(3) Be based upon the definition of market value as set forth in § 225.62(f);

(4)(i) Be written and presented in a narrative format or on forms that satisfy all the requirements of this section;

(ii) Be sufficiently descriptive to enable the reader to ascertain the estimated market value and the rationale for the estimate; and

(iii) Provide detail and depth of analysis that reflect the complexity of the real estate appraised;

(5) Analyze and report in reasonable detail any prior sales of the property being appraised that occurred within the following time periods:

(i) For 1-to-4 family residential property, one year preceding the date when the appraisal was prepared; and

(ii) For all other property, three years preceding the date when the appraisal was prepared;

(6) Analyze and report data on current revenues, expenses, and vacancies for the property if it is and will continue to be income-producing;

(7) Analyze and report a reasonable marketing period for the subject property;

(8) Analyze and report on current market conditions and trends that will affect projected income or the absorption period, to the extent they affect the value of the subject property;

(9) Analyze and report appropriate deductions and discounts for any proposed construction, or any completed properties that are partially leased or leased at other than market rents as of the date of the appraisal, or any tract developments with unsold units;

(10) Include in the certification required by the USPAP an additional statement that the appraisal assignment was not based on a requested minimum valuation, a specific valuation, or the approval of a loan;

(11) Contain sufficient supporting documentation with all pertinent information reported so that the appraiser's logic, reasoning, judgment, and analysis in arriving at a conclusion indicate to the reader the reasonableness of the market value reported;

(12) Include a legal description of the real estate being appraised, in addition to the description required by the USPAP;

(13) Identify and separately value any personal property, fixtures, or intangible items that are not real property but are included in the appraisal, and discuss the impact of their inclusion or exclusion on the estimate of market value; and

(14) Follow a reasonable valuation method that addresses the direct sales comparison, income, and cost approaches to market value, reconciles those approaches, and explains the elimination of each approach not used.

(b) *Unavailability of information.* If information required or deemed pertinent to the completion of an appraisal is unavailable, that fact shall be disclosed and explained in the appraisal.

(c) *Additional standards.* Nothing contained herein shall prevent a regulated institution from requiring additional appraisal standards if deemed appropriate.

§ 225.65 Appraiser independence.

(a) *Staff appraisers.* If an appraisal is prepared by a staff appraiser, that appraiser must be independent of the lending, investment, and collection functions and not involved, except as an appraiser, in the federally related transaction, and have no direct or indirect interest, financial or otherwise, in the property. If the only qualified persons available to perform an appraisal are involved in the lending, investment, or collection functions of the regulated institution, the regulated institution shall take appropriate steps to ensure that the appraisers exercise independent judgment and that the appraisal is adequate. Such steps include, but are not limited to, prohibiting an individual from performing appraisals in connection with federally related transactions in which the appraiser is otherwise involved and prohibiting directors and officers from participating in any vote or approval involving assets on which they performed an appraisal.

(b) *Fee appraisers.* If an appraisal is prepared by a fee appraiser, the appraiser shall be engaged directly by the regulated institution or its agent, and have no direct or indirect interest, financial or otherwise, in the property or transaction. A regulated institution may accept an appraisal that was prepared by an appraiser engaged directly by another institution subject to title XI of FIRREA, if the regulated institution that accepts the appraisal has:

(1) Established procedures for review of real estate appraisals;

(2) Reviewed the appraisal under the established review procedures, finding the appraisal acceptable; and

(3) Documented the review in writing.

§ 225.66 Professional association membership; competency.

(a) *Membership in appraisal organizations.* A State certified appraiser or a State licensed appraiser may not be excluded from consideration for an assignment for a federally related transaction solely by virtue of membership or lack of membership in any particular appraisal organization.

(b) *Competency.* All staff and fee appraisers performing appraisals in connection with federally related transactions must be State certified or licensed, as appropriate. However, a State certified or licensed appraiser may not be considered competent solely by virtue of being certified or licensed. Any determination of competency shall be based upon the individual's experience and educational background as they relate to the particular appraisal assignment for which he or she is being considered.

§ 225.67 Enforcement.

Institutions and institution-affiliated parties, including staff appraisers and fee appraisers, may be subject to removal and/or prohibition orders, cease and desist orders, and the imposition of civil money penalties pursuant to the Federal Deposit Insurance Act, 12 U.S.C 1811 *et seq.*, as amended, or other applicable law.

Board of Governors of the Federal Reserve System, June 27, 1990.

William W. Wiles,

Secretary of the Board.

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Part III

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 201

Labeling for Oral and Rectal Over-the-Counter Aspirin and Aspirin-Containing Drug Products; Final Rule

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 201

[Docket No. 90N-0169]

RIN 0905-AA06

Labeling for Oral and Rectal Over-the-Counter Aspirin and Aspirin-Containing Drug Products; Final Rule

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulations to require that the labeling of oral and rectal over-the-counter (OTC) aspirin and aspirin-containing drug products for human use bear a warning that such products should not be used during the last 3 months of pregnancy unless directed by a doctor. FDA is issuing this final rule after considering the report and recommendations of the Advisory Review Panel on OTC Internal Analgesic and Antirheumatic Drug Products, public comments on the agency's proposed regulation for these OTC drug products, which was issued in the form of a tentative final monograph, and all new data and information that have come to the agency's attention. FDA is taking this action in order to alert pregnant women that aspirin or aspirin-containing drug products taken without medical supervision during the last 3 months of pregnancy may cause problems in the unborn child or complications during delivery.

EFFECTIVE DATE: August 6, 1990. Manufacturers of affected drug products initially introduced or initially delivered for introduction into interstate commerce will have until July 5, 1991 to comply with the labeling requirement set forth in 21 CFR 201.63(e).

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION:

I. Background

In the Federal Register of July 8, 1977 (42 FR 35346), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC internal analgesic, antipyretic, and antirheumatic drug products, together with the recommendations of the Advisory Review Panel on OTC Internal Analgesic and Antirheumatic Drug Products (Internal Analgesic Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. One of the Panel's recommendations was that OTC drug products containing aspirin and carbaspirin calcium bear the following warning: "Do not take this product during the last three months of pregnancy except under the advice and supervision of a physician." This recommendation was based on the Panel's evaluation of data that led it to conclude that acute aspirin use during pregnancy could prolong the duration of labor, increase maternal blood loss both before and after delivery, and cause a change in the hemostatic mechanisms of the newborn child (42 FR 35346 at 35402). For these reasons, the Panel concluded that the acute use of aspirin during the third trimester of pregnancy poses a potential hazard and the above-cited warning should appear on all OTC aspirin-containing drug products (42 FR 35346 at 35405). Interested persons were invited to file comments by December 5, 1977. Reply comments in response to the comments filed in the initial comment period could be filed by February 6, 1978.

In accordance with § 330.10(a)(10) the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, after deletion of a small amount of trade secret information.

In response to the advance notice of proposed rulemaking for OTC internal analgesic, antipyretic, and antirheumatic drug products, two trade associations, several drug manufacturers, many health professionals, several consumers, a drug standard-setting association, two health professional associations, a health foundation, and one consumer group submitted comments. However, none of these comments discussed the Panel's proposed warning against the use of aspirin-containing products in the third trimester of pregnancy.

The agency's proposed regulation, in the form of a tentative final rule, for OTC internal, antipyretic, and antirheumatic drug products was published in the Federal Register of November 16, 1988 (53 FR 46204). As part of its proposed regulation, the agency expanded the Panel's proposed warning concerning the use of aspirin-containing products during the last 3 months of pregnancy in order to inform consumers of the reason for the warning, as follows: "IMPORTANT: Do not take this product during the last 3 months of pregnancy unless directed by a doctor. Aspirin taken near the time of delivery may cause bleeding problems in both mother and child" (53 FR 46253). This warning appeared in § 343.50(c)(1)(iv)(B) of the tentative final monograph. The agency further proposed that the warning follow the general pregnancy warning in § 201.63 that is required for all OTC drugs that are intended for systemic absorption, which includes oral and rectal aspirin and aspirin-containing drug products. Interested persons were invited to file by May 16, 1989, written comments, or objections, or requests for oral hearing before the Commissioner of Food and Drugs regarding the proposal. Interested persons were invited to file comments on the agency's economic impact determination by May 16, 1989. New data could have been submitted until November 16, 1989, and comments on the new data until January 16, 1990.

In a notice published in the Federal Register of January 16, 1990 (55 FR 1471), the agency advised that it was extending to March 16, 1990, the period for comments on new data for the notice of proposed rulemaking for OTC internal analgesic, antipyretic, and antirheumatic drug products.

Five manufacturers, two trade associations, and one consumer submitted comments on the proposed third trimester pregnancy warning for OTC aspirin-containing drug products. There was one request for a hearing. Copies of the comments and the hearing request are on public display in the Dockets Management Branch. Additional information that has come to the agency's attention since publication of the proposed rule is also on public display in the Dockets Management Branch. In proceeding with this final rule, the agency has considered all comments, new data, and the request for an oral hearing related to this issue.

II. Highlights of the Final Rule

This final rule requires a new warning statement for all OTC oral and rectal aspirin and aspirin-containing drug products. This new warning statement must appear in boldface type and all capital letters and immediately follow the general pregnancy-nursing warning statement required by § 201.63, under the heading "Warinings," as follows:

As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product. IT IS ESPECIALLY IMPORTANT NOT TO USE" (select "ASPIRIN" or " CARBASPIRIN CALCIUM," as appropriate) "DURING THE LAST 3 MONTHS OF PREGNANCY UNLESS SPECIFICALLY DIRECTED TO DO SO BY A DOCTOR BECAUSE IT MAY CAUSE PROBLEMS IN THE UNBORN CHILD OR COMPLICATIONS DURING DELIVERY."

The agency has determined that this new warning statement concerning use during the last 3 months of pregnancy should appear in the labeling of OTC aspirin and aspirin-containing drug products prior to finalization of the monograph for OTC internal analgesic, antipyretic, and antirheumatic drug products in order to alert pregnant women of the additional conditions under which these OTC drug products should not be used without medical supervision. The agency notes that similar warnings have been approved in new drug applications for OTC ibuprofen-containing drug products (an OTC analgesic similar to aspirin) for more than 5 years.

III. Summary of the Comments

The agency received 10 comments on its proposed third trimester warning for aspirin and aspirin-containing drug products. One comment endorsed the agency's proposed warning, which was as follows: "IMPORTANT: Do not take this product during the last three months of pregnancy unless directed by a doctor. Aspirin when taken near the time of delivery may cause bleeding problems in both mother and child." Several comments, including one from a trade association, recommended that the agency's proposed warning be deleted. Several of the comments contended that the warning, when used in conjunction with the general pregnancy warning required by § 201.63 ("As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product.") may confuse and unduly frighten consumers.

One comment noted that the Panel's recommendation in 1977 for an aspirin pregnancy warning was made before the agency implemented its requirement in 1982 for a general pregnancy-nursing warning for all drugs intended for systemic absorption. Other comments contended that the agency's proposed warning is unnecessary and that the general pregnancy warning is adequate to inform pregnant consumers of the need to consult a trained health professional prior to using OTC drug products containing aspirin. Another comment argued that the two warnings taken together would reduce the likelihood that consumers will follow the directions of the general warning to consult a doctor before use of these products during the first six months of pregnancy. The comment concluded that the agency's proposed warning could result in the inappropriate use of OTC aspirin drug products during pregnancy.

Another comment stated that the warning could cause consumer confusion. The comment asserted that the first sentence of the proposed warning could lead consumers to believe that there may be circumstances in which a woman in the third trimester of pregnancy should take aspirin when directed to do so by a doctor, while the second portion of the proposed warning clearly says that the use of aspirin near the time of delivery may cause bleeding problems in both mother and child. Another comment argued that the agency's proposed warning could lead a consumer to assume that aspirin taken prior to the last trimester is completely without risk. The comment stated its belief that the explicit speculation included in the proposed warning goes beyond responsible regulation and that it may frighten consumers who have been prescribed aspirin during pregnancy for legitimate medical needs.

One comment warned that the proliferation of warnings proposed for inclusion in the labeling of these OTC drug products carries with it the risk that the effectiveness of the warnings may be diluted, so that truly significant warnings will be overlooked by consumers. The comment recommended use of a single warning instead of several specific warnings dealing with the same subject. Citing the agency's proposed third trimester pregnancy warning as an example, the comment suggested that the general pregnancy warning and the agency's proposed warning be combined, to read as follows: "As with any drug, if you are pregnant or nursing a baby, do not take unless directed by a doctor. This is particularly important for aspirin during the last 3 months of pregnancy since it may cause bleeding problems in mother or child." The comment contended that the combined warning would be more effective and requested a hearing if the agency disagrees with its position on this issue.

One comment questioned the need for the additional warning for two reasons: (1) Lack of evidence demonstrating the need for such a warning and (2) lack of evidence that the general pregnancy warning is ineffective in accomplishing the goal of the more specific proposed warning. The comment further questioned the need for the proposed warning based on two studies (Refs. 1 and 2) that suggest that low daily doses (60 or 100 milligrams (mg)) of aspirin taken during the third trimester of pregnancy may reduce the incidence of pregnancy-induced hypertension and preeclamptic toxemia in women at risk from these conditions. The comment cautioned that the agency's proposed warning may jeopardize a woman's compliance with this promising new use of aspirin and may therefore interfere with the physician-patient relationship.

Another comment submitted a study (Ref. 3) designed to assess whether there is an association between third trimester aspirin use and an increase in the incidence of stillbirths or in the degree of neonatal bleeding, maternal bleeding, length of gestation, or length of labor. Subsequently, the comment submitted another analysis of the same data base (Ref. 4), which assesses the effect of aspirin use in the last 10 days of pregnancy. The comment asserted that these data demonstrate that a third-trimester pregnancy warning for aspirin is not necessary.

Subsequently, the trade association, which had requested deletion of the proposed warning, noted the more recently submitted new scientific information (Refs. 3 and 4) and requested that the agency resolve the third-trimester pregnancy warning for OTC aspirin-containing drug products without awaiting resolution of the other issues presented in the tentative final monograph. Numerous legal precedents were cited to support its suggestion (Ref. 5). The comment added that FDA has finalized labeling regulations outside the OTC drug review monograph process, mentioning the general pregnancy-nursing warning in § 201.63. That warning applied to OTC aspirin-containing drug products, and other marketed OTC drugs, prior to issuance of a final monograph. The comment recommended that the agency publish expeditiously a final rule that would require, if appropriate, the following third-trimester pregnancy warning on the labeling of all OTC aspirin and aspirin-containing analgesic-antipyretic drug products: "Do not use this product during the last 3 months of pregnancy unless advised to do so by a doctor because it may cause problems during delivery." The comment contended that the language of its proposed warning is consistent with the third-trimester warning language that now appears on the OTC analgesic ibuprofen. The comment asserted that this warning is likely to receive nationwide acceptance and thereby maintain national uniformity in the labeling of aspirin and other OTC analgesics. The comment also recommended that the final rule provide that warnings may be combined to eliminate duplicative words or phrases so that the resulting warnings are clear and understandable, as proposed in the tentative final monograph.

IV. The Agency's Conclusions on the Comments

The agency has determined that the third-trimester pregnancy warning should be finalized before resolution of the other matters pending in the tentative final monograph for OTC internal analgesic, antipyretic, and antirheumatic drug products. The agency is finalizing this warning for OTC aspirin-containing drug products now, in order to ensure that consumers have adequate information concerning the use of these products during the third trimester of pregnancy. This will enable consumers to make intelligent and informed decisions concerning their safe use.

The agency does not agree with the comments that contend that the agency's proposed third-trimester pregnancy warning is unnecessary in light of the general pregnancy warning already required to appear on these OTC drug products. However, after reviewing the Panel's conclusions, the submitted comments, and the recently available data on this issue, the agency now believes that a specific reference to bleeding as proposed in the tentative final monograph (53 FR 46204 at 46253) is not necessary. Use of aspirin during the third trimester poses potential risks. Therefore, the agency believes that it is important that consumers be specially advised not to use aspirin and aspirin-containing OTC drug products during the third trimester of pregnancy unless directed to do so by a doctor.

In a recent study by Brent, Shook, and Wilson (Ref. 3), the outcomes of pregnancies in which aspirin was used during the third trimester of pregnancy were compared to the outcomes of pregnancies in which no aspirin was used. The study also evaluated the effect of different aspirin exposure levels during the third trimester and the last month of pregnancy. The data base used in this study was generated by the National Collaborative Perinatal Project (NCPP), sponsored by the National Institutes of Health. This data base resulted from a comprehensive multicenter study that monitored approximately 58,000 pregnancies and their outcomes during a 16-year period (1959–1974) in an effort to clarify the etiology of cerebral palsy and mental retardation. The study collected information from participating women on many factors that may have affected cerebral palsy and mental retardation such as other conditions, disease states, medications, treatments, education, socio-economic level, sex of the neonate, and others. This information was collected from participating women on an ongoing basis from the time they were diagnosed as pregnant and continuing through delivery. Information also was collected on the neonates from the time of delivery until age eight.

Subjects were included in the analysis by Brent, Shook, and Wilson when the NCPP data base contained a record of the outcome of the pregnancy and information indicating whether or not aspirin was used. Aspirin exposure was recorded as "low dose" (subject took aspirin on only 1 day in a lunar month), "medium dose" (subject took aspirin on 2 to 7 days in a lunar month), and "high dose" (subject took aspirin on more than 7 days in a lunar month). However, neither the total dose of aspirin taken on any given day nor the total number of days of aspirin use if over 8 days was reported.

The study evaluated five endpoints: incidence of stillbirths, degree of neonatal bleeding, maternal bleeding, length of gestation, and length of labor. Because neonatal bleeding was not directly recorded in the NCPP data base, data on neonatal intracranial bleeding, neonatal hematocrit, and neonatal hemoglobin (after 48 hours) were analyzed to give an estimate of the degree of neonatal bleeding. The authors stated that a reduction in hematocrit by 0.6 percent after 48 hours or a reduction in hemoglobin by 0.2 gram (g) indicated a blood loss of approximately 1 percent. Both stillbirth and neonatal intracranial bleeding were noted as either present or absent, while the other outcomes were measured on a continuous scale.

Other factors which when present during pregnancy may have influenced the above uncorrected risk estimates were identified from previous literature and tested for possible influence on study outcomes. The other factors analyzed for included 62 non-drug factors and 27 categories of drugs. Each of these covariables was tested to determine whether it was associated with the unadjusted risk of the investigated outcomes and whether it was associated with the use of aspirin in the study. The unadjusted risk assessments for the evaluated outcomes were then corrected for each of these covariables simultaneously and both unadjusted and adjusted results were reported.

Pregnancies in which the above outcomes were recorded were evaluated by comparing aspirin-exposed pregnancies to unexposed pregnancies. The proportions of women who demonstrated one of these outcomes and who were exposed to aspirin in one of three dosage groups during the last 3 months of pregnancy were compared to the proportions of women in the group with no aspirin exposure. The exposure groups were: (1) Any exposure to aspirin regardless of doses, (2) low-dose group, and (3) high-dose group. In addition to the evaluation of the effects of aspirin exposure during the third trimester of pregnancy, women exposed at the high and low dose during the last month of pregnancy were compared to women not exposed to any aspirin during that time.

There was no statistically significant association of neonatal intracranial bleeding with any level of aspirin use in the third trimester or in the last month of pregnancy. The authors considered the data for these associations sufficient to detect a difference as small as 1 percent between any of the aspirin-user groups and the unexposed population, with a power of 90 percent or greater.

The mean neonatal hemoglobin of 18.2 g percent for the unexposed group was not changed significantly for any level of aspirin exposure during either the third trimester or the last month of pregnancy. However, the low-dose exposure during the last month suggests a decrease in the mean hemoglobin level of 0.1 g percent, indicating less blood loss among the unexposed group. An adjustment of the data for the last month of pregnancy for covariables indicated that there is no significant difference between the two means when aspirin was considered independently. The authors considered the data for this outcome sufficient to detect a difference of 0.2 g percent between any of the aspirin-user groups and the exposed population, with a power of 90 percent.

The unadjusted third-trimester exposure data for the mean neonatal hematocrit indicated that the unexposed group had a significantly higher mean hematocrit (58.6 percent) than the exposed groups ($p < 0.001$). The results for the last-month exposure groups were essentially identical to those for the third-trimester exposure group. The data from both levels (low and high dose) indicate a small (less than 1 percent) but statistically signifcant decrease in the mean neonatal hematocrit. The authors reported that adjustment of the data for covariables removed the statistical significance of the difference for both exposure groups. The authors contend that the data for the 3-month exposure were sufficient to detect a difference of 0.3 percent hematocrit between any of the exposure groups and the unexposed group, with a power of 90 percent or greater.

With regard to maternal blood loss, the study reported that the mean loss of 226.2 milliliters (mL) of blood for the unexposed group was not significantly

different from any of the aspirin groups (< 5.1 mL) based on both the adjusted and unadjusted data. The data from the low- and high-dose exposures of aspirin during the last month of pregnancy also showed no statistically significant change in either the adjusted or unadjusted data. The authors point out that the maternal blood loss measurements for this study were based on delivery room estimates of the quantity of blood lost during delivery. The authors report that the data for this variable were sufficient to detect a difference of 8 mL of blood loss for the 3-month data and a 7-mL blood loss for the 1-month data between the unexposed and exposed populations, with a power of 90 percent or greater.

The study also attempted to ascertain whether or not there was a dose effect of aspirin over the third trimester of pregnancy by comparing subjects who were not exposed to aspirin to subjects with exposure to aspirin (1) Any time during the last trimester, (2) with low- and high-use aspirin exposure during the third trimester, and (3) with low- and high-use aspirin exposure during the last month.

The third-trimester low-dose aspirin exposure group included those subjects who ingested aspirin on only 1 day in the last month of pregnancy and during at least 1 other month of the last 3 lunar months of pregnancy. Where inclusion was based on a 2-month exposure, the remaining month had to have had no exposure. To qualify for the high-dose aspirin group, the subjects must have ingested aspirin on at least 8 days in the last month of pregnancy and during at least one more of the last 3 lunar months of pregnancy, with an intermediate exposure (2 to 6 days) in the month in which a high exposure was not recorded. The last-month low-use group included subjects whose aspirin ingestion was only 1 day during the last month. The high-use group included subjects that had ingested aspirin on at least 8 days during the last month. The authors reported that their analysis of data from the any-aspirin exposure group and the groups with high and low dose aspirin exposure during the third trimester and last month of pregnancy indicated no aspirin association for neonatal intracranial bleeding, neonatal hematocrit, and neonatal hemoglobin. Noting the fact that the data for maternal blood loss were not based on a precise quantitative measurement, which may affect the reliability of the results, the authors reported that there was no significant difference in maternal blood loss between the any-aspirin-exposure group and the unexposed group. The evaluation of the 3-month high- and low-dose groups, and the last month data, also indicated no difference.

In summary, the authors concluded that this extensive data base shows that the ingestion of aspirin in OTC doses during the last 3 months of pregnancy does not lead to a clinically relevant adverse result due to bleeding in any of the outcomes studied. According to the authors, the study indicated no increase in maternal bleeding or neonatal bleeding (as measured by either neonatal intracranial bleeding, neonatal hemoglobin, or neonatal hematocrit).

In a subsequent study (Ref. 4) of the same NCPP data base, the same authors examined the risks to mothers who were exposed to aspirin during the last 10 days before delivery. The study compared exposed mothers and their neonates (both premature and full-term infants) with those who were never exposed to aspirin during pregnancy. The study involved the analysis of three bleeding endpoints: neonatal intracranial bleeding, neonatal hemoglobin, and neonatal hematocrit. In addition, based on the assumption that there was no aspirin effect on these endpoints, a fourth indicator of possible intracranial bleeding at birth, the intelligence quotient (IQ) at 7 years of age, was analyzed.

Subjects were included in the study if their records indicated that they had used aspirin within the last 10 days before delivery or had not used aspirin at all during their pregnancy but had the outcome being evaluated. Premature infants were defined by a length of gestation of less than or equal to 33 weeks and a birthweight of less than 1,500 g. Full-term infants were defined as having a gestation period greater than or equal to 34 weeks and a birth weight equal to or greater than 1,500 g. The infants whose mothers were exposed to aspirin during the last 10 days of pregnancy were compared to infants born to mothers with no aspirin exposure during this same period. An analysis of maternal bleeding in the full-term population was also done. Detailed information regarding the number of tablets or capsules of aspirin-containing products that the subjects took was abstracted from information in the NCPP data base.

Neonatal intracranial bleeding was evaluated on the basis of the presence or absence of the condition. Neonatal hemoglobin, neonatal hematocrit, maternal bleeding, and IQ at 7 years were measured on a continuous scale. As in the study above, the data were analyzed for the effect of other factors which may have influenced the uncorrected risk estimates. However, the method of analysis used in this study differs from that of the previous study (Ref. 3) because only the effect of variables likely to have had an influence on the unadjusted results were analyzed for, rather than all 89 potential covariables.

For the outcome of neonatal intracranial bleeding in full-term infants, the study reported that there was no difference in the percentage of infants who experienced intracranial bleeding when a comparison between the exposed and unexposed groups was made. For the outcome of neonatal hemoglobin (after 48 hours), the aspirin-exposure group had a mean of 18.3 g percent, and the no aspirin-exposure group had a mean of 18.2 g percent. The difference between these two means was not statistically significant. The data from the aspirin-exposure and the no-aspirin-exposure groups indicated that the unadjusted mean hematocrit of the exposed infants (57.8 percent) was less than the value for the nonexposed infants (58.8 percent) and that the difference was statistically significant with a probability of 0.0001. The results showed on covariant analysis that aspirin exposure during the last 10 days of pregnancy had an opposite effect, i.e., it caused less effect on neonatal hematocrit than no aspirin exposure during this period. An assessment of the IQ at age 7 indicated a statistically significant increase ($p=0.0001$) in the IQ of infants at age 7 of the aspirin exposure group (96.0) over the unexposed group (96.1), but an adjustment of the data for the effects of covariables indicated no significant difference in IQ between the two groups.

Maternal bleeding was assessed in the same way it had been in the other study (Ref. 3). The authors stated that the analysis of these data was extremely difficult due to the large standard deviations and the skewed distributions of the blood loss which they attributed to the fact that the blood loss values were estimated and not measured. Comparison of the unadjusted means for the blood loss indicated the unexposed group lost 7.5 mL more blood than the exposed group. The difference was found to be statistically significant ($p = 0.002$). The authors reported that this result indicated that the use of aspirin during the last 10 days of pregnancy resulted in less blood loss at delivery; however, the difference of 7.5 mL (which is equivalent to 1½ teaspoons) is clinically insignificant.

A comparison of the incidence of neonatal intracranial bleeding in exposed and unexposed premature infants was not statistically significant (14.0 and 12.1 percent, respectively). The authors concluded that there is no significant increase in the risk of neonatal intracranial hemorrhage between the exposed and unexposed groups.

In the assessment of the data on premature neonatal hemoglobin (after 48 hours), the study indicated that the aspirin group showed significantly less neonatal hemoglobin than the no-aspirin-exposure group. However, when these results were adjusted for covariables that were deemed to have a significant effect on this outcome, there was no significant difference between the aspirin-exposure and no-exposure groups. The unadjusted mean hematocrit of the exposed infants was less than the value for the unexposed infants, but this difference was not statistically significant. When these results were corrected for covariables, the results also were not statistically significant. With regard to the assessment of IQ at 7 years, the study contained little data; and both the unadjusted and adjusted values indicated that there was no statistically significant difference.

The agency concludes that upon evaluation of all the available data, including the new uses discussed below, that aspirin used in the third trimester of pregnancy poses some potential risks, only one of which is bleeding. It is important to advise women in their third trimester of pregnancy to consult a doctor before using any OTC drug products containing aspirin or carbaspirin calcium. The agency continues to agree with the Panel and concludes that these products should bear a third-trimester pregnancy warning.

The Panel's conclusion that acute aspirin use during the third trimester of pregancy poses a potential risk for both mother and infant was based on its evaluation of data on the effects of aspirin on various aspects of pregnancy as extensively reported in the literature through 1977 (42 FR 35346 at 35399). In addition to its concerns about the changing of the hemostatic mechanisms in the newborn and increasing maternal blood loss, the Panel's discussion of the evaluated data regarding the effects of aspirin or carbaspirin calcuim on pregnancy also included other effects of these ingredients on pregnancy. Such other effects are due to multiple effects of prostaglandin inhibition on the fetus and on delivery.

The Panel noted that Tuchman-Duplessis et al. (Ref. 6) reported that the administration of 200 mg/kilogram (kg)/day of aspirin to rats during the last 6 days of pregnancy resulted in a prolongation of the duration of pregnancy, a prolongation of parturition, and appearance of dystocia (abnormal labor) in some animals, which the authors speculated resulted in the possible secondary death of the fetuses in utero. The authors reported that 70 percent of the control dams delivered on day 21 of pregnancy, while only 18 percent of the treated dams did ($p < 0.05$).

The Panel noted that Lewis and Schulman (Ref. 7) reported the results of a 20-year retrospective study designed to evaluate the influence of aspirin on the duration of human gestation and labor of 103 aspirin-treated subjects. The study compared subjects (most of whom had nonspecific collagen disease or degenerative musculoskeletal disease) taking doses of greater than 3,250 mg of aspirin a day during the last 6 months of pregnancy to two control groups. One of the control groups consisted of 52 pregnant females with rheumatoid arthritis, nonspecific collagen diseases, or degenerative musculoskeletal disease who did not take aspirin or other compounds known to affect prostaglandin synthesis. The second control group consisted of 50 pregnant women without known disease who did not take therapeutic doses of aspirin or related drugs. The authors reported that subjects taking aspirin had an average gestation period of over 1 week longer than either of the control groups ($p < 0.025$) and that the control groups did not differ from each other. In the aspirin group, 42 percent of the subjects had gestation periods of greater than 42 weeks (at least 15 days post mature), while only 3 percent of the combined control group demonstrated this. The authors considered this result as very significant ($p < 0.0001$). The subjects in the aspirin group also had a significant longer mean length of labor than either of the control groups (12 hours versus 7 hours, p-value of less than 0.005) and had an estimated average blood-loss at delivery of 100 mL more than either of the control groups ($p < 0.025$).

The Panel evaluated a study by Collins and Turner (Ref. 8) in which two groups of pregnant women who self-medicated with analgesics regularly were compared to a group of matched controls. One group of subjects (constant takers) admitted to taking analgesics every day of their pregnancy. Many of the women in this group had self-medicated with analgesics for years and were habituated to analgesics. The constant takers took analgesic powders containing either aspirin, salicylamide, and caffeine or aspirin, phenacetin, and caffeine. The second group of self-medicated women (intermittent takers) admitted to taking analgesics at least once a week throughout their pregnancy. However, the authors reported that many of the women in this group took analgesics much more frequently than this, but denied taking them every day. The women in this group took the same analgesic powders or a variety of tablets containing salicylate alone or in combination with other drugs. None of the subjects took aspirin for chronic disease such as rheumatoid arthritis.

Collins and Turner reported that the major effects of regular aspirin consumption on pregnancy were an increased frequency of anemia during pregnancy, a prolonger gestation, an increased incidence of complicated deliveries, a high incidence of antepartum and postpartum hemorrhage and transfusion at delivery, and an increased perinatal mortality. The authors theorized that the observed effects may have been caused by the other constituents of the powders or by the fact that so many of the regular takers were heavy smokers. The authors stated, however, that the observed effects of the study were also explainable by the pharmacologic effects of aspirin.

The mean length of pregnancy of the two groups of women was significantly increased compared to the control group ($p < 0.05$). The authors of the study reported that women in the control group had a mean duration of pregnancy of 38.7 weeks while the women in the aspirin groups had a mean duration of pregnancy of 39.7 and 39.8 weeks, respectively. The proportion of subjects going beyond 42 weeks of pregnancy was increased but not significantly so. The authors stated that the inhibition of prostaglandin release by aspirin might be expected to delay the onset of labor and increase the mean length of labor.

The authors reported a highly significant increase in both prenatal and postnatal bleeding ($p < 0.001$). However, because the numbers in the survey were small, the findings in the present and past pregnancies of the women in the study were combined when assessing the incidence of antepartum hemorrhage, postpartum hemorrhage, and transfusion at delivery. The authors remarked that it was not possible to determine in each patient the time between the last dose of aspirin and delivery.

In a subsequent study (Ref. 9), Turner and Collins evaluated the effects of regular salicylate ingestion during

pregnancy on the infants of 144 mothers. Infants born to mothers who took salicylates daily during their pregnancy were compared to infants whose mothers took salicylates at least once a week and to a control group matched for age, parity, gravity, ethnic group, and social class. The authors reported that the birth-weights of infants born to mothers taking salicylates were significantly lower than those of the matched controls even after a correction for the mothers who smoked during the study. The perinatal mortality of these infants was increased. The authors reported that while a direct comparison between salicylate levels in maternal blood and cord blood was not possible because of inconsistencies in the sampling of maternal blood, high levels of salicylates in maternal blood corresponded to high salicylate levels in cord blood. However, no clinical signs of bleeding in the infants with increased salicylate blood levels were reported.

Bleyer and Breckenridge (Ref. 10) studied the effects of prenatal medications, including aspirin, on newborn hemostasis by the comparison of prenatal histories obtained from prenatal medication diaries with clinical and laboratory studies done postpartum. Forty-Three newborns, all born of healthy mothers after normal pregnancies and uneventful deliveries, were included in the study. A medication diary designed to provide an accurate record of all pharmacological agents taken during pregnancy was kept by each mother in the study and brought to the hospital at the time of delivery. Only after all clinical and laboratory data had been tabulated were the medication records opened and the mothers who had taken aspirin identified and allocated to the following groups. The drug group consisted of infants whose mother took more than 0.3 g of aspirin during the week prior to delivery. The dosage range for this group ranged from 0.32 g taken once 7 days before delivery to 1.3 g daily. The control group consisted of infants whose mothers had not taken aspirin in any form during the last 3 weeks of their pregnancy. Fourteen infants exposed to aspirin during the week prior to birth were compared to 17 infants in the control group. The authors of the study stated that they had chosen the above criteria based on information that had established that blood levels can be detected for 2 days or longer in adults and for as long as 7 days in neonates, and that a single small dose of aspirin (0.15 to 1.5 g) in normal adults can cause hemostatic abnormalities for as long as 7 days.

Umbilical cord and maternal blood samples were obtained at the time of delivery. All bleeding, including hemorrhage from circumcision, was recorded. Guaiac and fetal hemoglobin tests were performed on meconium from each newborn. A variety of laboratory tests relating to platelet function and number and clotting factor activities were performed on both the maternal and neonatal blood. The authors reported that maternal ingestion of aspirin was associated with the inhibition of collagen-induced platelet aggregation and diminished factor XII activity and noted that both were evidenced after ordinary doses of aspirin occurring in the newborn when the mother ingested as little as 0.65 g of aspirin as long as 2 weeks prior to delivery.

The authors stated that the diminished factor XII activity is of uncertain clinical importance but that aspirin-induced platelet dysfunction may have clinical relevance, particularly during difficult, traumatic deliveries or in the presence of another hemostatic defect such as von Willebrand's disease, hemophilia, or thrombocytopenia. They concluded that even though none of the newborns included in the study developed major hemorrhages, the hemostatic defects uncovered by the study are not necessarily benign, and recommended that until the clinical significance of the study finding is further evaluated, aspirin and other anti-inflammatory agents known to produce platelet dysfunction should be avoided when labor is imminent.

The Panel also noted a report (Ref. 11) by Haslam, Ekert, and Gillam of a case of a "life-threatening gastrointestinal hemorrhage" requiring two transfusions in one infant whose mother had taken calcium carbaspirin (3 tablets of 300 mg on each of the last 3 days of pregnancy, a total of 2,700 mg).

The more recent data address some of the Panel's concerns. As noted above, the studies by Brent, Shook, and Wilson on the effects of aspirin exposure in the third trimester and the last month of pregnancy (Refs. 3 and 4) included an evaluation of stillbirths, length of gestation, and length of labor. The authors reported that the data indicated that there was no statistically significant association between aspirin and still birth for aspirin exposure during the third trimester of pregnancy.

The unadjusted 3-month exposure data on the length of gestation from this study suggest that the average gestation period of 39.8 weeks for the unexposed group was significantly increased by 0.1 week for any exposed aspirin group ($p=0.004$) and decreased 0.2 week for the high dose aspirin group ($p=0.012$). However, the authors reported that the adjustment of the data for covariables by multiple regression indicated that the effect of aspirin alone does not significantly change the length of gestation in any of the three groups analyzed. The unadjusted data from the low and high dose aspirin use during the last month of pregnancy suggest a significant decrease in the length of gestation of 0.1 week for the high dose group ($p=0.022$) which is supported by the multiple regression analysis of the data. When the data were adjusted, statistically significant decreases were indicated for both groups (low dose mean decrease of 0.097 week, $p=0.014$; high dose mean decrease of 0.191 week, $p=0.0001$). The authors reported that the data were sufficient to detect a difference of 0.84 day (0.12 week) for the 3-month data and 0.7 day (0.1 week) for the 1-month data between the exposed populations and the unexposed populations, with a power of 90 percent or greater.

With regard to the length of labor, the authors reported that based on the unadjusted data none of the third-trimester aspirin exposure levels resulted in a statistically significant change in the mean delivery time of 7.7 hours for the unexposed group. However, they did report that the high dose data suggest an average decrease of 0.4 hour in length of labor, which was not significant. When the above data were adjusted for covariables, there was a small but statistically significant increase in the length of labor for the any-aspirin group (mean increase=0.467 hour, $p=0.042$) and for the high-dose group (mean increase=0.644 hour, $p=0.040$). In the last-month exposure data, no significant increase in the length of labor was found for the high-dose group, but the data for the low-dose group indicated an increase of 0.5 hour (unadjusted data) and 0.315 hour (adjusted) ($p=0.016$). The authors report that the data were sufficient to detect a difference of 18 minutes (0.3 hour) between any-aspirin users and nonusers, with a power of 90 percent or greater.

In the portion of the study in which the authors attempted to assess if there was a dose effect among differing aspirin groups, the authors compared the data (adjusted for covariables) on gestation from subjects with any exposure to aspirin to unexposed women and reported that aspirin alone did not increase the average gestation period. The authors further reported that when the 3-month high- and low-dose

groups were considered, the high-dose group had a slightly decreased gestation period (0.2 week). However, when these data were adjusted for covariables, the data did not indicate an aspirin effect on the length of gestation. The authors reported similar results when evaluating the subjects with exposure only in the last month.

No effect of aspirin on the length of labor was reported in the study when the unadjusted data from the any-exposure-to-aspirin group were compared to unexposed subjects. However, the adjustment of the data for covariables indicated that aspirin alone would be associated with a slight increase in the length of labor of about 28 minutes for the exposed groups. When dose during the last trimester was considered for this outcome, the high-dose aspirin group had an average labor of 24 minutes less than the unexposed group. When the data were adjusted for covariables, aspirin exposure along was indicated to be associated with an average increase of about 39 minutes. No difference was indicated for the low-dose group. Data from the last-month exposure groups indicated no increase for the high dose group but a slight increase for the low-dose group. Adjustment for covariables indicated that aspirin exposure alone was associated with an average increase of 21 minutes in the low-dose group, but there was no increase in the high-dose group.

In addition, the agency is aware of new uses of aspirin that have been reported in the scientific literature (Refs. 1 and 2). Schiff et al (Ref. 1) reported a prospective, randomized, double-blind, placebo-controlled study to investigate the capacity of aspirin to prevent pregnancy-induced hypertension and to alter prostaglandin metabolism in women at risk from these disorders. The results of the study indicated that the number of women in whom pregnancy-induced hypertension developed was significantly lower among women treated with 100 mg of aspirin daily during the last trimester of pregnancy (to within 0 days of delivery) than in the placebo group. The same result was reported for the incidence of preeclamptic toxemia. Based on this study, the authors concluded that low daily doses of aspirin taken during the third trimester significantly reduce the incidence of pregnancy-induced hypertension and preeclamptic toxemia of pregnancy in women at risk from these disorders.

Benigni et al. (Ref. 2) evaluated the effect of low-dose aspirin on the fetal generation of thromboxane by platelets in women at risk for pregnancy-induced hypertension. The authors reported that low doses (60 mg daily until delivery) of aspirin suppressed maternal platelet thromboxane B_2, but only partially suppressed neonatal platelet thromboxane B_2, thus allowing hemostatic competence of the fetus and newborn. The authors also reported that low doses of aspirin were associated with a longer pregnancy and an increased weight of newborns.

The agency concludes that the effects of these ingredients on maternal and fetal vascular and platelet prostaglandins have been demonstrated. These effects could be beneficial in some instances, e.g., pregnancy-induced hypertension, or under other circumstances could cause problems in some mothers and infants. These effects could lead to complications for some women during delivery, and these problems would be most likely to occur if aspirin were taken during the last trimester of pregnancy close to the time that delivery occurs. Although the agency has not yet evaluated these potential new uses of aspirin, the agency is concerned that a reference to bleeding as included in the proposed warning may discourage compliance with medically supervised uses of aspirin, e.g., the treatment of chronic arthritis, and therefore is not including a specific reference to bleeding in the new warning for these OTC drug products.

The agency notes that another OTC analgesic drug, ibuprofen, which is not currently included in the OTC drug review but is the subject of an approved new drug application, bears a similar warning, which states:

IT IS ESPECIALLY IMPORTANT NOT TO USE IBUPROFEN DURING THE LAST 3 MONTHS OF PREGNANCY UNLESS SPECIFICALLY DIRECTED TO DO SO BY A DOCTOR BECAUSE IT MAY CAUSE PROBLEMS IN THE UNBORN CHILD OR COMPLICATIONS DURING DELIVERY.

Both aspirin and ibuprofen are members of a class of drug ingredients known as non-steroidal anti-inflammatory drugs. The basis for the pharmacologic action of this drug class is their ability to inhibit the synthesis of prostaglandins (Ref. 12). The inhibition of prostaglandin synthesis is a critical factor with regard to the effects of aspirin on pregnancy. Aspirin and the other members of this class share similar effects on prostaglandin synthesis, and their effects on pregnancy are similar (Refs. 13 and 14). The agency now believes that having different warnings on OTC drug products containing these ingredients could cause consumers to perceive that there is a difference in the safety of using these ingredients during the third trimester of pregnancy when, in fact, there is no established significant safety difference.

For all of the above reasons, the agency has concluded that it would be advisable to include in the labeling of all OTC aspirin and aspirin-containing drug products a warning statement that it is especially important not to use these products during the last 3 months of pregnancy unless specifically directed to do so by a doctor and to inform pregnant women why they should not do so, i.e., because such use of the drug may cause problems in the unborn child or cause complications during delivery. Therefore, the agency is amending the pregnancy-nursing warning labeling requirement in § 201.63 to require that all oral and rectal OTC aspirin and aspirin-containing drug products bear a warning similar to that currently required for OTC ibuprofen drug products, as follows:

IT IS ESPECIALLY IMPORTANT NOT TO USE (select "ASPIRIN" or "CARBASPIRIN CALCIUM," as appropriate) "DURING THE LAST 3 MONTHS OF PREGNANCY UNLESS SPECIFICALLY DIRECTED TO DO SO BY A DOCTOR BECAUSE IT MAY CAUSE PROBLEMS IN THE UNBORN CHILD OR COMPLICATIONS DURING DELIVERY.

The agency is requiring that this warning immediately follow the general pregnancy warning required by § 201.63(a) and appear in boldface type and all capital letters.

The agency disagrees with the comments that contended that the proposed third-trimester warning is unnecessary when used in conjuction with the general pregnancy-nursing warning, that the two warnings used together would reduce the likelihood that consumers will follow the directions of the general warning, that the third-trimester warning would result in the inappropriate use of the OTC aspirin drug products during pregnancy, and that the two warnings used together may confuse and unduly frighten consumers. The general pregnancy-nursing warning regulation (§ 201.63(b)) provides that where a specific warning relating to use during pregnancy has been established for a particular drug, the specific warning shall be used in place of the general warning unless otherwise stated. In this particular situation, the agency concludes that each warning statement serves a specific purpose. The general pregnancy-nursing warning is intended to convey the message that at any time during pregnancy a consumer should seek the advise of a health professional

before using any OTC drug product. The third-trimester warning is intended to emphasize that it is especially important not to use these types of drugs during this time unless specifically directed to do so by a doctor. The agency has revised the proposed warning in this final rule to reflect that intent. Thus, the agency does not intend, in this case, for the third-trimester warning to be used in place of the general warning. The third-trimester warning is to be used in addition to the general warning. The final regulation specifically states this requirement.

The similar warning for OTC ibuprofen drug products has been in use for over 5 years. It too is used in conjuction with the general pregnancy-nursing warning. The agency has not received any reports that the use of both of these warnings has been confusing or frightening to consumers.

The agency is not adopting the warning recommended by the trade association which reads "Do not use this product during the last 3 months of pregnancy unless advised to do so by a doctor because it may cause problems during delivery." The agency concludes that the ibuprofen-type warning that has been adopted is more informative to consumers because it provides more information about the potential risks that may occur.

The agency believes that it is important that this new labeling information be brought to consumers' attention. In order to ensure that the new thrid-trimester pregnancy warning for OTC aspirin and aspirin-containing drug products is prominently displayed, the agency is requiring that the warning be printed on all labeling in boldface type and all capital letters. Based on the format of the new warning, the agency does not consider it appropriate to combine any portion of the warning with the general pregnancy-nursing warning statement. Further, the agency does not want the general pregnancy-nursing warning to appear in different wording in the labeling of OTC aspirin and aspirin-containing drug products. Therefore, the agency is not including in this final rule a provision that the two pregnancy-warning statements can be combined to eliminate duplicative words and phrases.

Further, the agency is not adopting the combined warning suggested by the comment that requested a hearing, which read, "As with any drug, if you are pregnant or nursing a baby, do not take unless directed by a doctor. This is particularly important for aspirin during the last three months of pregnancy since it may cause bleeding problems in mother or child." This combined warning would change the general pregnancy-nursing warning required by § 201.63. As noted above, the agency does not want this warning when used in the labeling for aspirin-containing products to be different than the warning that appears on all other OTC drug products intended for systemic absorption. In addition, "bleeding problems" are no longer included specifically in the warning; thus, the comment's suggested warning would not be appropriate to use. For these reasons, the agency concludes that the comment's request for a hearing is moots.

The effective date of this final rule is August 6, 1990. Although the regulation will become effective on that date, manufacturers of affected drug products will be permitted to defer labeling changes until July 5, 1991. Thereafter, covered OTC drugs initially introduced or initially delivered for introduction into interstate commerce will be required to comply with the new labeling requirement. The agency will consider requests for additional time to comply with the requirement based on a showing of good cause. Such requests should be sent to Office of Compliance, Center for Drug Evaluation and Research, HFD–300, Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857. Any request for additional time must state the reasons that the drug product's compliance with the labeling requirement cannot be achieved, steps that have been taken to achieved compliance, and when compliance is anticipated. Requests for additional time must be specifically granted by the agency; an extension of time will not be considered granted merely upon submission of a request. Manufactures are therefore encouraged to submit requests for extensions of time far enough in advance to allow the agency time to act on them.

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V. Economic Impact

FDA has examined the regulatory impact and regulatory flexibility implications of the final rule in accordance with Executive Order 12291 and the Regulatory Flexibility Act (Pub. L. 96–354). This final regulation imposes direct one-time costs associated with changing product labels to include the third-trimester pregnancy warning statement. FDA estimates those costs to total less than $5 million. Therefore, the agency has determined that the final rule is not a major rule as defined in Executive Order 12291. Further, the agency certifies that this final rule will not have a significant economic impact

on a substantial number of small entities as defined by the Regulatory Flexibility Act.

VI. Environmental Impact

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, subchapter D of chapter I of title 21 of the Code of Federal Regulations is amended in part 201 as follows:

PART 201—LABELING

1. The authority citation for 21 CFR part 201 continues to read as follows:

Authority: Sections 201, 301, 501, 502, 503, 505, 506, 507, 508, 510, 512, 701, 704, 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 358, 360, 360b, 371, 374, 376); secs. 215, 301, 351, 354–360F, 361 of the Public Health Service Act (42 U.S.C. 216, 241, 262, 263b–263n, 264).

2. Section 201.63 is amended by adding new paragraph (e) to read as follows:

§ 201.63 Pregnancy-nursing warning.

* * * * *

(e) The labeling of orally or rectally administered OTC aspirin and aspirin-containing drug products must bear a warning that immediately follows the general warning identified in paragraph (a) of this section. The warning shall be as follows:

"IT IS ESPECIALLY IMPORTANT NOT TO USE" (select "ASPIRIN" or "CARBASPIRIN CALCIUM," as appropriate) "DURING THE LAST 3 MONTHS OF PREGNANCY UNLESS SPECIFICALLY DIRECTED TO DO SO BY A DOCTOR BECAUSE IT MAY CAUSE PROBLEMS IN THE UNBORN CHILD OR COMPLICATIONS DURING DELIVERY."

[sentence in bold face type and all capital letters]

Dated: May 23, 1990.

James S. Benson,

Acting Commissioner of Food and Drugs.

[FR Doc. 90–15481 Filed 7–2–90; 8:45 am]

BILLING CODE 4160–01–M

federal register

Thursday
July 5, 1990

Part IV

Department of Education

Proposed Funding Priorities for the National Institute on Disability and Rehabilitation Research for Fiscal Years 1991–1992; Notice

DEPARTMENT OF EDUCATION

National Institute on Disability and Rehabilitation Research; Proposed Funding Priorities for FYs 1991–1992

AGENCY: Department of Education.

ACTION: Notice of proposed funding priorities for the National Institute on Disability and Rehabilitation Research for fiscal years 1991–1992.

SUMMARY: The Secretary of Education proposes funding priorities for several programs under the National Institute on Disability and Rehabilitation Research (NIDRR) for Fiscal Years 1991–1992. NIDRR intends to propose additional priorities for Fiscal Year 1992 at a later date.

DATES: Interested persons are invited to submit comments or suggestions regarding the proposed priorities on or before August 6, 1990.

ADDRESSES: All written comments and suggestions should be sent to Betty Jo Berland, National Institute on Disability and Rehabilitation Research, Department of Education, 400 Maryland Avenue SW., Switzer Building, Room 3422, Washington, DC 20202–2601.

FOR FURTHER INFORMATION CONTACT: Betty Jo Berland, National Institute on Disability and Rehabilitation Research (telephone: (202) 732–1139). Deaf and hearing-impaired individuals may call (202) 732–1198 for TDD services.

SUPPLEMENTARY INFORMATION: Authority for the research programs of NIDRR is contained in section 204 of the Rehabilitation Act of 1973, as amended. Under these programs, awards are made to public and private nonprofit and for-profit agencies and organizations, including institutions of higher education, Indian tribes, and tribal organizations. NIDRR may make awards for up to 60 months, through grants or cooperative agreements. The purpose of the awards is for planning and conducting research, demonstrations, and related activities that lead to the development of methods, procedures, and devices that will benefit individuals with disabilities, especially those with the most severe disabilities.

NIDRR regulations authorize the Secretary to establish research priorities by reserving funds to support particular research activities (see 34 CFR 351.32). NIDRR invites public comment on the priorities individually and collectively, including suggested modifications to the proposed priorities. Interested respondents also are invited to suggest the types of expertise that would be needed for independent experts to review and evaluate applications under these proposed priorities.

NIDRR will review the comments received on these proposed priorities and will then announce final funding priorities, which will be based on the responses to this notice, available funds, and other Departmental considerations. The publication of these proposed funding priorities does not bind the Department of Education to fund projects under any or all of these priorities except as otherwise provided by statute. Funding of particular projects depends on both the final priorities and the quality of the applications received.

The following proposed priorities represent areas in which NIDRR proposes to support research and related activities through grants or cooperative agreements in four programs: Rehabilitation Research and Training Centers (RRTCs); Rehabilitation Engineering Centers (RECs); Research and Demonstration projects (R&D); and Knowledge Dissemination and Utilization projects (D&U).

Research and Demonstration Projects

Research and Demonstration projects support research and/or demonstrations in single project areas on problems encountered by individuals with disabilities and handicaps in their daily activities. These projects may conduct research on rehabilitation techniques and services, including analysis of medical, industrial, vocational, social, emotional, recreational, economic, and other factors affecting the rehabilitation of individuals with disabilities.

Proposed Priorities for Research and Demonstration Projects

Involving People With Psychiatric Disabilities as Consumer Advocates in Vocational Rehabilitation

Psychosocial rehabilitation, an emerging modality for the rehabilitation of individuals with severe psychiatric disabilities, focuses on assisting people with long-term mental illness to develop their skills at decision-making, self-care, and self-determination while emphasizing normalization, less reliance on professional service providers, and other principles and practices that involve persons with severe psychiatric disability in their own rehabilitation. There is a need to identify proven strategies that involve members of this target population as advocates, planners, administrators, and implementers of service programs and to facilitate their contribution to improving vocational rehabilitation services for all persons with psychiatric disabilities. Partnerships of researchers and consumers are needed to identify effective models and the prerequisite organizational elements, demonstrate operational examples, and document outcomes.

This priority is based, in part, on recommendations from the Rehabilitation Services Administration Interagency Work Group on Psychiatric Rehabilitation, and on reviews of work completed or in progress on consumer advocacy in the broad field of mental health. The principles of psychosocial rehabilitation encourage substantial consumer involvement, and thus require an improved understanding on the part of consumers, advocates, clinicians, and other service providers of methods to most effectively involve consumers in developing and providing services. Further, the Best Practice Study of Vocational Rehabilitation Services to Severely Mentally Ill Persons (Policy Studies Associates, 1989) clearly identified the potential contribution of consumer-driven and operated services and recommended their use by vocational rehabilitation agencies.

An absolute priority is proposed for a project to:

- Review the current state-of-the-art in involving persons who have experienced severe psychiatric disability in key roles in advocacy, planning, information and referral, peer support, training, program administration, service delivery, evaluation, and related aspects of the provision of psychosocial vocational rehabilitation services;
- Demonstrate models to effectively involve individuals with severe psychiatric disabilities in the development of their own rehabilitation service plans and/or in the delivery of psychosocial rehabilitation services; and
- Develop materials, based on research findings, and provide technical assistance to enhance the capacity of a national cross-section of vocational and psychosocial rehabilitation agencies to facilitate the involvement of consumer-advocates in implementing psychosocial rehabilitation programs.

National Job Coach Study

Supported employment has become an important approach to the vocational rehabilitation of individuals with severe disabilities. A key element of the supported employment approach is the use of the job coach to provide employment-related support. There are indications that rehabilitation administrators need a better understanding of the role, function and status of the job coach (also called an

employment training specialist) in transitional and supported employment. A recent study (Rusch, 1988) found that job coaches in Illinois have varied educational backgrounds (34 percent baccalaureate degrees related to disability, 10 percent baccalaureate degrees unrelated to disability, 8 percent associate degrees, 4 percent masters degrees, 34 percent high school diplomas, and 10 percent from unknown backgrounds). The study also found that job coaches are paid relatively low salaries (mean $12,628 per year) and have a high turnover rate (46.5 percent terminated in one year). Although the total number of supported employment training specialists is unknown, serving individuals with severe disabilities in small, integrated settings as required by Federal regulations, has been accomplished largely through the use of these job coaches. The need for research on the employment condition of job coaches was highlighted by the Rehabilitation Services Administration's 1988 Forum on Supported Employment in Williamsburg, and the 1989 Supported Employment Forum in Washington, DC. The President's Committee on Employment of People With Disabilities Supported Employment Forum (May 1988) recommended national action to improve job coaching.

This proposed project will identify key facts about job coaches—pay, working conditions, experience, duties, career opportunities, and methods of coaching—that can be used to develop operational guidelines for recruiting, training, and retaining job coaches and to improve job coaching services for individuals with severe disabilities.

An absolute priority is proposed for a project to:

- Conduct public participation activities such as forums, workshops, hearings, and institutes involving persons with disabilities, job coaches, parents, employers, rehabilitation administrators, educators, and researchers in order to identify issues, best practices, alternative models, and outcomes for improving the use of job coaches;
- Analyze conditions affecting the role, status, and management of job coaches, including such issues as recruitment and hiring, pre-service and in-service training, position descriptions, merit and productivity review criteria, use of co-workers as job coaches, benefits and incentives, career paths and advancement, turnover, coaching resources, technology applications, and mechanisms for professional communication and exchange; and
- Convene a national conference, which has been planned and organized with the substantial involvement of job coaches, consumers, parents, or family members of persons with severe disabilities, administrators, and researchers, to represent project recommendations and findings for consideration at local, State, and national levels.

National Study of Transition of Individuals With Severe Disabilities Leaving School

Individuals with severe disabilities of all types leaving school often need additional services to help them enter and maintain adult roles, including independent living and employment. Many such persons however, may be unable to access these additional services in a timely manner. A recent analysis of data from the State of Maryland concluded that 11 percent of those leaving school with severe disabilities face uncertain futures due to discrepancies between their continuing service needs and the ability of adult service programs to meet their needs. (Ward, M. and Halloran, W., "Transition to Uncertainty: Status of Many School Leavers with Severe Disabilities," *CDEI*, 1989.)

Individuals involved in assisting youth to make the transition from school to adult life often allude to discrepancies between the needs of individuals leaving school and the availability of services. However, there are no definitive data regarding this alleged service gap, and a national study of this issue is needed to determine the extent to which such a gap exists.

Youth with severe disabilities leaving school often require coordinated services from education agencies, vocational rehabilitation agencies, and community-based service providers. Some States and agencies may have more effective systems that others for assigning priority to youth with severe disability in transition, as well as other approaches to eliminate or reduce any gaps in services. A national study of specific policies and practices for coordinating transition services would provide information regarding effective intervention.

The study will include a survey to determine the magnitude of the problem of service gaps, an analysis of existing policies and practices, and case studies of States whose current policies or practices deliver effective transition services for youth with severe disabiliities. The project should consider the use of problem-solving techniques that include youth and adults with disabilities who have experienced both gaps in services and successful transitions.

An absolute priority is proposed for a project to:

- Analyze transition problems of youths with severe disabilities in several States in order to document the magnitude and characteristics of any service gaps that may exist;
- Identify States that have exemplary policies, administrative practices, and funding strategies that facilitate the transition of students with severe disabilities into employment and related adult outcomes;
- Develop a framework for model State transition policies and practices appropriate for the range of problems facing States; and
- Conduct a variety of appropriate information exchange activities to encourage States to develop policies that will facilitate timely access to adult services and thus improve transition outcomes for youth with severe disabilities.

Alcohol and Substance Abuse as Barriers to Job Re-Entry for Persons with Traumatic Brain Injury

There is a serious problem of substance (alcohol and drug) abuse and addiction among persons who have experienced traumatic brain injury (TBI). Individuals who have experienced TBI often have residual functional difficulties in short-term memory, decision-making, social skills, communicating, problem solving, and relating to family members and friends. Consequently, many interventions which have proven effective in assisting people with substance addictions have not helped persons with TBI. Treatment and support interventions, particularly for early problem identification and to assist family members of TBI survivors, are needed in order to help individuals with TBI avoid or overcome addictions and continue their rehabilitation programs for return to work.

Alcohol and other substance addictions of persons with TBI were identified as major problems at the November 1987 NIDRR National Invitational Conference on Traumatic Brain Injury and at the February 1989 University of Wisconsin-Stout's Clearwater Beach Conference on Community-Based Employment for Persons with TBI. A recent article in Alcohol Health & Research World (1989) titled "Alcohol Abuse and Traumatic Brain Injury" identified the need for improved case management, research, and education on this problem. Progress reports from NIDRR's Research and Development projects on supported employment for persons with TBI have identified addictive behavior as a major

barrier to their return to work. The National Head Injury Foundation has recommended national action on this topic, including the effects on family members of substance abuse by persons who have survived TBI.

An absolute priority is proposed for a project to:

- Develop, field test, and evaluate appropriate treatment and support interventions to prevent or ameliorate substance abuse for persons who have experienced traumatic brain injury and their families;
- Prepare program materials for use by rehabilitation counselors, job coaches, teachers, psychologists, employers, family members, and consumers in their efforts to reduce substance abuse among individuals with TBI;
- Develop model referral procedures, guidelines for the use of general alcohol and substance abuse treatment resources by the TBI population, strategies for avoiding second injuries consequent to substance abuse, and measures of program outcomes and effectiveness; and
- Disseminate project findings to rehabilitation and addiction programs, to medical programs in TBI, and to professional and consumer organizations dealing with traumatic brain injury.

Case Management in the Vocational Rehabilitation of Persons With Psychiatric Disability

"Case management" has frequently been identified as essential for providing outcome-oriented, individualized, continuous assistance to persons with psychiatric disability whose complex needs require the services of a gamut of agencies over long periods of time (Robinson and Bergman, 1989; Gowdy and Rapp, 1989; Rapp and Wintersteen, 1989). "Best practices" in vocational rehabilitation for persons with psychiatric disability incorporate case management features such as specialized caseloads, post-employment services, interagency coordination of vocational rehabilitation with other service systems, and extension of the role of the job coach to accommodate the special need of persons with severe psychiatric disability (Policy Studies Associates, 1989). Despite the widespread agreement on the value of case management approaches, administrators have few proven case management models and little guidance on their implementation.

Questions frequently asked by managers of mental health rehabilitation programs include the following: How do case management approaches in mental health and vocational rehabilitation compare? What are the mental health case management functions of a job coach? What are the vocational support functions of a mental health case manager? Can peer, family, and co-worker support activities serve case management functions? How do case management needs change after employment? When and how should case management start, stop, or transfer lead responsibility between mental health and vocational rehabilitation agencies?

There is a need for research to examine case management practices in the vocational rehabilitation of persons with psychiatric disability in order to identify feasible, effective models and specify crucial cost, staffing, skills, and administrative components.

An absolute priority is proposed for a project to:

- Analyze case management practices and models for vocational rehabilitation of persons with psychiatric disability, including analyses of costs, effectiveness, staffing, interagency coordination, and the roles of peers, co-workers, and family members;
- Compare and contrast case management functions and responsibilities in mental health and vocational rehabilitation (MH/VR) service systems from the time of initial vocational assistance to persons with psychiatric disability through periods of their sustained employment to compile longitudinal data that will assist MH/VR agencies to adapt or adopt appropriate program features that foster greater employment stability among their clients; and
- Prepare research monographs, presentations, training materials, and journal articles for dissemination of project findings to MH/VR agencies and other relevant audiences.

Health Care Policy and Rehabilitation

The health care system in the United States is undergoing substantial changes, not the least of which are in the mechanisms for delivering and financing medical care. Many of the new developments in the delivery of health care services are based on models for acute care or communicable diseases services and fail to take into account the long-term medical and rehabilitation needs of persons with the most severe disabilities. At present, disabled populations are either ignored or forced into modes of care that may be inappropriate or unresponsive to their needs.

The purpose of this priority is to generate new knowledge to resolve important health care policy issues that have an impact on the delivery of medical rehabilitation/physical restoration services. Issues that require study in this area include: The costs and efficacy of rehabilitation services and specific rehabilitation modalities; the impact of various innovative payment methods on rehabilitation hospitals and regional service delivery systems, e.g., Model Spinal Cord Injury projects; and the development of new and innovative methods of delivering comprehensive medical rehabilitation services that include identification of financial and administrative characteristics.

An absolute priority is proposed for a project to:

- Identify innovative models of resource consumption, using established and recognized functional outcome measures, to serve as a basis for prospective and other payment systems in rehabilitation medicine services;
- Demonstrate and evaluate the feasibility of using functionally-based models for payment systems, with emphasis on appropriate classification schemes that include such factors as severity, progress during rehabilitation, and outcome compared to admission status;
- Analyze variations in patterns of resource utilization during acute rehabilitation and identify the variables that influence these changes;
- Determine the relationship between changes in functional status and patterns of resource utilization during acute in-patient rehabilitation; and
- Identify and evaluate factors in various payment models that contribute to the quality of care during acute in-patient medical rehabilitation.

Rehabilitation Research and Training Centers

Authority for the Rehabilitation Research and Training Centers programof NIDRR is contained in section 204(b)(1) of the Rehabilitation Act of 1973, as amended. Under the RRTC program, awards are made to institutions of higher education, or to public and private organizations, including Indian tribes and tribal organizations, that are affiliated with institutions of higher education.

RRTCs conduct programmatic, multidisciplinary, and synergistic research, training, and information dissemination in designated areas of high priority. NIDRR's regulations authorize the Secretary to establish research priorities by reserving funds to support particular research activities

(see 34 CFR 352.32). A program of RRTCs has been established to conduct coordinated and advanced programs of rehabilitation research and to provide training to rehabilitation personnel engaged in research or the provision of services. Each Center conducts a synergistic program of research, evaluation, and training activities focused on a particular rehabilitation problem area. Each Center is encouraged to develop practical applications for all of its research findings. Centers generally disseminate and encourage the utilization of new rehabilitation knowledge through such means as writing and publishing undergraduate and graduate texts and curricula and publishing findings in professional journals. All materials that the Centers develop for dissemination training must be accessible to individuals with a range of handicapping conditions. RRTCs also conduct programs of in-service training for rehabilitation practitioners, education at the pre-doctoral and post-doctoral levels, and continuing education. Each RRTC must conduct an interdisciplinary program of training in rehabilitation research, including training in research methodology and applied research experience, that will contribute to the number of qualified researchers working in the area of rehabilitation research. Centers must also conduct state-of-the-art studies in relevant aspects of their priority areas. Each RRTC must also provide training to individuals with disabilities and their families in managing and coping with disabilities.

NIDRR will conduct, not later than three years after the establishment of any RRTC, one or more reviews of the activities and achievements of the Center. Continued funding depends at all times on satisfactory performance and accomplishment, in accordance with the provisions of 34 CFR 75.253(a).

Proposed Priorities for Rehabilitation Research and Training Centers

Rehabilitation of Blind and Visually-Impaired Individuals

The National Health Interview Survey (LaPlante, 1988) indicates that there are approximately 600,000 men and women between the ages of 18 and 69 whose work activities are limited due to visual disabilities, including blindness, glaucoma, cataracts, and other visual impairments. Of this group, about 405,000 individuals are unemployed. A significant number of the remaining 195,000 individuals are underemployed.

A program of coordinated, interdisciplinary research and training is needed to develop and disseminate rehabilitation approaches designed to improve services for this population. A Center in this area should develop models for the effective delivery of rehabilitation services in the areas of career preparation, placement, and career advancement. The Center will assist rehabilitation service delivery systems to adapt to the changing needs of blind and visually-impaired individuals for career preparation and enhancement, either by restructuring service programs, retraining staff, or implementing new service techniques.

An immediate objective for the Center is to assist service delivery agencies to make better use of the information that is available, including research data, models of career preparation, placement, retraining, and advancement, and standards and guidelines that have been developed to guide rehabilitation efforts for this population. Over the longer term, it is important to develop better rehabilitation service delivery models that are based on field and laboratory research, and tested by blind and visually-impaired persons in regular use. One prerequisite to improving rehabilitation services in a comprehensive way is to assist those who design, manage, and provide training, placement, and employment services to become aware of the potential for creating more accessible environments for this population through the use of technology, adaptive viewing devices, and related accommodations.

A critical element of any Center to be funded under this priority will be the involvement of individuals who are blind and those with low vision and their advocates in the planning, conduct, and review of Center activities. All instruments, program descriptions, training materials and courses, databases, and technical assistance materials produced by the Center must be developed in formats that are accessible to individuals with various types of visual impairments. The Center will develop a national database in this field of activity and serve as a central repository of information on the rehabilitation of persons with blindness and visual impairments.

An absolute priority is proposed for an RRTC to:

- Identify and analyze existing career preparation and placement service programs and systems for persons who are blind or visually impaired, and, when needed, develop new and innovative services and service delivery systems for enhancing the rehabilitation of this population;
- Develop research-based models for and conduct training to enhance the capabilities of blind and visually-impaired persons, including those from racial and ethnic minorities and women, to develop their rehabilitation plans, select career goals, and match personal abilities and expectations to changing vocational opportunities in the labor market;
- Develop strategies and techniques to enhance coordination and cooperation between secondary and postsecondary educational institutions and vocational rehabilitation agencies to assist both visually-impaired persons and their employers in the process of transition from school to work;
- Analyze methods to increase job retention among this population, including strategies such as job-site modification, job restructuring, cooperative efforts with organized labor, and retraining;
- Develop and test technical assistance and training for rehabilitation agencies, business and employer associations, and consumer groups to promote the employment, retention, and advancement of blind and visually-impaired workers;
- Analyze the cost-effectiveness and quality of life factors in different rehabilitation delivery systems, including Comprehensive Rehabilitation Centers, for individuals who are blind or visually impaired, including individuals in different age groups, from racial and ethnic minorities, women, and both rural and urban residents;
- Develop and disseminate model curricula for training vendors in the Business Enterprise Program (BEP), model program operation manuals for BEP supervisors, and model BEP marketing programs for people who are blind, for building supervisors, and for rehabilitation service providers, with an emphasis on expanded representation of women and minorities;
- Identify the appropriate use of, and instruction in, Braille, optical devices and technologies that could contribute to the higher literacy level necessary for various types of employment.
- Develop and maintain a national research database on the career preparation, placement, and advancement of blind and visually-impaired persons, and serve as a Center for current information concerning this population and the professional personnel, programs, and related resources available to assist in rehabilitation efforts on their behalf;
- Provide advanced training for predoctoral, postdoctoral, and professional practitioners in the

rehabilitation of blind and visually-impaired persons, with an emphasis on recruiting blind and visually-impaired persons for that training;

• Provide advanced training in research in fields pertinent to the rehabilitation of blind and visually-impaired individuals, with emphasis on recruiting blind and visually-impaired individuals and individuals from other underrepresented populations for that training;

• Conduct at least one national study of the state-of-the-art to identify current knowledge and recommend future research; and

• Organize and conduct research and training conferences and short-term institutes in cooperation with professional and consumer organizations in order to disseminate Center findings and products on an annual basis.

Rehabilitation of Deaf and Hearing-Impaired Individuals

Individuals with hearing impairment comprise the single largest chronic physical disability group in the United States, numbering an estimated 21 million Americans (National Center for Health Statistics, "Data Reports", Series 10, No. 160, 1987.) The unpublished data from the combined 1979–1980 Health Interviews Surveys indicate that over 26 percent of those whose only disability is hearing impairment report themselves to have activity limitations, while those who also have other chronic conditions or impairments are twice as likely to report functional limitations. (Mathematica Policy Research, Digest of Data on Persons with Disabilities, 1984.) This segment of the population presents major challenges to public rehabilitation efforts on their behalf.

An RRTC is proposed to address the rehabilitation needs of this population, particularly those individuals who are profoundly deaf or have significant hearing impairments. A program of coordinated, interdisciplinary research and training is needed to develop and disseminate rehabilitation approaches designed to improve services for this population. In particular, an RRTC is needed to develop models for effective delivery of rehabilitation services in the areas of career preparation, placement, and career advancement. The Center will assist rehabilitation service delivery systems to adapt to the changing career preparation and enhancement needs of deaf and hard-of-hearing persons, whether by restructuring service programs, retraining staff, or implementing new service techniques.

An immediate objective is to make better use of the information that is available, including research data, models of career preparation, placement, retraining, and advancement, and standards and guidelines that have been developed to improve rehabilitation efforts for this population. Over the longer term, it is important to develop better rehabilitation service delivery models that are based on field and laboratory research, and tested by deaf and hard-of-hearing persons in regular use, including those from racial and ethnic minorities. One prerequisite to improving rehabilitation services in a comprehensive way is to assist those who design, manage, and provide training, placement, and employment services to become aware of the potential for creating more accessible communication environments for this population through the use of interpreters, adaptive listening devices, and related accommodations.

A critical element of any Center to be funded under this priority will be the involvement of individuals who are deaf and those who are hard-of-hearing in the planning, conduct, and review of Center activities. All instruments, descriptions, training materials and courses, databases, and technical assistance developed by the Center must be provided in formats that are accessible to individuals with various types of hearing impairments. The Center will develop a national database in this field of activity and serve as a central repository of information on the rehabilitation of persons with severe-to-profound hearing impairments. The Center also is expected to cooperate with the RRTC on Low-Functioning Deaf Individuals, funded in 1990, to share information and findings, and to consider coordinated research studies and training activities.

An absolute priority is proposed for an RRTC to:

• Identify and analyze existing career preparation and placement service programs and systems for persons who are deaf or hard-of-hearing, and, when needed, develop new and innovative services approaches and systems to enhance the rehabilitation of this population;

• Conduct research and training to enhance the capabilities of deaf and hard-of-hearing persons, including those from racial and ethnic minorities and women, to develop rehabilitation plans, select career goals, and match personal abilities and expectations to changing vocational opportunities in the labor market;

• Develop strategies and techniques to enhance coordination and cooperation between secondary and postsecondary educational institutions and vocational rehabilitation agencies to improve the transition from school to work for deaf and hearing-impaired persons;

• Develop an employment profile of the deaf and hard-of-hearing populations and identify the skills necessary for job entry, advancement, retention, and satisfaction for this population in the year 2000;

• Develop models of technical assistance and training for rehabilitation agencies, business and employer associations, and consumer groups in methods to stimulate the hiring, retention, and advancement of deaf and hard-of-hearing workers;

• Investigate the special problems and needs that professionals, support personnel, and families encounter in their efforts to facilitate the independence, and personal, social, cultural, and career adjustment of deaf and hard-of-hearing persons in both urban and rural settings, and develop effective models for the provision of support services;

• Develop and maintain a national research database on the career preparation, placement, and advancement of deaf and hard-of-hearing persons, and serve as a Center of current information concerning this population and the professional personnel, programs, and related resources available to assist in rehabilitation efforts on their behalf;

• Provide advanced training for predoctoral, postdoctoral, and professional practitioners in the rehabilitation of deaf and hard-of-hearing persons, with an emphasis on recruiting persons who are hearing-impaired for the training;

• Provide advanced training in research in fields pertinent to the rehabilitation of deaf and hard-of-hearing persons, with emphasis on recruiting individuals who are hearing-impaired and individuals from other underrepresented populations for this training;

• Conduct at least one national study of the state-of-the-art to identify current knowledge and recommend future research; and

• Organize and conduct research and training conferences and short-term institutes in cooperation with professional and consumer organizations in order to disseminate Center findings and products on an annual basis.

Cardiovascular Rehabilitation

There are 1.4 million new myocardial infarctions each year in the United States, with 700,000 individuals

surviving the acute incident. In addition, many newly identified coronary artery disease patients are undergoing angioplasty and by-pass surgery and are in need of comprehensive and effective rehabilitation to stay on the job and to maintain independence in daily life. Given the extent of the problem of cardiovascular disease and infarctions, and their serious disabling consequences, the rehabilitation field would benefit from a Center that will develop and implement well-designed studies in clinical outcomes, patient evaluation, and rehabilitation interventions, as well as education and training programs, in order to promote comprehensive rehabilitation for the population affected by these conditions.

The conceptual basis for this proposed priority was the work of the American College of Cardiology Bethesda Conference No. 20 (October, 1988) on the rehabilitation and employability of the patient with ischemic heart disease.

An absolute priority is proposed for a Center to:

- Develop improved methods to assess functional outcomes and evaluate disease paramenters in individuals with coronary heart disease, including individuals who have had angioplasty and bypass surgery;
- Identify and evaluate intervention models to reduce impairment and disability in individuals with coronary heart disease, including those whose rehabilitation and medical management are complicated by peripheral vascular or hypertensive disease;
- Document the natural course of cardiovascular and coronary heart disease in individuals with physical disabilities, including neurologic and musculoskeletal disorders that impair ambulation and physical function;
- Develop and evaluate rehabilitation methods and techniques to assist older persons with coronary heart disease or cardiovascular impairment to remain employed and functionally independent;
- Develop protocols for collaborative research on the evaluation of cardiovascular disability and the development of interventions to promote optimal functional recovery and rehabilitation;
- Develop a professional education and training program in cardiovascular rehabilitation and a public education program in order to enhance rehabilitation understanding and outcomes;
- Provide advanced training in research in fields related to the rehabilitation of individuals with cardiovascular impairment, with an emphasis on recruiting individuals from underrepresented populations, including individuals with disabilities, minorities, and women, for that training; and
- Serve as a national resource and information center for the rehabilitation field in matters relating to cardiovascular rehabilitation and related research.

Rehabilitation Engineering Centers

Authority for the Rehabilitation Engineering Center (REC) program of NIDRR is contained in section 204(b)(2) of the Rehabilitation Act of 1973, as amended. Under this program, awards are made to public and private organizations, including institutions of higher education, Indian tribes, and tribal organizations to conduct coordinated programs of advanced research of an engineering or technological nature. RECs also work to develop systems for the exchange of technical and engineering information and to improve the distribution of assistive devices and equipment to individuals with disabilities. Each REC must be located in a clinical setting and is encouraged to collaborate with institutions of higher education in the conduct of a program of research, scientific evaluation, and training that advances the state-of-the-art in technology or its application. Each Center is expected to contribute substantially to the solution of rehabilitation problems through developing practical applications for their research and through scientific evaluation to validate the findings of their research and that of other Centers. RECs generally conduct both academic and in-service training to disseminate and encourage the use of new rehabilitation engineering knowledge, and to build capacity for engineering research in the rehabilitation field. Each REC must ensure that all training materials developed by the Center are presented in several formats that will be accessible to individuals with various types of sensory and mobility impairments.

NIDRR will conduct, not later than three years after the establishment of any REC, one or more reviews of the activities and achievements of the Center. Continued funding depends at all times on satisfactory performance and accomplishment in accordance with the provisions of 34 CFR 75.253(a).

Priority for Rehabilitation Engineering Center

Technology for Older Persons With Disabilities

The prevalence of medical, neurological and orthopedic impairments increases with the age of the population. Common conditions in the older population that frequently result in disability include arthritis, stroke, pulmonary disease, hip fractures, Alzheimer's disease, and deficits in vision and hearing. (Breuer, 1982; Haber, 1986). It is estimated that half of all Americans over seventy years of age have one or more disabilities. (Williams 1986). The frequency of multiple disabilities is also much higher in the older population (Breuer, 1982; Williams, 1986).

Technology has been used in rehabilitation to help reduce the adverse effects of impairment and disability. Technology, however, has not been widely used to solve problems in geriatric rehabilitation.

A new REC to be funded in this area will emphasize technological solutions to the special needs of older persons that are a consequence of the aging process as it produces functional limitations similar to those experienced by persons of all ages with disabilities. At the same time, the Center must be concerned with applications of technology to mitigate the effects of the aging process on persons who have disabilities.

The older person often has problems unique to an older population that must be considered in the application of technological solutions. First, many devices or techniques aimed at ameliorating specific disabilities are designed to augment or take advantage of compensatory abilities. However, multiple and gradual changes related to aging may leave older persons without one or more areas of strength with which to compensate for other functional losses. For example, an older person requiring a wheelchair, because of gradual loss of muscle mass, may not have, or may not be able to develop, the requisite arm strength to use the grab bars.

Second, many older persons who experience problems with daily living in their houses or apartments do not consider themselves to be disabled. Because they don't view their problems as disabilities, they neither perceive nor accept the need for adaptive technologies, and are less likely to seek technology-related assistance.

Finally, the development of technological solutions to functional limitations of older persons is often focused on the disability as a characteristic of the individual rather than an artifact of the person-environment interaction.

Efforts to develop and disseminate technological aids to older persons with

functional limitations must be conducted in the context of using different dissemination media and service systems to reach older persons, and with a sensitivity to the need for accurate prescriptions, appropriate training in the use of the technology that is prescribed, and followup to assure that desired outcomes are achieved.

One study of 500 older persons who owned technological aids (Page, Galer, Fitzgerald, and Feeny, 1980) found that about 50 percent of them did not use their aids because the devices had been inaccurately prescribed, did not work, were unsafe or broken, or because the individual regarded the disability as a minor inconvenience that he/she would rather accept than try to overcome.

Other studies have emphasized the need for more sensitive and more selective criteria for assessing the need for assistive technology; a need for assessments for aids to take place in the usual living environment or in a facsimile situation; a need to understand that the selection of the appropriate aid is critical to the consumer's expectations; that adequate training in the use of an aid is vital; and that followup visits are necessary to ensure that the aids are used and function well in the daily milieu. NIDRR has also identified a need for better-designed assistive technology, more information about assistive technology, and improved methods for the maintenance of assistive devices for older persons.

According to Childress (1986), the most effective deployment of technology is to prevent the need for assistive devices in the first place. He states that using simple technical aids to prevent serious injuries and the resulting disabilities can be a major factor in maintaining functional independence.

The appropriate infrastructure for delivery of assistive technology to this population has not yet been determined, and the delivery system is one of the most important barriers to optimal use of assistive technology by older persons with disabilities. Users of all ages and experts have expressed difficulties in acquiring new technologies. Evaluation research has identified the communication gap between reimbursement decision-makers unfamiliar with innovative rehabilitation technologies and product designers and developers unfamiliar with the process of how users actually acquire these technologies. (Englehardt and Leifer, 1983).

Research, development, and dissemination of information by the Center must address the needs of older individuals who are typically underserved, including those from ethnic, racial, and linguistic minorities, rural areas, or congregate care settings. Older persons, including older persons with disabilities, must be involved in the planning, conduct, and review of Center activities. Any Center to be funded under this priority must coordinate and share information with NIDRR-funded RRTCs on Rehabilitation and Aging, and with programs funded under the Technology-Related Assistance for Individuals with Disabilities Act of 1988.

An absolute priority is proposed for a Center to:

- Examine the relationship between the older individual and the environment to determine strategies to adapt the environment to improve the quality of life for older persons with disabilities;
- Develop and evaluate assistive technologies that are less sophisticated, more easily repairable, easier to use, less expensive, and more appropriate for and more acceptable to older persons;
- Explore various strategies to enhance the use of available assistive devices by using the knowledge, personnel, devices, and information sources available through the rehabilitation field;
- Explore various strategies for strengthening public-private sector partnerships in marketing to, and in the purchase and use of assistive devices by, older individuals with disabilities.
- Develop and disseminate new knowledge about the prevention of disabilities through the appropriate use of assistive devices;
- Develop and deliver training and technical assistance to service providers in both rehabilitation and general services to older persons, and to consumers, on sources and use of assistive devices and other technological applications to problems of functional loss caused or exacerbated by aging; and
- Provide, either directly or through collaboration with other institutions, advanced training in research in rehabilitation technology to meet the needs of older persons, with special emphasis on recruiting individuals from underrepresented populations such as individuals with disabilities, minorities, and women, for that training.

Knowledge Dissemination and Utilization Program (D&U)

Knowledge Dissemination and Utilization (D&U) projects ensure that rehabilitation knowledge generated from projects and centers funded by NIDRR and others is utilized fully to improve the lives of individuals with disabilities. The authority for this program is contained in section 202 and 204(a) and (b)(5) of the Rehabilitation Act of 1973, as amended.

Proposed Priority for Knowledge Dissemination and Utilization Program

Regional Information Exchange

As part of its effort to disseminate new knowledge on improved rehabilitation practices, NIDRR seeks to promote the widespread use of validated exemplary practices in rehabilitation in order to improve the service delivery system for individuals with disabilities. Many of these exemplary programs were developed at the "grassroots" in communities; others emerged as a result of research sponsored by NIDRR or other agencies. NIDRR proposes to address this objective by establishing one or more Regional Information Exchanges.

A Regional Information Exchange (RIE) is intended to facilitate the adoption of exemplary program models that were developed within the locality or region of the adopting agency.

The RIEs must identify and validate exemplary programs within the established priority areas, "market" the model programs to potential adopting agencies, and provide technical assistance in the adoption or adaptation of the model.

Priority areas for RIE diffusion efforts during the period of this priority, include: emergent issues in supported employment programs, such as the involvement of co-workers, obtaining long-term funding support for individuals, and appropriate family involvement; interagency collaboration and coordination in programs for transition from school to work; parent-professional collaboration in the integration of individuals with disabilities in education, community living, and employment; strategies for assisted housing for individuals with long-term mental illness; application of rehabilitation principles in generic services to elderly persons with disabilities in order to promote and maintain independence; and model programs for the delivery of rehabilitation engineering services in vocational rehabilitation agencies.

The RIE programs are restricted to the diffusion of carefully validated model programs in one or more of the designated priority areas, and must provide necessary technical assistance to facilitate the successful adoption or adaptation of the exemplary programs. Each RIE will work within its designated region, as defined in the grant application and cooperative agreement, and must demonstrate the

appropriateness of the selected region for diffusion of exemplary programs in the specified priority areas.

An absolute priority is proposed for a project to:

- Develop a process for identifying exemplary programs, including criteria, a methodology for data collection, and evaluation instruments that include measurements related to the identified criteria;
- Solicit nominations of exemplary programs in the priority area(s) from program operators, consumer organizations, and other relevant parties in the region, giving consideration to the inclusion of demonstration projects funded by NIDRR, the Rehabilitation Services Administration, the Office of Special Education Programs, and other Federal agencies;
- Develop and implement a procedure to validate exemplary programs in the region in the specified priority areas, involving individuals with disabilities and technical experts in the validation process, and document the methodology and findings of the validation process;
- Develop and implement strategies to make the wide audience of rehabilitation service providers and special educators aware of the exemplary programs and stimulate their interest in adopting or adapting similar models, with the assistance of the RIE;
- Develop and maintain a cadre of expert consultants in the RIE's priority areas and in the general area of knowledge transfer who can facilitate the adoption or adaptation of exemplary programs;
- Facilitate the exchange of technical assistance between the exemplary program and the requesting adopter program through onsite demonstrations, training materials, and direct consultation; and
- Maintain appropriate data on the activities of the RIE to support an evaluation of its effectiveness.

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Dated: May 15, 1990.

Lauro F. Cavazos,

Secretary of Education.

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