OIT Chemicals IOF Final Project Report
Principle Investigator Form

1. Project Title: "Oxidative Reactions with Nonaqueous Enzymes"
aka '**Biocatalysis Under Extreme Conditions for the Chemical Industry'**

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3. Other Participating Organizations: Douglas Clark, University of California - Berkeley; Brian H Davison, Oak Ridge National Laboratory, Alexander Klibanov, Massachusetts Institute of Technology. Dow Chemical Co., BioCatalytics, Hercules, Eastman Chemical, EnzyMed, Altus Biologics, Kraft Foods.

4. Project Initiation Date: 6/1998

5. Expected Project Completion Date: 12/30/2001

6. Statement of Problem: The objective of this work is to demonstrate a proof-of-concept of enzymatic oxidative processing in nonaqueous media using alkene epoxidation and phenolic polymerization as relevant targets. This project will provide both the fundamental and applied investigations necessary to initiate the implementation of oxidative biocatalysts as commercially relevant alternatives to chemical processing, in general, and to phenolic polymerizations and alkene epoxidation specifically. Thus, this work will address the Bioprocessing Solicitation Area to: 1) makes major improvements to phenolic polymerization and alkene epoxidation technologies; 2) is expected to be cost competitive with competing conventional processes; and 3) produces higher yields with less waste.

Two reactions are central to this proposed research. 1) Alkene epoxidation catalyzed by chloroperoxidase (CPO) employs one mol H_2O_2 per mol of alkene oxidized. A wide range of alkenes are substrates for CPO, and high yields of the epoxide product can be obtained. Because of the poor solubilities of alkenes in water, the ideal process would take place in organic solvents. The reaction co-product is water, and thus represents a substantial reduction in waste generated as compared to the chemical process.

2) Phenol polymerization catalyzed by soybean peroxidase (SBP) employs one mol H_2O_2 per two mol of phenol oxidized, theoretically; however, more typically, 1.5 mol phenol is oxidized per mol H_2O_2 consumed. As with CPO catalysis, the co-product of this oxidation is water. The major waste prevention compared to the chemical route is the elimination of formaldehyde as the co-reactant. As with CPO, the poor solubilities of phenols in water necessitate organic solvents as the reaction medium.

7. Technical Approach: Briefly describe the technical concept and how this project is addressing the problem, including technical performance goals and the applicability across the industry.

The use of chemical approaches to modify enzyme stability rather than the use of genetic methodologies has been pursued for several years. Nevertheless, only recently have novel approaches been used that have shown the potential for dramatically improving enzyme activity and stability for use in organic solvents. These new approaches include the use of ligands to enhance enzyme solubility in organic media (to generate effective homogeneous biocatalysts), lyoprotectants to stabilize enzyme in organic solvents, the addition of low molecular excipients (such as salts) to activate enzymes in organic media, and cross-linking and polymerization techniques to stabilize enzymes for heterogeneous operation. These techniques are nascent, however, and their merits have not been fully explored or demonstrated. They need further examination in potential industrial applications to demonstrate commercial value. The vast majority of enzymes that have been utilized for these kinds of studies are hydrolases (proteases, esterases, etc.). However, many reactions of commercial interest are oxidative. **Enzyme activation and stabilization for use in organic solvents has largely been ignored for oxidative biocatalysts**.

8. Technical Work Plan: Briefly describe project work plan and list contributions of each participating organization. Include experimental design, approach to data analysis, key equipment and facilities, etc.

The proposed work is innovative in several respects. First, new techniques for enzyme activation and stabilization are to be developed specifically for use in nonaqueous media. Second, these approaches will be tailored to the specific requirements for oxidative enzymes, such as CPO (chloroperoxidase) and SBP (soybean peroxidase). Third, the use of biocatalysts represents a redesign of the commercial processes in use today and is expected to reduce energy costs in manufacturing as well as reduce waste generation.

- Test approaches on hydrolases and extend to oxido-reductases; move from aqueous to organic solvents
- Activate and stabilize enzymes by engineering the microenvironment of the biocatalysts.
  - Salt stabilization based on chaotropic and kosmotropic behavior (**Clark and Dordick**).
  - Activation via sample preparation (imprinting and lyophilization) (**Klibanov**).
  - Use PEG (and other polymeric modifiers) (**Davison**).
- Use solid supports to develop high performance biocatalysts
  - Incorporation into polymeric gels (**Klibanov**) and sol-–gels (**Davison**)
- Fundamentals of enzymes in organic media.
  - Characterize via NMR and EPR spectroscopies, and SEM (**Clark**), via X-Ray structures (**Klibanov**).
  - Predict enzyme activity in organic media via molecular modeling (**Klibanov**).
- Process and experimental improvements
  - Develop better protocols for epoxidation (**Davison**)
  - Combinatorial approaches to test conditions (**Dordick, Clark)**

9. Technical Problems/Barriers: Briefly describe technical barriers or problems (including key technical hurdles, performance requirements for economic competitiveness, theoretical limits, regulatory requirements for commercialization/implementation, etc.) and how they are being addressed.

In this completed project, we have shown several approaches that can stabilize enzymes in nonaqueous solvent and greatly increase their activity. We have shown that the proof-of-concept experiments that these approaches (salt activation, immobilization etc.) can be extended from hydolases to oxidases. We have developed initial methods to more rapidly optimize the formulations for enzyme use in these systems. This important precompetitive work has meet its initial goals. The key remaining barriers are several. 1] We need to extend this effort further into industrial and commodity systems. Of the two experimental systems - the phenolic polymerization is further along. The epoxidase will require further work in the mid-alkenes before attempting to extend into commodity alkenes. 2] We need to test and combine the different approaches for potential optimization. 3] The issue of catalytic density for these enzyme systems will need to be addressed and assessed.

10. Status of Milestones: Discuss progress in achieving each technical milestone as scheduled in the proposal plan. Discuss any variances and how they are being addressed. Emphasis should be given to current and next year activities.

Summary: We have successfully improved precompetitve technologies for use in nonaqueous enzymatic systems. We have shown that these approaches can be extended from hydrolytic enzymes into oxidative enzymes.

- Salt activation results in extraordinarily high catalytic activities of enzymes in organic solvents (up to 33,000-fold)
  - Subtilisin Carlsberg
  - Penicillin Amidase (Here a combination of additives resulted in an **activity in hexane > water with the native enzyme!**)
  - Chloroperoxidase (CPO) demonstrated activation via salts

- Lyophilization conditions influence enzyme activity for salt-activated enzymes due to water content and water structure
- Elucidated the mechanism of salt activation (via kaotropic and kosmotropic additives)
- Sol-gel Enzymes with enhanced thermal and solvent stability fro both hydrolase and for CPO
- Improved epoxidation protocols with high conversion
- Extablished a combinatorial activation strategy as a method for future research
- Invented a solid-phase peroxidase system for polyphenol synthesis

11. Commercialization Plans: Describe end-use application, competing technology assessments, regulatory evaluations, patentability assessments, market assessments, cost-benefit analyses, commercialization plan, and progress towards commercialization including intellectual property agreements or formal commercialization agreements.

It is noteworthy to point out that organic solvents form the mainstay of the solution chemistry media used in the chemical process industry. Developing active and stable enzymes for use in organic solvents, coupled with the hallmark high selectivity of biocatalysts would result in high volumetric productivities, lower reactor size (and hence a real lifecycle reduction of energy consumption), fewer byproducts, and therefore, less waste produced. As compared to traditional biocatalysis in aqueous media, the higher productivities and high reactant concentrations afforded by nonaqueous enzymology results in smaller reactor sizes and reduced cost and reduced energy consumption for solvent removal and product purification. The benefit of biocatalysis in organic media as compared to traditional chemical catalysis is the dramatically increased reaction selectivity that leads to fewer toxic byproducts. Compared to both aqueous-based biocatalysis and traditional chemical catalysis, nonaqueous biocatalysis will benefit society by providing processes that are more energy efficient and produce less waste. These benefits will surely spawn the development of new industrial processes and their affiliated plants, and the formation of new companies and new business units within existing companies that will take the lead in utilizing this new technology in the chemical industry.

- Develop pre-competitive methods to allow the large-scale use of oxidative biocatalysts in nonaqueous solvents
- Licensable technologies are anticipated and will be available through our institutional offices
  Invention disclosures have been submitted on salt activation techniques and on the sol-gel enzyme.
- Sharing of information among group members, DOE, and industrial partners
  We have had numerous public presentations, several project meetings including one with over ten industrial partners in Chicago.
- Encourage alliances between complementary industrial concerns [Enzymol International was bought by Biocatlalytics and produces SBP for use in speciality oligomers and polymers].
- Spin off technology when appropriate

12. Efficiency Improvement Merits: Describe original proposal's estimates and revised estimates for improving energy efficiency, reducing emissions, enhancing productivity, reducing costs, and/or reducing materials usage. Use Web-based energy assessment tool provided by DOE OIT for revised energy efficiency estimates (*www.energetics.com/chemtool*).

This analysis is largely based on prior Energetic tools and estimates. The ultimate goal of this work is to develop active and stable biocatalysts using oxidases to: a) epoxidize directly propylene and other alkenes; and b) carry out phenolic polymerization. We will discuss these two cases separately for energy/waste savings calculations, even though the core technology to utilize these enzymes in nonaqueous media will be the same. There are additional applications beyond these two cases for nonaqueous enzymatic oxidation. Additional work will be needed to refine these preliminary estimates. There are very large potential long-term energy and waste savings from these approaches. Most of the impacts come from two areas: a) yield and specificity improvements due to biocatalysis which for commodity process result in substantial petroleum displacement savings, and b) waste decreases by completely eliminating certain hazardous wastes as either unused substrate or byproducts. (such as propylene dichloride from the chlorohydrin process of propylene oxide and from formaldehyde use in the Novalac polyphenol process). At the bottom is a more complete analysis and asumptions.

13. Budget Tables:

Funded Budget, $K

OIT	**FY99**	**FY00**	**FY01**	
RPI	102	88	288	
UCBerkeley	88	58	188	
MIT	85	57	184	
ORNL	84	153	217	
Industry				
RPI, UCB	185	382	270	
ORNL	25	10	10	
MIT	25	10	10	
Total				**Total Project**
OIT	359	356	878	1593
Industry	235	402	290	927

Actual Costs, $K

OIT	**FY99**	**FY00**	**FY01**	**FY02**
RPI	141	156	150	30
UCBerkeley	50	88	133	64
MIT	50	87	154	30
ORNL	1	132	308	13

Est. Materials, $K

OIT	**FY99**	**FY00**	**FY01**	**FY02**
	12	25	35	6
	5	10	20	5
	6	9	30	3
		10	28	1

Explanation of Budget Variances:

Transfer of project from U Iowa from RPI; Contractual delays in arranging subcontracts out of RPI. Contractual delays from transfer of DOE project from Chicago Ops to Idaho Ops. Project was granted a no-cost extension until 12/31/01. Project was awarded in a competitive solicitation under a 30% costshare requirement as precompetitive work. The actual industrial cost share is estimated at 37%. An estimated $350K of the industrial cost share was funds-in, the remainder was in-kind materials and effort.

Est. Effort, months PI (others)

	FY99	**FY00**	**FY01**	**FY02**
RPI	2 (10)	2 (14)	2(14)	1(3)
UCBerkeley	1(6)	2(12)	3(20)	1(6)
MIT	1(6)	2(12)	3(24)	1(3)
ORNL	1	2(12)	3(22)	1(1)

Publications

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Y. Xie, P.K. Das, and A.M. Klibanov, "Excipients activate peroxidases in specific but not in nonspecific reactions in organic solvents". Biotechnol. Lett. 23: 1451-1454 (2001).

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J.P. Lindsay, D.S. Clark, and J.S. Dordick (2001), "Penicillin Amidase is Activated for Use in Nonaqueous Media by Lyophilizing in the Presence of Potassium Chloride", Enzyme Microb. Technol. (in press).

M.T. Ru, K.C. Wu, J.S. Dordick, J.A. Reimer, and D.S. Clark (2001), "Towards more active biocatalysts in organic media: increasing the activity of salt activated enzymes:, Biotechnol. Bioeng. (in press).

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M. T. Ru, S. Y. Hirokane, A. S. Lo, J. S. Dordick, J. A. Reimer, and D. S. Clark (2000), "On the Salt-Induced Activation of Lyophilized Enzymes in Organic Solvents: Effect of Salt Kosmotropicity on Enzyme Activity", J. Am. Chem. Soc. **122**, 1565-1571.

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ChemTool Summary

User Name: DAVISON

Project ID: 406

Project Name: OXIDATIVE REACTIONS WITH NONAQUEOUS ENZYMES - TARGET ALKENE EPOXIDATION

User Inputs

Chain: Propylene

% Energy Savings Feedstocks: 9.0%

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Derivative:	Propylene_Oxide	% Energy Savings Heat/Steam:	50.0%
% of Market Impacted:	8.0%	% Energy Savings Electricity:	95.0%
Annual Growth Rate:	5.0%	Solid or Liquid Wastes:	50 lbs per 1000 lbs of product
Year of Introduction:	2010	Non-Combustion Air Pollutants:	0 lbs per 1000 lbs of product
Market Penetration Curve:	40 Year Market Saturation		

Energy Impacts for Propylene: Propylene_Oxide

(Based on the input provided above, this technology will have the following impacts:)

	2005	**2010**	**2015**	**2020**
MARKET PENETRATION	N/A	4.4%	7.4%	12.2%
MARKET (Million lbs)	N/A	23	49	103
ENERGY SAVINGS				
Feedstock Energy Savings (trillion Btu)	N/A	0.055	0.118	0.248
Steam/Fuel Energy Savings (trillion Btu)	N/A	0.024	0.052	0.109
Electricity Savings (trillion Btu)	N/A	0.031	0.066	0.139
POLLUTANT REDUCTIONS (lbs)				
Carbon (MMTCE/yr)	N/A	0.00093	0.00199	0.00420
Nitrogen Oxides (NOX)	N/A	14,393	30,894	65,005
Sulfur Oxides (SOX)	N/A	13,351	28,659	60,302
Carbon Monoxide (CO)	N/A	2,776	5,959	12,539
Volatile Organic Compounds (VOCS)	N/A	312	670	1,410
Particulates	N/A	245	526	1,106
Other (million lbs)	N/A	1	2	5

N/A = not applicable

USER EXPLANATIONS

Technology Description:	Demonstrate proof-of-concept of enzymatic oxidative processing in nonaqueous media using alkene epoxidation and phenolic polymerization as relevant ultimate targets. The poor solubilities of substrates in water necessitate use of organic solvents. Both utilize H2O2 as cosubstrate with water as coproduct. Alkene epoxidation catalyzed by chloroperoxidase (CPO) may react a wide range of alkenes substrates. Phenol polymerization catalyzed by soybean peroxidase (SBP) eliminates formaldehyde compared to the chemical route.
Market Percentage:	Calculations show that replacing one chlorohydrin process plant (400MM lb/y) would have a significant impact. PPO market of 9.8 B lb/y by 2020 Assuming 5% growth/yr. If this process could displace only the current aging chlorohydrin process PO plants by 2020, this would be 800 M lb/yr produced enzymatically and would be two plants of the size described above.

Introduction Year:	This is precompetitive high risk R&D; oxidation works but requires sustained R&D to reach goal and introduction.
Energy Impacts Percentages:	Compare enzymatic process with chlorohydrin process. Chlorohydrin process first makes propylene chlorohydrin and then converts it into PO under alkaline conditions, consuming 1.4 lb chlorine/ lb PO produced. Major problems are production of undesired byproducts (about 0.1 lb propylene dichloride/lb PO), alkali requirements and waste treatment (salt brine, VOCs, chloroorganics). enzyme oxidation is assumed at a higher yield (98% vs 90%). Electricity reduction is largely due to eliminating the electricity requirements for the production of chlorohydrin. Unreported is offsite energy to produce Ca(OH)2 in a lime kiln for purchase by chlorohydrin which reduces energy another 5-10%
Other Wastes and Pollutants:	The chlorohydrin process produces about 10 byproducts, but these are used commercially. The enzyme process will produce few to no byproducts. For this analysis, it was assumed that the waste would be approximately equal except for the the production of less desired byproducts (e.g. about 0.1 lb propylene dichloride/lb PO), we assumed that half of PDC would be sold.

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User Name: DAVISON   Project ID: 407

Summary

Project Name:	OXIDATIVE REACTIONS WITH NONAQUEOUS ENZYMES - TARGET POLYPHENOL

User Inputs

Chain:	Broad Industry Sectors	% Energy Savings Feedstocks:	79.0%
Derivative:	Plastics_and_Resins	% Energy Savings Heat/Steam:	0.0%
% of Market Impacted:	2.0%	% Energy Savings Electricity:	-130.0%
Annual Growth Rate:	3.0%	Solid or Liquid Wastes:	35 lbs per 1000 lbs of product
Year of Introduction:	2007	Non-Combustion Air Pollutants:	28 lbs per 1000 lbs of product
Market Penetration Curve:	20 Year Market Saturation		

Energy Impacts for Broad Industry Sectors: Plastics_and_Resins

(Based on the input provided above, this technology will have the following impacts:)

	2005	**2010**	**2015**	**2020**
MARKET PENETRATION	N/A	8.2%	21.1%	44.5%
MARKET (Million lbs)	N/A	200	598	1,461
ENERGY SAVINGS				
Feedstock Energy Savings (trillion Btu)	N/A	1.172	3.496	8.547
Steam/Fuel Energy Savings (trillion Btu)	N/A	0.000	0.000	0.000
Electricity Savings (trillion Btu)	N/A	-0.582	-1.735	-4.242
POLLUTANT REDUCTIONS (lbs)				
Carbon (MMTCE/yr)	N/A	-0.01047	-0.03123	-0.07635
Nitrogen Oxides (NOX)	N/A	-162,843	-485,763	-1,187,650
Sulfur Oxides (SOX)	N/A	-193,086	-575,977	-1,408,214
Carbon Monoxide (CO)	N/A	-27,916	-83,274	-203,597
Volatile Organic Compounds (VOCS)	N/A	-3,490	-10,409	-25,450
Particulates	N/A	-3,490	-10,409	-25,450
Other (million lbs)	N/A	13	38	92

N/A = not applicable

USER EXPLANATIONS

Technology Description:	Phenolic polymers used in thermoset resins (>3.5 B lb/yr). Enzymatic polymerization eliminates use of formaldehyde and enables use of mild polymerization conditions for products with improved material properties. The enzymatic process uses H_2O_2, creates free radicals for direct ring polymerization. Compare the enzymatic process to the current Novolac

	process which uses formaldehyde and phenol to form polyphenols with methylene bridges between rings.
Market Percentage:	Replacing the Novolac process with an enzymatic process could have a significant impact. The phenolic resin market is stable and growing at 3%/y. Therefore, we estimate that the phenolic resin market would be about 5 B lb/y by 2020. If this process could displace only half of the new capacity needed by 2020, this would be 1 B lb/yr produced enzymatically. Finally, formaldehyde is a toxic and potentially carcinogenic compound. Hence, stringent OSHA regulations limit its exposure in the workforce, and its elimination from newer processes is a significant advantage.
Introduction Year:	This is a nearer term process than the PO process. Indeed, Enzymol International is already producing speciality oligomers and polymers. Thus, phenolic polymers generated by enzymatic catalysis has commercial applications at the present time. The proposed work will enable the research team to work with Enzymol as well as other companies to provide information needed to generate phenolic resins on a large scale using the enzymatic process
Energy Impacts Percentages:	Feedstock energy includes producing the formaldehyde at 1 mole formaldehyde/mole phenol [5.2 kBTU/lb=70%] . 90% yield of phenol in the novolac process versus a 98% yield from enzyme [+9% energy]. With heat recovery, assume same; electricity for the Novolac process reported by Lipinsky and Wesson; estimate of the electricity process energy cost of an enzymatic process for another commodity based on earlier DOE metrics. There is also an increases as an estimate of the electricity needed to produce the hydrogen peroxide. This assumes a 30% efficient process and 0.5 moles H2O2 per mole phenol.
Other Wastes and Pollutants:	Novalac- a 90% yield, there is 10% excess phenol or 87 lb phenol/1000lb and 28 lb formaldehyde; Enzyme with a 98% yield there is 17 lb phenol. Assumed that half of the phenol is recycled in each case. Novalac-formaldehyde, a great health and environmental concern (VOC). As volatile formaldehyde is not easily recovered. There is no equivalent waste for the enzyme and H2O2 process.

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I. Details **ENERGY SAVINGS/WASTE REDUCTION**

Impact: The ultimate goal of this work is to develop active and stable biocatalysts using oxidases to: a) epoxidize directly propylene and other alkenes; and b) carry out phenolic polymerization. We will discuss these two cases separately for energy/waste savings calculations, even though the core technology to utilize these enzymes in nonaqueous media will be the same. There are additional applications beyond these two cases for nonaqueous enzymatic oxidation. Additional work will be needed to refine these preliminary estimates.

a) **Propylene oxide** (PO) is a major commodity chemical with 2.9 B lb/y produced. Direct oxidation of propylene has been an unachieved commercial goal for catalytic chemists. Any new process would need to compete with the either the chlorohydrin or styrene co-product processes; each process has about half of the current production. In the most common co-product process, the thermochemical conversion of propylene to propylene oxide is energy intensive (7000 BTU/lb product) and produces the co-product styrene. Due to the current co-product markets and demands, it would be more difficult to compete with the styrene process. Therefore, we will compare the proposed enzymatic process with the chlorohydrin process. The chlorohydrin process first produces propylene chlorohydrin and then converts it into PO under alkaline conditions. About 1.4 lb of chlorine are consumed per lb of PO produced. The major problems are the production of less desired byproducts (e.g. about 0.1 lb propylene dichloride/lb PO), the alkali requirements and the waste treatment requirements (salt brine, VOCs, chloroorganics, etc.).

The analysis here is based on a 1985 report by ChemSystems, “Assessment of the Likely Role of Biotechnology in Commodity Chemical Production,” for the DOE which compared chemical and biological PO production. This assessment was based on aqueous methane monooxygenase and was modified by NREL for a direct enzyme oxidation process. Costs were updated to 1995. [Other data derived from “Brief Characterizations of the Top 50 U.S. Commodity Chemicals,” E. S. Lipinsky and J. D. Ingham, Battelle Report for U.S. DOE Biological and Chemical Technology Program. Sept. 1, 1994; and from “Propylene Oxide” in Ullmann’s Encyclopedia of Industrial Chemistry - Fifth Ed., Verlagsgesellschaft gmbH (1986).]

Estimated 1995 savings for one 400 M lb PO/y plant. Energy (M BTU/y)					
	A. Conventional	B. New	Savings A-B	Savings to Others	Total Savings C+D
Petrol. Feed	8,400,000	7,600,000	800,000[a]	0	800,000
Nat’l gas	920,000		920,000		920,000
Coal	3,700,000	2,000,000	1,700,000		1,700,000
Electricity	300,000	1,600,000	-1,300,000	0	-1,300,000
Other	28,000,000 [b]			2,300,000[c]	30,300,000
				Total	32,400,000
Non combustion Wastes: (M Ton/y)					
Haz.(nonTRI)					
Other			[d]		

[a] enzyme oxidation is assumed to have a slightly higher yield; but the feedstock requirements are essentially equivalent.

[b] This large amount is for the electricity requirements for the production of chlorohydrin.

[c] This is the energy required offsite to produce $Ca(OH)_2$ in a lime kiln for purchase by the PO plant.

[d] The chlorohydrin process produces about 10 byproducts, but these are used commercially. The enzyme process will produce few to no byproducts. For this analysis, it was assumed that the waste would be approximately equal.

The above calculations show that replacing one chlorohydrin process plant would have a significant impact. We estimate that the PO market would be about 9.8 B lb/y by 2020. {Assuming 5% growth/yr, by 2020, the total market would have increased by 3.4x.} If this process could displace only the current aging chlorohydrin process PO plants by 2020, this would be 800 M lb/yr produced enzymatically and would be two plants of the size described above for a total energy saving of 66 trillion BTUs/y. These numbers are summed with the case below and reported on the Table.

b) **Phenolic polymers** are used in thermoset resins and electronic materials with a market valued at over $3 B/yr (> 3.5 B lb/yr). Enzymatic polymerization would eliminate the current use of formaldehyde and enable the use of mild polymerization conditions for products with improved materials properties. In particular, the enzymatic process uses hydrogen peroxide to create free radicals which allow direct ring to ring polymerization of the polyphenols, and this leads to better and more stable resin materials. We will compare the enzymatic process to the current Novolac process which uses formaldehyde and phenol to form polyphenols with methylene bridges between rings. The Novolac process has a yield of about 90%, the enzyme process will have a yield >98%. This is a nearer term process than the PO process. Indeed, Enzymol International is already producing speciality oligomers and polymers. Thus, phenolic polymers generated by enzymatic catalysis has commercial applications at the present time. The proposed work will enable the research team to work with Enzymol as well as other companies to provide information needed to generate phenolic resins on a large scale using the enzymatic process.

[Data derived from “Brief Characterizations of the Top 50 U.S. Commodity Chemicals,” E. S. Lipinsky and J. D. Ingham, Battelle Report for U.S. DOE Biological and Chemical Technology Program. Sept. 1, 1994; from "Characterization of the Top Twelve U.S. Commodity Polymers," E. S. Lipinsky and R. Wesson, Battelle Report for U.S. DOE Biological and Chemical Technology Program. July, 1995 and from “Phenolic Resins” in Ullmann’s Encyclopedia of Industrial Chemistry - Fifth Ed., Verlagsgesellschaft mbH (1986).]

Estimated 1995 savings for production on a basis of **1000 lb** of phenolic resins. Energy (M BTU/y)					
	A. Conventional	B. New	Savings A-B	Savings to Others	Total Savings C+D
Petrol. Feed	5.2 [a]		5.2		5.2
Nat’l gas					
Coal					
Electricity	2.0 [b]	4.0 [d]	-2.0	-0.725 [e]	-2.725
Other	0.28 [c]				0.28
				Total	2.8
Non combustionWastes:		(lb waste/1000 lb phenolics produced)			
Haz. (RCRA)	43 [f]	9 [f]	32		32
Toxic (TRI)	28 [g]	0			28
Hazardous					
Other			[d]	Total	50

[a] This is the feedstock energy intensity needed to produce the formaldehyde at 1 mole formaldehyde per mole phenol. The amount of phenol is ignored here as near equivalent for both. The effect of the yield improvement from 90% to 98% is noted under Other - see [b].

[b] The process energy for the Novolac process reported by Lipinsky and Wesson.

[c] This is the amount of "extra" phenol needed to account for a 90% yield in the novolac process versus a 98% yeild in the enzyme process.

[d] This is an estimate of the process energy cost of an enzymatic process for commodity based on earlier DOE metrics.

[e] This is an estimate of the electricity needed to produce the hydrogen peroxide. This assumes a 30% efficient process and 0.5 moles H_2O_2 per mole phenol.

[f] With a 90% yield, there is 10% excess phenol or 87 lb phenol; with a 98% yield there is 17 lb phenol. Both Phenol and formaldehyde can be treated biologically but must be kept at controlled levels. Sometimes part of the phenol is recovered, we assumed that half of the phenol is recovered and recycled in both cases.

[g] With a 90% yield, there is 28 lb of formaldehyde, a waste of great health and environmental concern. Due to the high volatility formaldehyde is not easily recovered. There is no equivalent waste for the enzyme and hydrogen peroxide process.

The above calculations show that replacing the Novolac process with an enzymatic process could have a significant impact. The phenolic resin market is stable and growing at 3%/y. Therefore, we estimate that the phenolic resin market would be about 5 B lb/y by 2020. If this process could displace only half of the new capacity needed by 2020, this would be 1 B lb/yr produced enzymatically. This would save 2.8 trillion BTU/y and 25,000 M Ton/y of waste. These numbers are summed with the PO case above and reported on the Table. Moreover, the higher yield of phenol monomer incorporated into the final polymeric resin and the elimination of formaldehyde as a coreactant result in less waste and higher process efficiency. Finally, formaldehyde is a toxic and potentially carcinogenic compound. Hence, stringent OSHA regulations limit its exposure in the workforce, and its elimination from newer processes is a significant advantage.