Announcement from China Ministry of Environmental Protection

Notice No. 42 of 2017

The Announcement on the Adjustment of the Data Requirement in 'Guidance for New Chemical Substance Notification and Registration'

To make the data requirement of new chemical substances notification more scientific and normative, MEP adjusted the minimum toxicology and ecotoxicology data requirements for Typical Registration specified in 'Guidance for New Chemical Substance Notification and Registration' as well as the exemption conditions for physicochemical properties, toxicology and ecotoxicology data.

This announcement shall come into force from October 15, 2017. The difference between the previous 'Guidance for New Chemical Substance Notification and Registration' and this announcement, this announcement shall prevail.

Ministry of Environmental Protection (MEP)

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The English version is prepared by Randis ChemWise (Shanghai) Co., Ltd., a consulting firm located in Shanghai China, providing professional service on China chemical regulation compliance especially on China REACh registration service.

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Annex1:

Toxicology minimum data requirements for Typical Registration

Data requirement	Level I 1≤Q<10t/a	Level II 10≤Q<100t/a	Level III 100≤Q<1000t/a	Level IV Q≥1000t/a
Acute toxicity[1)]	√[2)]	√	√	√
Skin irritation	√	√	√	√
Eye irritation	√	√	√	√
Skin sensitization	√	√	√	√
Mutagenicity[3)]	√	√	√	√
28-day repeated dose toxicity[4)]	X	√	√	√
Reproductive/developmental toxicity[5)]		√	√	√
Toxicokinetics[6)]		√	√	√
90-day repeated dose toxicity[7)]		X	√	√
Chronic toxicity[8)]				√
Carcinogenicity[9)]				√
Others[10]				

Note: "Q" refers to notified quantity .

1): Acute toxicity data include acute oral toxicity, acute dermal toxicity and acute inhalation toxicity.

2): For Level I registration, acute toxicity data of one exposure route shall be provided by considering the notified usage --- preferred data is acute oral toxicity.

Starting from Level II, acute oral toxicity, acute dermal toxicity and acute inhalation toxicity data should be submitted.

3): For Level I notification, bacterial mutation reverse test data* (~~and in vitro Chromosome Aberration test data~~) should be submitted. If the test result is positive and a risk of wide-range exposure exists, mutagenicity test data for higher Level rank should be provided.

*If the notified substance is not suitable for bacterial mutation test due to the obvious bacterial toxicity, in vitro mammalian cell gene mutation test data could be submitted instead.

Starting from Level II, in vitro mammalian cell chromosome aberration test data or in vitro mammalian cells micronucleus test should be submitted. At the same time, based on the results of the above in vitro tests, test data of the following four cases should be provided:

a) If all above test results are negative, in vitro mammalian cell gene mutation test data should be submitted; if the result of in vitro mammalian cell gene mutation test is positive, in vivo gene mutation test data (such as transgenic rodent somatic and germ cell gene mutation test data etc.) or DNA damage/repair test data (such as mammalian liver cells non-programmed DNA synthesis (UDS) test data, in vivo comet test data, etc.) should also be submitted.

b) If bacterial mutation reverse test result is negative, and in vitro mammalian cell chromosome aberration test result is positive, in vitro mammalian cell gene mutation test data and in vivo chromosome aberration test data (such as mammalian erythrocyte micronucleus test data, mammalian bone marrow chromosome aberration test data, etc.) should be submitted; if in vitro mammalian cell gene mutation test result is positive, the in vivo gene mutation test data or DNA damage/repair test data should also be submitted.

c) If bacterial mutation reverse test result is positive, and in vitro mammalian cell chromosome aberration test result is negative, in vivo gene mutation test data or DNA damage/repair test data should be submitted.

d) If all above test results are positive, one in vivo genetic toxicity test data should be submitted and if the test result is negative, another in vivo genetic toxicity test data for different endpoint should also be submitted.

4): 28-day repeated dose toxicity includes oral, dermal and inhalation toxicity. Toxicity test data of at least one exposure route shall be provided by considering the notified usage.

5): For level II notification, reproductive/developmental screening test data should be submitted. If it is known that notified substance has deleterious effect on reproduction or has similar chemical structure to substances with known reproductive toxicity, developmental toxicity research shall be carried out; if it is known that notified substance causes developmental

toxicity or has similar chemical structure to substances with substances with known developmental toxicity, reproductive toxicity research shall be carried out.

Screening test can be replaced by pregnancy developmental toxicity data, two-generation reproductive toxicity or extended one generation reproductive toxicity data.

Starting from Level III, pregnancy developmental toxicity data (414) and extended one generation reproductive toxicity data (443) or two-generation reproductive toxicity data (416) should be submitted.

6): From level II notification, toxicokinetic evaluation should be performed based on relevant data which are available.

7): Test data of at least one exposure route shall be provided based on notified usage.

8): Test data of at least one exposure route shall be provided based on notified usage.

9): Carcinogenicity test data should be submitted if the notified substance has widely dispersed uses, or may be frequently or long-termly exposed to the human body, and is classified as germ cell mutagenesis category 2 or there is evidence that the substance is capable of inducing hyperplasia and/or pre-tumor lesions in the repeated exposure test.

Besides the situations stated above, the carcinogenic test data or carcinogenicity assessment report should be submitted. While if the assessment concludes that cancer test should be further conducted, the carcinogenic test data should be submitted.

'Widely dispersed uses' means the substance is used by trained professional operators in many scattered places or is used by public in daily life, of which the activities result in uncontrolled exposure or decentralized releases. For example, the new chemical substance or preparation containing the new chemical substance is used in paint spray, pesticide application, textile dyeing etc. these activities relating to occupational exposure or is used as detergents, detergents, disinfectants, coolants, cosmetics, flavors and fragrances, air spray products, household paints, coatings, adhesives, lubricants etc. the activities relating to consumer and to environmental exposure.

10): In case that it is proved by relevant data that the notified substance may have obvious target organ toxicity, corresponding toxicity data shall be submitted, for example neurotoxicity data shall be submitted for organic phosphorus substance.

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Annex 2:

Ecotoxicology minimum data requirements for Typical Registration

Data requirement	Level I 1≤Q<10t/a	Level II 10≤Q<100t/a	Level III 100≤Q<1000t/a	Level IV Q≥1000t/a
Algal growth inhibition toxicity	√	√	√	√
Daphnia acute toxicity	√	√	√	√
Fish acute toxicity	√	√	√	√
Activated sludge respiration inhibition toxicity	√	√	√	√
Adsorption/desorption	√	√	√	√
Degradability[1)]	√	√[2)]	√	√
Earthworm acute toxicity test	√[3)]	√[3)]	√	√
Daphnia reproductive test		√	√	√
Bioaccumulation		√	√	√
Fish chronic toxicity test[4)]			√	√
Seed germination/root elongation toxicity test			√	√
enchytraeid reproduction test or earthworm reproduction test [5)]				√
Note: "Q" refers to notified quantity				

1): Readily biodegradation test data should be submitted, and the data shall be obtained by using test method suitable for properties of notified substance.

2): Starting from level II notification, in case that test result shows the notified substance has no ready biodegradability, inherent biodegradability test data should be submitted; In case that test result shows the notified substance has no biodegradability, hydrolysis test data related to pH value should be submitted.

3): required when water solubility is less than 1mg/L and soil absorption logKoc is > 3.5.

4): For Level III registration, one of the following tests can be selected: fish early-life stage toxicity test, fish short-term toxicity test on embryo and sac-fry stages or fish juvenile growth test.

Fish juvenile growth test should be submitted for Level IV registration.

5): required when terrestrial biological acute toxicity test data results in hazardous classification according to relevant national standards and industry standards.

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Annex 3:

Exemption conditions for data of physicochemical properties

Endpoint	Exemption conditions and description [a]
Melting point (°C)	- Melting point/condensation point is below -20°C.
Boiling point (°C)	- Gaseous substance; - for solids which either melt above 300 ℃ or decompose before boiling. In such cases the boiling point under reduced pressure may be estimated or measured; - Substance decomposes before boiling.

Endpoint	Exemption conditions and description [a]
Density (kg/m^3)	- Gaseous substance; - The substance is only stable in solution in a particular solvent and the solution density is similar to that of the solvent. In such cases, an indication of whether the solution density is higher or lower than the solvent density is needed.
Vapor pressure (kPa, °C)	- Melting point is higher than 300°C ; - If melting point is between 200°C and 300°C, limit value based on measurement or recognised calculation method can be provided.
Surface tension (N/m)	- Water solubility at 20°C is lower than 1mg/L.
Self-ignition temperature (°C)	- the substance is explosive or ignites spontaneously with air at room temperature; - gases having no flammable range; - liquid which is non flammable in air, e.g. flash point > 200°C; - for solids, if the substance has a melting point no more than 160 ℃, or if preliminary results exclude self-heating of the substance up to 400 ℃.
Flash point (°C)	- Inorganic substance; - The substance only contains volatile organic components with flash-points above 100 ℃ for aqueous solutions - the estimated flash-point is above 200 ℃; - the flash-point can be accurately predicted by interpolation from existing characterized materials.
N-octanol/water partition coefficient (Log Pow)	- Inorganic substance.

Endpoint	Exemption conditions and description [a]
Water solubility (g/L)	- Substance hydrolyzing in case that pH value is 4, 7 or 9 (half-life period is shorter than 12h); - Readily oxidizable in water; - If substance shows “insolubility” in water, limit test shall be taken till minimum detectability of analysis method.
Oxidising properties	- Explosive; - Highly flammable; - Organic peroxide (type should classified through test); - the compounds do not contain the high-electronegative atom; - the substance is incapable of reacting exothermically with combustible materials, for example on the basis of the chemical structure (e.g. organic substances not containing oxygen or halogen atoms, or these elements are not chemically bonded to nitrogen or oxygen, or inorganic substances not containing oxygen or halogen atoms). ~~The full test does not need to be conducted for solids if the preliminary test clearly indicates that the test substance has oxidising properties~~
Flammability	- solid which possesses explosive or pyrophoric properties; - substances which spontaneously ignite when in contact with air.

Endpoint	Exemption conditions and description [a]
Explosive properties	- there are no chemical groups associated with explosive properties present in the molecule; - the substance contains chemical groups associated with explosive properties which include oxygen and the calculated oxygen balance is less than –200; - the substances contains chemical groups associated with explosive properties, but the exothermic decomposition energy is less than 500 J/g or the onset of exothermic decomposition is below 500 ℃.
Particle size (μm)	- Sale or use as non-solid or non-granular
Stability in organic solvent and characteristics of degradation products	- Inorganic substance.
a: If several exemption conditions are listed, the exemption is permitted if one of the conditions is met (unless otherwise specified). Remark by Randis: for the Blue font: New contents comparing to previous Guideline. ~~Middle delete line~~: not in new 'Guidance' but in previous 'Guidance'	

Annex 4:

Exemption conditions of toxicology data For Typical Registration

Endpoint	Exemption conditions and description [1]
Acute oral toxicity	- the substance is gaseous at normal temperature and pressure; - the substance is corrosive to skin.
Acute dermal toxicity	- as Gaseous at normal temperature and pressure; - Difficult to pass through skin barrier. - the substance is corrosive to skin.

Endpoint	Exemption conditions and description [1]
Acute inhalation toxicity	- liquid substance with vapor pressure less than 10^{-1}Pa at 20℃; - The inhalation part (particle size < 10μm) of the substance is less than 1% (weight percentage) and the aerosols, particles or droplets generated during usage have a MMAD > 100μm. - the substance is corrosive to skin.
Skin irritation or skin corrosion	- the substance is gaseous at normal temperature and pressure; - the substance is flammable in air at room temperature; - the acute toxicity study by the dermal route does not indicate skin irritation up to the limit dose level (2000 mg/kg body weight); - the substance is a strong acid (pH < 2.0) or base (pH > 11.5); - Acute dermal toxicity is classified as category 1; - the substance is highly irritant or corrosive demonstrated by structure-effect analysis result (considered as skin irritant or skin corrosive). - the substance is revealed corrosive to skin to by existing data (considered as skin irritant or skin corrosive substance).
Eye irritation	- the substance is flammable in air at room temperature; - the substance is a strong acid (pH < 2.0) or base (pH > 11.5); - the substance is classified as Skin irritation category 2 (included) or the substance is corrosive to skin; - the substance is revealed irritant to eyes by existing data (considered as eye irritant).

Endpoint	Exemption conditions and description [1]
Skin sensitization	- the substance is gaseous at normal temperature and pressure; - the substance is flammable in air at room temperature; - the substance is a strong acid (pH < 2.0) or base (pH > 11.5); - Highly irritant or corrosive at expected contact concentration; - has similar chemical structure to known sensitizer (considered as skin sensitizer)
28-day repeated oral toxicity	- the substance is gaseous at normal temperature and pressure; - the substance undergoes immediate disintegration and there are sufficient data on the cleavage products; - Reliable repeated dose toxicity combined with reproductive/ developmental toxicity screening test, or 90-day repeated dose oral toxicity or chronic oral toxicity research data are available. - the substance is corrosive to skin;
28-day repeated dermal toxicity	- the substance is gaseous at normal temperature and pressure; - The physic-chemical properties and toxicological properties reveals it is difficult to be absorbed by the skin; - the substance undergoes immediate disintegration and there are sufficient data on the cleavage products; - Reliable 90-day repeated dose dermal toxicity or chronic dermal toxicity research data are available; - the substance is corrosive to skin.

Endpoint	Exemption conditions and description [1]
28-day repeated inhalation toxicity	- The liquid substance has a vapor pressure less than 10^{-1}Pa at 20℃; - The inhalation part (particle size < 10μm) of the substance is less than 1% (weight percentage) and the aerosols, particles or droplets generated during usage have a MMAD > 100μm. - the substance undergoes immediate disintegration and there are sufficient data on the cleavage products; - Reliable 90-day repeated dose inhalation toxicity or chronic inhalation toxicity research data are available.
90-day repeated dose toxicity	- the substance undergoes immediate disintegration and there are sufficient data on the cleavage products; - Reliable chronic toxicity research data with same test animal and exposure route are available and; - The 28d repeated dose toxicity test with the same test animals and exposure route has observed toxic effects, or the 'no observable adverse effects level' is very low[2]; - the substance is classified as Carcinogens Category 1 or Category 2.
Mutagenicity	- the substance is classified as Carcinogen Category 1 or Category 2; reproductive/developmental toxicity Category 1 or Category 2 (considered as reproductive cell mutagenicity, carcinogenicity, reproductive/developmental toxicity). - The available in vivo genotoxicity test can exempt the same genetic endpoint in vitro genotoxicity test.

Endpoint	Exemption conditions and description [1]
Reproductive/developmental toxicity	- Pregnancy developmental toxicity data, two-generation reproductive toxicity data or extended one generation reproductive toxicity data are available (reproductive/developmental screening data can be exempted); - the substance is classified as Carcinogen Category 1 or Category 2; - the substance is classified as Mutagenic substance Category 1 or Category 2; - It has been known that the substance meets the classification criteria of reproductive toxicity Category 1 or Category 2. The latter three conditions are all considered the substance has reproductive cell mutagenicity, carcinogenicity, reproductive/developmental toxicity.
Carcinogenicity	- The substance is classified as Germ cell mutations Category 1A or Category 1B; - Combined test of chronic toxicity and carcinogenicity is available.
Chronic toxicity	-"No-observed effect level" of repeated dose toxicity is quite high (e.g. 90-day system toxicity effects NOAEL ≥ 300 mg/kg), excluding the situations below: toxic effects which maybe caused by particular molecular structure is not detected in the 90-day test, and it is known that the substance may have the hazardous characteristics which maybe not be detected by the 90-day repeated dose toxicity test; - There is sufficient toxicokinetic data to explain the long-term toxicity of the substance; - Combined test of chronic toxicity and carcinogenicity is available.

Endpoint	Exemption conditions and description [1]
1: If several exemption conditions are listed, the exemption is permitted if one of the conditions is met (unless otherwise specified); 2: the 'no observable adverse effects level' is very low means the 'no observable adverse effects level' in 28-day repeated dose toxicity test is <100mg/kg(oral), <200mg/kg(dermal), <0.25mL/L (inhalation, gas), <1mg/L (inhalation, vapor), <0.2mg/L (inhalation, dust/mist). Remark by Randis: for the Blue font: New contents comparing to previous Guideline.	

Annex 5:

Exemption conditions of ecotoxicology data for Typical Registration

Endpoint		Exemption conditions and description [1]
Algal growth inhibition toxicity		- Water solubility is lower than 1mg/L and impossible to penetrate the biomembrane [2].
Daphnia acute toxicity		- Water solubility is lower than 1mg/L and impossible to penetrate the biomembrane [2]; - Chronic toxicity data which contain effective acute toxicity data of same species are available, e.g. daphnia reproductive test.
Fish acute toxicity		- Water solubility is lower than 1mg/L and impossible to penetrate the biomembrane [2]; - Chronic toxicity data which contain effective acute toxicity data of same species are available, e.g. fish 14-days prolonged toxicity test, fish chronic toxicity test etc.
Daphnia reproductive test		- Water solubility is lower than 1mg/L and impossible to penetrate the biomembrane [2].
Terrestrial Organism toxicity	Earthworm acute toxicity	- soil absorption is very low (e.g. logKoc<1.5); - Long-term test shall be considered for replacing short-term test if soil adsorption is very high (e.g. logKoc >4.5).
	Earthworm chronic toxicity	

	Seed germination/root elongation toxicity	
	Terrestrial plant chronic test	
	Soil microorganism effect	
Activated sludge respiration inhibition toxicity		- the substance is impossible to produce microorganism toxicity as demonstrated by relevant data, for example, soil microbial-carbon/nitrogen conversion test does not show toxicity (~~solubility is quite low~~); - the test can be replaced by nitrification inhibition effect test if available data show that the substance is likely to be a microbial inhibitor (especially for nitrobacteria)
Adsorption/desorption		- the substance and its degradation products decomposes rapidly, e.g. hydrolysis half-life <12h.
Degradability	Non-bio degradation	- Readily biodegradable; - Hydrolysis test is not required if its solubility is quite low.
	Ready biodegradation	- Inorganic substance.
	Inherent biodegradation	- inorganic substance; - Readily biodegradable.
Bioaccumulation	Fish accumulation	- Low possibility of accumulation in organism (e.g. log Kow<3); - Impossible to penetrate biomembrane; - Readily biodegradable.

1: If several exemption conditions are listed, the exemption is permitted if one of the conditions is met (unless otherwise specified);

2: to submit biofilm permeability test report of the notified substance or its analog; If the test can not be carried out to obtain the membrane permeability data of the notified substance, the reason and in the same time the description and summary on biomembrane permeability software forecast report or literature data should be submitted.

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