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Dr. William S. Stokes
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Re: APERC Comments on Proposed List of Substances for Validation of *In Vitro* Endocrine Disruptor Screening Methods (67 FR 64902; October 22, 2002)

Dear Dr. Stokes:

The Alkylphenols & Ethoxylates Research Council (APERC) appreciates the opportunity to submit comments on the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Endocrine Disruptor Working Group's "Proposed Substances for Validation of Estrogen Receptor (ER) and Androgen Receptor (AR) Binding and Transcriptional Activation (TA) Assays," October 16, 2002 (67 FR 64902). APERC represents the major manufacturers of alkylphenols and alkylphenol derivatives in North America. APERC members include: Dover Chemical Corporation; GE Plastics; Great Lake Chemical Corporation; Mitsubishi Chemical Corporation; Rhodia Inc.; Rohm and Haas Company; Schenectady International, Inc.; Stepan Canada; Sunoco, Inc.; and, The Dow Chemical Company. Information on APERC and its activities can be found at www.aperc.org.

Based on the recommendations of the ICCVAM Expert Panel and in consultation with the Endocrine Disruptor Working Group (EDWG), a combined list of proposed substances was developed to facilitate future validation of *in vitro* endocrine disruptor screening methods, which included *n*-nonylphenol, CAS number 104-40-5. Nonylphenol (NP) is produced by the reaction of phenol with branched nonene. The nonyl group is positioned predominantly in the *para* position on the phenol ring. Commercial synthesis results in a mixture of various branched nonylphenol isomers rather than one discrete chemical structure and is usually represented by CAS number 84852-15-3. Normal or *n*-NP represents a phenol group with a linear nonyl group. The ICCVAM and EDWG should be aware that this compound is difficult to produce and is therefore not likely to be commercially relevant. APERC considers CAS number 84852-15-3 to be most descriptive of commercially available NP. Other CAS numbers are less descriptive with

respect to the branching and position of the nonyl group on the phenol ring. The following table summarizes the CAS numbers that are commonly associated with NP.

CAS NUMBER	DESCRIPTION
25154-52-3	Phenol, nonyl- (Historically viewed as not descriptive regarding branching. EPA now assumes that CAS numbers that do not specify branching on alkyl groups represent linear structures. Not viewed as descriptive of commercial NP)
104-40-5	Phenol, 4-nonyl- (Assumes linear alkyl, not viewed as descriptive of commercial NP)
84852-15-3	Phenol, 4-nonyl-, branched (Viewed as descriptive of commercial NP)

The ICCVAM and EDWG should be aware that most of the *in vivo* endocrine research conducted on NP has used commercially available, branched NP when deciding which substances should be included in future validation studies of *in vitro* endocrine disruptor screening methods.

Please contact me at 732-557-5524 or blosey@regnet.com if you have questions or would like additional information about NP nomenclature, chemistry or sources.

Sincerely,

Barbara S. Losey
Deputy Director