CHEMICALS PROPOSED FOR LISTING VIA THE "FORMALLY REQUIRED TO BE LABELED OR IDENTIFIED" MECHANISM

Reproductive and Cancer Hazard Assessment Section
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

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The chemicals listed in the table below have been identified or labeled to communicate a risk of cancer or reproductive harm, in accordance with formal requirements of the U.S. Food and Drug Administration. They appear to meet the requirements for listing outlined in Title 22, California Code of Regulations, Section 12902 for the listing of a chemical which a state or federal agency has formally required to be labeled or identified as causing cancer or reproductive harm.

According to Title 22 CCR Section 12902,

- "'labeled' means that a warning message about the carcinogenicity or reproductive toxicity of a chemical is printed, stamped, written, or in any other manner placed upon the container in which the chemical is present or its outer or inner packaging including any material inserted with, attached to, or otherwise accompanying such a chemical;"
- "'identified' means that a required message about the carcinogenicity or reproductive toxicity of the chemical is to be disclosed in any manner to a person or legal entity other than the person or legal entity who is required to make such disclosure."

Chemical	CAS No.	Toxicological Endpoint	Reference
Spironolactone	52-01-7	cancer	FDA (1990)
Stanozolol	10418-03-8	cancer	FDA (1992)
Clarithromycin	81103-11-9	developmental toxicity	FDA (1995)
Dihydroergotamine mesylate	6190-39-2	developmental toxicity	FDA (1994)
Hydroxyurea	127-07-1	developmental toxicity	FDA (1971)
Oxymetholone	434-07-1	developmental toxicity	FDA (1993)

Language taken directly from the FDA-approved product labels which meets the requirements outlined in Title 22 CCR Section 12902 is quoted below for each of these substances.

Spironolactone (under WARNINGS, boxed section)
"Spironolactone, an ingredient of Aldactazide, has been shown to be a tumorigen in chronic toxicity studies in rats (see WARNINGS)." Aldactazide should be used only in those conditions described under INDICATIONS AND USAGE. Unnecessary use of this drug should be avoided."

Stanozolol (under WARNINGS, boxed section)
"Liver cell tumors are also reported. Most often these tumors are benign and androgen-dependent, but fatal malignant tumors have been reported. Withdrawal of drug often results in regression or cessation of progression of the tumor. However, hepatic tumors associated with androgens or anabolic steroids are much more vascular than other hepatic tumors and may be silent until life-threatening intra-abdominal hemorrhage develops."

Clarithromycin (under WARNINGS)
"Clarithromycin should not be used in pregnant women except in clinical circumstances where no alternative therapy is appropriate. If pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus. Clarithromycin has demonstrated adverse effects on pregnancy outcome and/or embryo-fetal development in monkeys, rats, mice, and rabbits at doses that produced plasma levels 2 to 17 times the serum levels achieved in humans treated at the maximum recommended human doses."

Dihydroergotamine Mesylate (under CONTRAINDICATIONS and PRECAUTIONS)
Under CONTRAINDICATIONS: "Dihydroergotamine possesses oxytocic properties and, therefore, should not be administered during pregnancy."

Under PRECAUTIONS: Pregnancy Category X.

Hydroxyurea (under WARNINGS)
USAGE IN PREGNANCY
"Drugs which affect DNA synthesis, such as hydroxyurea, may be potential mutagenic agents. The physician should carefully consider this possibility before administering this drug to male or female patients who may contemplate conception."

"Hydrea is a known teratogenic agent in animals. Therefore, hydroxyurea should not be used in women who are or may become pregnant unless in the judgment of the physician the potential benefits outweigh the possible hazards."

Oxymetholone (under CONTRAINDICATIONS)
"Oxymetholone can cause fetal harm when administered to pregnant women. It is contraindicated in women who are or may become pregnant. If the patient becomes pregnant while taking the drug, she should be apprised of the potential hazard to the fetus."

References

Food and Drug Administration (FDA, 1990). Final printed labeling for the drug Aldactazide (spironolactone with hydrochlorothiazide). FDA approved March 1990.

Food and Drug Administration (FDA, 1992). Final printed labeling for the drug stanozolol. FDA approved February 1992.

Food and Drug Administration (FDA, 1995). Final printed labeling for the drug clarithromycin. FDA approved February 1995.

Food and Drug Administration (FDA, 1994). Final printed labeling for the drug dihydroergotamine mesylate. FDA approved May 1994.

Food and Drug Administration (FDA, 1971). Final printed labeling for the drug hydroxyurea. FDA approved November 1971.

Food and Drug Administration (FDA, 1993). Final printed labeling for the drug oxymetholone. FDA approved July 1993.