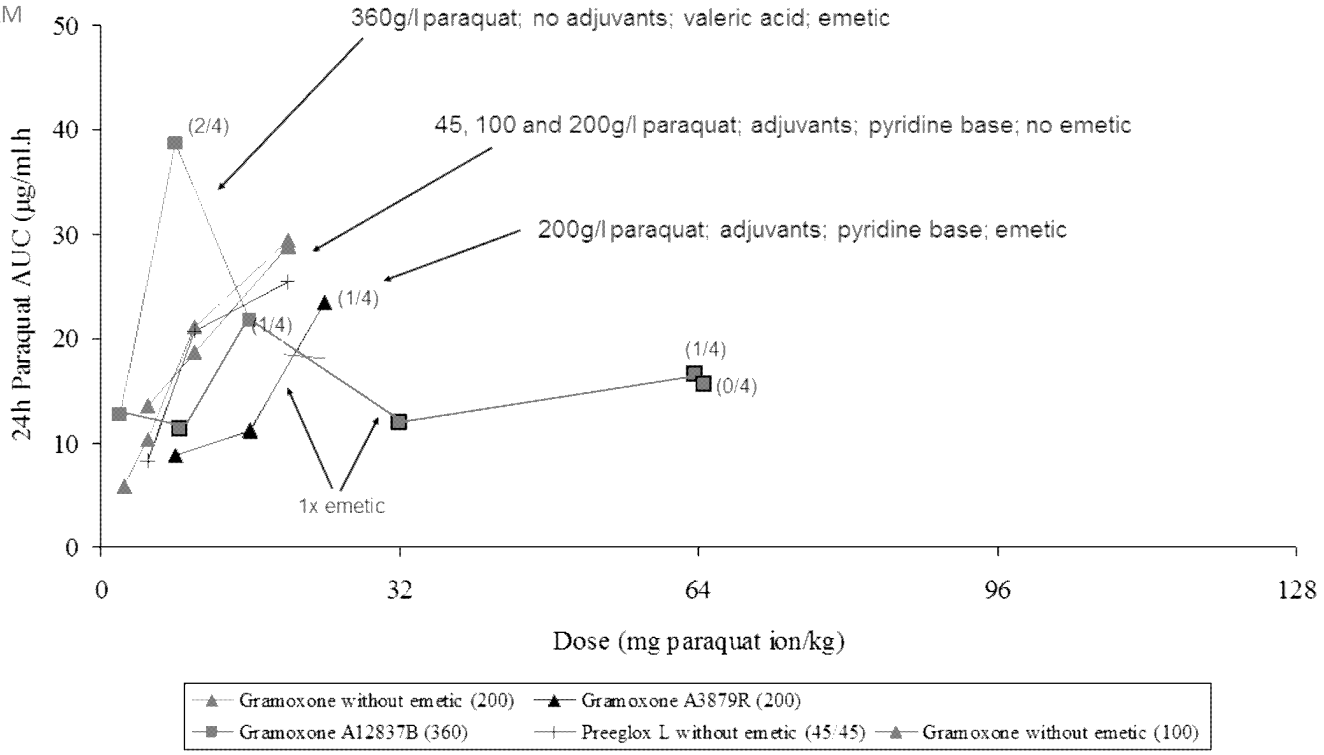


3

MPI data added (2007)

Past Work

Monday, October 08, 2012
9:00 AM



Gramoxone information

Wednesday, September 19, 2012
2:52 PM

Subject	**Gramoxone information**
From	Wall Michelle CAGU
To	Dixon Monty USGR
Cc	Lajoie Cindy CAGU
Sent	Wednesday, September 19, 2012 2:10 PM
Attachments	 projTest 1

Hi Monty,

As requested, please find attached a list of the toxicology studies sent to the PMRA in support of paraquat and our GRAMOXONE Herbicide with Wetting Agent formulation.

With respect to the variant, we historically sold A3789G (and had a high and low stench version registered); however when the EU stopped selling this recently (2010, I believe), we moved the manufacturing site to Mexico and registered the A3879GN variant to align with what they were manufacturing for their own sales. This version is NPE-free, which aligns with the proactive action of Syngenta Canada to remove NPE from products as well. I believe that first sales of the GN variant began in 2011 and that is what has been sold since. If required, I could confirm with Canadian Supply for you. Please let me know.

Hope this helps,

Michelle

Comparison of GMX Formulations

Wednesday, October 31, 2012
3:25 PM

Confidential Business Information

		EPA Reg. No. 100-1217			Glob. non Int	Glob. Inteon	Canadian
Product Design Code		**A7813K**	**A7813Q**	**A7813AD**	**A3879R**	**A3879EN**	**A3879GN**
Syngenta CSF Identification Code		**364/4**	**1181/2**	**1508/2**			
Formulation Classification		**Basic**	**Alt. of A7813K**	**Alt. of A7813Q**			
EPA Reg. No.		**Inteon**	**Inteon or SL**	**SL 2.0**			
Paraquat Load		**240 g/L**	**240 g/L**	**240 g/L**	**200 g/L**	**200 g/L**	**200 g/L**
Component (Note 1)	**CAS Number**	**% by wt.**	**% by wt.**	**% by wt.**	**% by wt.**	**% by wt.**	**% by wt.**
Active Ingredient (AI)	1910-42-5	66.0	66	66	56.10	53.20	58.25
AI as 100% pure active*		30.1	30.1	30.1	18.50	17.50	18.6
Emetic	27277-00-5	0.14	0.14	0.14	0.05	0.13	0.05
Stabilizer MgSO4	7487-88-9					10.90	
Stabilizer (MgSO4 heptahyt)	10034-99-8	5.63					
Stabilizer (Alginate)	9005-38-3	0.82				0.79	
Antifoam	63148-62-9	0.023	0.023		0.02	0.04	0.02
Surfactant	68515-73-1	0.91	0.91				
pH Adjustment (NaOH)	1310-73-2	0.32	0.32			0.88	
Stench (Cis-3-hex)	928-96-1	0.18	0.18				
Stench (Valeric Acid)	109-52-4			0.22			
Stench (pyridine, alky deriv)	68391-11-7				0.93	0.01	0.09
Dye	3844-45-9	0.35	0.35	0.35			
Dye - sulfacide brillinat blue	not avail				0.46	0.22	0.23
Water		25.767	32.217	33.43	30.50	32.95	29.1
Wetting Agents	70955-14-5				3.98	3.98	4.01
Wetting Agents	25155-30-0				7.96	7.96	
Wetting Agents	85117-50-6						8.02
Acetic Acid	64-19-7				0.00	0.88	0.23
Total % by wt. Compostion		**100.00**	**100.00**	**100.00**	100.00	111.94	100.00

Search Criteria

CAS Number: **85117-50-6**

Nonfood Use Only – Food use is prohibited

CAS Reg. No.	Ingredient
85117-50-6	Benzenesulfonic acid, mono-C10-14-alkyl derivs., sodium salts

Pesticide Registration Improvement Extension Act (PRIA 3)
Fee Determination Decision Tree

Below is the fee for your selected Fee Category for Fiscal Year 2013

Action Code	Description	FY13 Fee	Decision Time (months)
1002	Amend currently approved inert ingredient tolerance or exemption from tolerance - new data	$ 5,000	10

Do you plan to request either of the following types of waiver(s)

	You pay	$ 2,500
	You pay	$ 1,250

To pay the fee shown above go to [illegible] and follow the instructions.

Action Code Interpretation

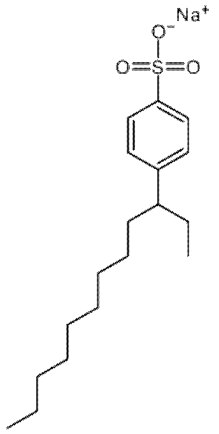
An application that proposes a change in food use approval for an inert ingredient. The use requires an amendment to a tolerance or the exemption from the requirement of a tolerance under section 408 of the FFDCA. The application must contain a petition to amend existing tolerances or exemptions from the requirement of a tolerance for all food/feed commodities for which food use approval is sought as well as the submission of data supporting the amendment (e.g. Toxicity data, residue chemistry data). This category fits for changes in food use that require a change to the existing tolerance or tolerance exemption such as an increase in the limitation of the percentage of the inert ingredient under an existing tolerance exemption or the expansion of use limitations under an existing tolerance exemption such as the removal of a pre-emergent only use. Examples of food uses include: use on foods, for example, corn or apples; aquatic uses involving potable water irrigation; or requiring tolerances for fish or shellfish; uses on areas where food may be grown or raised such as pastures; rangeland home garden beehive; uses involving livestock such as livestock housing, livestock dips, and livestock ear tags and food handling storage establishment premises and equipment (e.g. eating establishments, meat processing equipment, food handling equipment). Prior to a submission under this category, OPP highly recommends the applicant request a meeting with the Agency to discuss data needs. Additional information regarding applications for approval of new food use inert ingredients can be found at [illegible]

If another covered application intends to associate with and depend upon an already pending application for an inert ingredient approval in this category, the dependent application must identify the pending inert ingredient action with its inert approval tracking number assigned by the Agency, name of the inert ingredient(s) that is pending and the inert ingredient's applicant's name. Due to CBI concerns, the Agency will not provide information to the applicant of the dependent covered application regarding the status of the pending inert ingredient approval action beyond information that must be shared to adjust decision review times for the dependent application as discussed below. All other information on the inert ingredient's approval action MUST come from the inert ingredient applicant.

The decision review time due date for the dependent covered application will be extended to match the decision review time due date of the pending inert ingredient approval action unless the decision review time due date for the dependent covered application is further out, in which case the dependent covered application will initially be subject to its own decision review time.

If the application covers multiple ingredients grouped by EPA into one chemical class, a single registration service fee will be assessed for approval of those ingredients.

CAS Number : 85117-50-6

Product Information	Structure
Name 1: sodium 4-dodecan-3-ylbenzenesulfonate Name 2: sodium 4-(1-ethyldecyl)benzenesulfonate MOLECULAR FORMULA: $C_{18}H_{29}NaO_3S$ MOLECULAR WEIGHT: 348.47583 SMILES: CCCCCCCCCC(CC)C1=CC=C(C=C1)S(=O)(=O)[O-].[Na+]	

N,N-bis(2-hydroxyethyl)alkyl (C_{13}-C_{15}) amine (CAS Reg. No. 70955-14-5)	For use only: 1. As an antistatic agent at levels not to exceed 0.2 percent by weight in molded or extruded high-density polyethylene (having a density ≥0.95 g/cm^{3}and polypropylene containers that contact food only of the types identified in § 176.170(c) of this chapter, Table 1, under types I, VI-B, VII-B, and VIII, under the conditions of use E through G described in Table 2 of § 176.170(c) of this chapter, provided such foods have a pH above 5.0. 2. As an antistatic agent at levels not to exceed 0.1 percent by weight in molded or extruded polypropylene homopolymers and copolymers that contact food only of the types identified in § 176.170(c) of this chapter, Table 1, under Types II, III, IV, V, VII-A, and IX, under the conditions of use C through G described in Table 2 of § 176.170(c) of this chapter.

CAS Reg. No.(s):
70955-14-5 [EPA Chemical Data Access Tool]

Approved for Food Use

Click on the CFR Number below for required use limitations in the CFR.

Search for the following in the e-CFR...

N,N -Bis-Alpha-ethyl-Omega-hydroxypoly(oxy-1,2-ethanediyl) C8-C18saturated and unsaturated alkylamines, the poly(oxy-1,2-ethanediyl) content is 2-60 moles (CAS Reg. Nos. 10213-78-2, 25307-17-9, 26635-92-7, 26635-93-8, 288259-52-9, 58253-49-9, 61790-82-7, 61791-14-8, 61791-24-0, 61791-26-2, 61791-31-9, 61791-44-4, 68155-33-9, 68155-39-5, 68155-40-8,70955-14-5, 73246-96-5)

Food Use tolerance information (40 CFR Part 180)

CFR Title	CFR Number	Limits	Uses*
Inert ingredients used pre-harvest exemptions from the requirement of a tolerance	180.920	Not to exceed 25% in herbicide formulations and 10% in insecticide and fungicide formulations	Surfactants, related adjuvants of surfactants
Inert ingredients applied to animals exemptions from the requirement of a tolerance	180.930	Not to exceed 25% in herbicide formulations and 10% in insecticide and fungicide formulations	Surfactants, related adjuvants of surfactants

* A value of "Do" is the CFR representation of ditto, which refers to uses listed immediately preceding that entry in the CFR. See the e-CFR or contact IIAB for more details.

Approved for Nonfood Use

Data Submitter

If there is a gray checkmark in the data submitter box, do not use the inert ingredient unless you own the data or have discussed data compensation requirements with EPA. Click the | Contact Us icon in the upper right of the screen to send an email to EPA's Inert Ingredient Assessment Branch.

Data Compensation	Notes
✔	Company 84940/CST 4

Sodium Dodecylbenzenesulfonate (hard type) (mixture)
[CAS Number [illegible]]

Structure

Synonym: 4B, Benzenesulfonic Acid Sodium Salt, hard type mixture
Synonym: Dodecylbenzenesulfonic Acid Sodium Salt, hard type, mixture
Synonym: Laurylbenzenesulfonic Acid Sodium Salt, hard type mixture
Synonym: Sodium dodecylbenzenesulfonate, hard type, (mixture)
Synonym: Sodium [illegible] hard type, mixture

General Information

Product Number [illegible]

Packing Unit	Price	Available Stock: Chennai	Available Stock: Japan *
25g	1,140.00 INR	Please contact us	10
500g	1,300.00 INR	Please contact us	10

* Please contact us if you need further information.
email id:es@sigma.com

Request Bulk Quotation

Purity: Analysis Method	[illegible]
Storage Temperature	
M.F.: M.W.	[illegible]
CAS Number	25155-30-0
Related CAS Number	
MDL Number	MFCD00011808
Packaging and Container	

GHS

Pictogram 

Signal Word: Warning

Hazard Statements:
H302 :Harmful if swallowed.
H315 :Causes skin irritation
H317 :May cause an allergic skin reaction.
H319 :Causes serious eye irritation.
H335 :May cause respiratory irritation
H401 :Toxic to aquatic life
H411 :Toxic to aquatic life with long lasting effects.

Precautionary Statements
P261 :Avoid breathing.
P264 :Wash hands thoroughly after handling.
P270 :Do not eat, drink or smoke when using this product.
P271 :Use only outdoors or in a well ventilated area.
P272 :Contaminated work clothing should not be allowed out of the workplace.
P273 :Avoid release to the environment.
P280 :Wear protective gloves/eye protection/face protection.
P301+P312+P330 :IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell. Rinse mouth.
P302+P350 :IF ON SKIN: Gently wash with plenty of soap and water
P304+P340 :IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P305+P351+P338 :IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P312 :Call a POISON CENTER or doctor/physician if you feel unwell.
P333+P313 :If skin irritation or rash occurs: Get medical advice/attention.
P337+P313 :If eye irritation persists: Get medical advice/attention.
P363 :Wash contaminated clothing before reuse.
P391 :Collect spillage.
P403+P233 :Store in a well-ventilated place. Keep container tightly closed.
P405 :Store locked up.
P501 :Dispose of contents/container through a waste management company authorized by the local government

Transport Information

[Approved for Food and Nonfood Use - see below for use limitations.]

CAS Reg. No.(s)
25155-30-0 [EPA Chemical Data Access Tool]

Approved for Food Use

Click on the CFR Number below for required use limitations in the CFR.

Search for the following in the e-CFR...

Benzenesulfonic acid, dodecyl-, sodium salt

Alkyl (C8-C24) benzenesulfonic acid and its ammonium, calcium, magnesium, potassium, sodium, and zinc salts

Food Use tolerance information (40 CFR Part 180)

CFR Title	CFR Number	Limits	Uses*
Inert ingredients used pre- and post-harvest exemptions from the requirement of a tolerance	180.910	-	Surfactants, related adjuvants of surfactants
Inert ingredients applied to animals exemptions from the requirement of a tolerance	180.930	-	Surfactants, emulsifier, related adjuvants of surfactants
-	180.940c	When ready for use, the end-use concentration is not to exceed 430 ppm	-

* A value of "Do" is the CFR representation of ditto, which refers to uses listed immediately preceding that entry in the CFR. See the e-CFR or contact IIAB for more details.

Approved for Nonfood Use