1 The New Chemical Review Process under TSCA

Section 5 of the Toxic Substances Control Act of 1976 gives EPA the authority to review "new" chemicals before they enter the market place. A *new* chemical is one that is not already on the TSCA Inventory. Anyone wishing to manufacture or import a new chemical substance must submit a Pre-Manufacture Notice (PMN) to EPA 90 days before the date of intended start of production or import of the subject chemical. Certain substances are excluded from TSCA, including food, drugs, cosmetics and pesticides.

This document will summarize certain information on the New Chemicals Program and explain how Sustainable Futures was developed based on the experience gained in the OPPT New Chemicals Program. Extensive information is available on the New Chemicals Program website at http://www.epa.gov/oppt/newchems/index.htm. Some of the useful websites include:

Program Overview http://www.epa.gov/oppt/newchems/
TSCA Inventory http://www.epa.gov/oppt/newchems/pubs/invntory.htm
Policies http://www.epa.gov/oppt/newchems/pubs/policies.htm
Guidance http://www.epa.gov/oppt/newchems/pubs/guideman.htm

1.1 Types of New Chemical Notices

Pre-Manufacture Notices (PMNs) must be submitted for industrial chemicals not already on the TSCA Inventory before that chemical substance can be manufactured or imported. Supporting documents must be electronically prepared and submitted to EPA online. Software has been developed to create and submit Form EPA 7710-25 electronically and is available at http://www.epa.gov/oppt/newchems//epmn/epmn-index.htm. PMNs are reviewed within 90 days of the submission acceptance.

Specific Exemptions for under section 5 of TSCA for new chemical substances include:

Low Volume Exemption (LVE) – 10,000 kilograms or less of the substance will be manufactured or mported each year under the requirements at 40 CFR Part 723.50; these requirements were substantially rewritten on March 29, 1995. LVEs get a 30-day review.

Research and Development – the substance is manufactured in small quantities for research and development, and special procedural and recordkeeping requirements are met 40 CFR Parts 720.36 and 720.78.

Low Releases and Low Exposures (LoREX) – the substance is expected to have low release and exposure under the requirements at 40 CFR Part 723.50, published March 29, 1995. LoREX cases get a 30-day review.

Test Marketing Exemption (TME) – the substance is manufactured or imported for TME, under the requirements at 40 CFR Part 720.38. TMEs get a 45-day review.

Polymer Exemption – the substance is one that meets certain specified criteria where the substance is not considered chemically active or bioavailable under the requirements at 40 CFR Part 723.250. Polymer exemptions require annual reporting.

Biotechnology Exemptions – manufacturer, importer, or processor of a living microorganism is required file a Microbial Commercial Activity Notice (MCAN) unless the activity is eligible for one of the exemptions described at 40 CFR Part 725. These exemptions are (1) R&D, TSCA Experimental Release Application (TERA), and (2) Closed System Exemptions. See http://www.epa.gov/biotech_rule/. R&D cases get a 90-day review and TERA cases get a 60-day review. Closed System Exemptions require record-keeping but not reporting.

1.2 Information Required in PMN Submissions

Information that must be submitted with a new chemical PreManufacture Notice is described in 40 CFR Part 720.45 and includes:

- Chemical identity
- Impurities
- Synonyms or Trade Names
- Byproducts
- Production/Import volume
- Description of uses
- Process diagrams
- Worker exposure
- Environmental releases, control technologies, and disposal practices to be used, AND
- Test data *in the possession* of the submitter.

As explained in 40 CFR Part 720.50 TSCA does not *require* that the submitter conduct specific tests or conduct additional tests. TSCA does describe test data that would be useful to submit but does not mandate that a submitter provide specific test data to EPA. As a result, many new chemical notices lack the data necessary to fully characterize toxicity and risk to humans and the environment.

Due to the design of TSCA, it has become necessary to make chemical management decisions in the absence of measured data. Historically, of the approximately 1500 submissions received each year:

No Test Data (of any kind)	51 %
Health Test Data	45 % (mostly Acute or Mutagenicity)
Ecotoxicity Data	<5 % (mostly Acute Fish or Daphnids)
Environmental Fate	<5 % (various types)

Source: Auer, C; Zeeman, M; Nabholz, J; et al. (1994) SAR - The U.S. Regulatory Perspective. SAR QSAR Environ Res 2:29-38.

1.3 The P2 Framework & Sustainable Futures Promotes Prescreening

Structure Activity Relationship (SAR) Methods
The Office of Pollution Prevention and Toxics (OPPT) developed chemical screening methods specifically to address the lack of measured data received with PMNs. Faced with short review periods mandated by TSCA, and the customary lack of data, OPPT developed screening methods that use Structure Activity Relationships (SARs). The SAR approach calculates or estimates toxicity (hazard) based on an analysis of chemical structure, comparing the structure of untested chemicals with that of tested chemicals. SAR techniques are used to address endpoints such as environmental fate, aquatic toxicity, cancer hazard, exposure, and risk among other factors.

OPPT has computerized many of these SAR methods and uses these to evaluate PMNs and existing chemicals where data are lacking. These SAR methods are generally computer models that assess a particular aspect of a chemical's possible impact on humans or the environment. For example, one model ECOSAR, estimates toxicity to fish, aquatic invertebrates, and algae. This is important information if the chemical could be discharged to streams during manufacture, processing, use, or disposal. Another method, OncoLogic™, estimates the likelihood that a chemical would cause cancer in humans. OPPT uses other models in addition to SAR-based techniques to estimate potential exposures to a chemical in consumer products. Models are also presented for estimating properties such as vapor pressure and water solubility, which are important for projecting the nature, magnitude, and duration of exposure.

Knowledge from Confidential Business Information (CBI) received with PMN submissions is used to develop SARs which are not CBI. In the years since TSCA was implemented OPPT has received a wealth of CBI data on tens of thousands of chemicals covering the vast range of chemistry. These CBI data can not be released to the public however the methods developed using the knowledge from these sources can be made public.

Exposure Assessment Models
OPPT has developed several exposure assessment methods, databases, and predictive models to help in predicting what happens to industrial chemicals when they are used and released to the environment; and how workers, the general public, consumers and the aquatic ecosystems may be exposed to chemicals. These exposure models can be used when monitoring data are not available, to consider potential exposure when designing and selecting products and processes, and in evaluating pollution prevention opportunities.

The results of an exposure assessment are combined with a hazard (toxicity) assessment to predict the potential of an industrial chemical to cause risk to humans or the environment. If a potential for risk may exist OPPT will examine these new chemical notices in greater detail and regulate if necessary.

P2 Framework Integrates OPPT Predictive Methods
OPPT integrated these predictive methods into a program called the Pollution Prevention Framework (P2 Framework), a science-based analytical framework for identifying safer new chemicals. OPPT wanted to learn if its SAR techniques could be transferred to industry and if these methods could be used early in Research and Development to evaluate PMN product alternatives based on risk.

This document describes each method and the importance of the data generated, and provides case studies showing how methods can be used collectively to answer complicated risk assessment questions

and identify pollution prevention opportunities. The P2 Framework, as currently constructed, does not address all biological endpoints. It is a set of screening-level methods that are used when chemical-specific data are lacking.

Sustainable Futures

OPPT developed P2 Partnerships under Project XL with many industry sectors to help them explore the application of the P2 Framework methods to their chemicals of interest. Based on the success of the P2 Framework-based Kodak and PPG Project XLs, OPPT developed the Sustainable Futures Initiative to help industry develop new chemicals that are sustainable economically and environmentally. The Dec. 11 2002 Federal Register notice announcing Sustainable Futures is available at www.epa.gov/fedrgstr/EPA-TOX/2002/December/Day-11/t31243.pdf.

Sustainable Futures offers comprehensive training in the use of the P2 Framework methods and incentives in the form of regulatory flexibility to companies that graduate from Sustainable Futures. The regulatory flexibility allows Sustainable Futures graduates to submit prescreened new chemical notices that are considered a PreManufacture Notice AND a Test Manufacturing Exemption application. The new chemical that is the subject of these combined notices, once dropped from further review, can be manufactured in 45-days under the terms of the TME, rather than requiring the submitter wait until the 90-day time-period ends under the PMN. This reduced review period for qualifying prescreened new chemical notices can be a powerful incentive for many companies. In addition to getting to market sooner, regulatory uncertainty is greatly reduced because the P2 Framework helps anticipate, and engineer away from, chemicals and process of concern.

New Method Development

Working with participants in Sustainable Futures has allowed OPPT to identify the need for potentially useful new methods. OPPT along with partners from the chemical industry and environmental groups worked to develop the PBT Profiler to help identify chemicals that potentially may persist, bioaccumulate, and be toxic to aquatic life. The release of even small amounts of persistent, bioaccumulative, and toxic chemicals to the environment is of concern because they can accumulate over time to higher concentrations and, therefore, have a higher potential to adversely impact human health and the environment. The PBT Profiler is web-based and available at no cost at http://www.pbtprofiler.net.

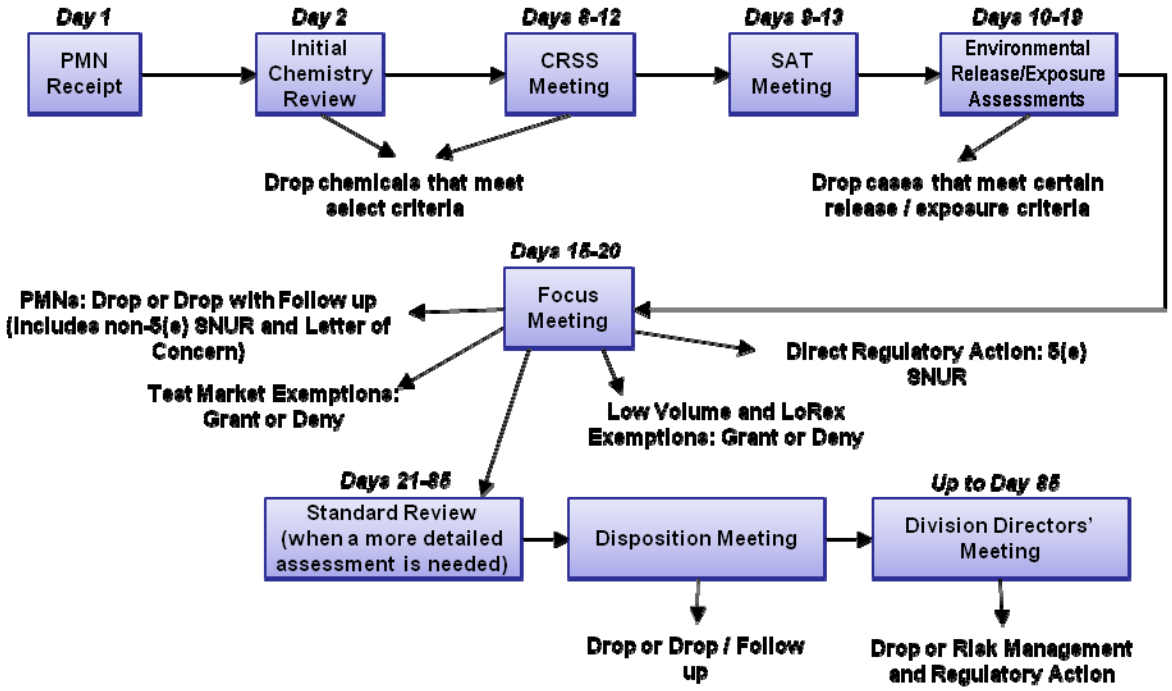
Through the P2 Framework and Sustainable Futures outreach efforts OPPT is working to make additional chemical screening methods available to stakeholders. The goals are to inform decision making and help promote the design, development, and application of safer chemicals, products, and processes. Screening methods used early in the R&D process can help anticipate, and engineer away from, chemicals of concern.

1.4 The EPA New Chemical Review Process

New Chemicals Program Meetings and Review Process

The New Chemicals Program has evolved into an efficient process which focuses resources on the problem chemicals by identifying cases which are of greatest concern as early in the 90-day review process as possible. EPA utilizes an integrated approach that draws on knowledge and experience across disciplinary and organizational lines to identify and evaluate health and environmental hazards and risks, and economic impacts. The New Chemicals Program is managed by the New Chemicals Management Branch in OPPT's Chemical Control Division. The duties of each section of that branch are explained at http://www.epa.gov/oppt/newchems/pubs/roster.htm.

Following receipt of a PMN or Exemption notice, the case undergoes the following steps in the Agency's 90-day review process. The review process, which is summarized here, is shown in the diagram below and explained in greater detail at http://www.epa.gov/opptintr/newchems/pubs/process.htm.



STEPS IN THE 90-DAY REVIEW PROCESS AND ACTIONS UNDER EACH STEP

INITIAL CHEMISTRY REVIEW (Day 2)

- Submission is reviewed for completeness

CHEMICAL REVIEW AND SEARCH STRATEGY (CRSS) MEETING (Day 8-12)

- Chemical Identity
- Structure / Nomenclature
- Analogs / TSCA (Toxic Substances Control Act) Inventory Status
- Synthesis, which includes byproducts and impurities
- Use / TSCA jurisdiction as provided by Submitter, literature, analog use
- Physical / chemical properties, including physical state, molecular weight, melting and boiling point, vapor pressure, solubility, octanol / water partition co-efficient, pH
- Pollution prevention aspects: pollution prevention information provided by Submitter, EPA makes suggestions for Alternate Synthetic Pathways.
- CRSS decisions: Notice completeness, validity, reportability, eligibility for exemption or exclusion, candidacy for exposure-based review, whether notice meets certain CRSS drop criteria.

STRUCTURE ACTIVITY TEAM (SAT) MEETING (Day 9-13) Interdisciplinary team of chemists, biologists, toxicologists, and information specialists that use structure activity relationships (SAR), test data on PMN substance, data on analogs, SAR (Structure Activity Relationship) or QSAR (Quantitative Structure Activity Relationship) estimates and expert judgment to evaluate:

- Environmental fate
- Human health hazard / toxicity
- Aquatic (environmental) hazard / toxicity

PROFILE OF EXPOSURE AND RELEASE (Day 10-19)

- Releases to all media
- Occupational exposure
- Environmental / consumer exposure (includes environmental persistence and bioaccumulation or bioconcentration)

FOCUS MEETING (Day 15-20) Representatives from each discipline are involved in the assessment of risk. Decisions are made based on chemical categories, exposure-based reviews, Exemptions.
Focus meeting decisions include:

- For PMNs: (1) ban pending upfront testing, (2) "drop" from further Agency review, (3) short question, (4) TSCA 5(e) consent order / Significant New Use Rule (SNUR), and (5) standard review.
- For Exemptions: (1) grant, (2) denial, or (3) conditional grant or denial.
- If regulated, Submitter will be notified by EPA.

STANDARD REVIEW (Day 21-85) This is an in-depth review for non-category/special issue PMN chemicals. The regulatory decision (see Focus Meeting decisions, listed above) is made at the Division Director management level.

1.5 Possible Regulatory Outcomes

The range of possible regulatory decisions for PMNs is summarized from http://www.epa.gov/opptintr/newchems/pubs/possible.htm. Most PMNs (~90%) are not regulated which includes outcomes of:

Drop From Further Review A case is dropped from further review when it:

- Does not meet any of the exposure-based criteria.
- Does not present an unreasonable risk to human health or the environment.
- Does not present increased potential for risk from an increased production volume or other uses.

Drop with a Concern Letter

- The submitter is informed by letter of potential hazard or risk.
- Data exist for structurally analogous substances.
- Small population may be affected and potential risk is controllable by:
  - Standard industrial practices
  - PPE (Personal Protective Equipment) required for workers
  - Environmental controls

Regulated Cases occur when EPA issues a TSCA § 5(e) Order to prohibit or limit activities associated with the substance, if EPA review has determined that:

1. There is insufficient information to evaluate the human health and environmental effects of the substance, and
2. The substance **may** present an unreasonable risk of injury to human health or the environment (the "risk-based" finding), or
3. The substance will be produced in substantial quantities and may be anticipated to enter the environment in substantial quantities or there may be significant or substantial human exposure (the "exposure-based" finding).

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