Esposizione agli ftalati nell'infanzia

G. Latini, Divisione di Neonatologia, Brindisi, IFC-CNR, sezione di Lecce

Background

PHTHALATES ARE A FAMILY OF INDUSTRIAL COMPOUNDS WITH A COMMON CHEMICAL STRUCTURE, DIALKYL OR ALKYL/ARYL ESTERS OF 1,2-BENZENEDICARBOXYLIC ACID.

Background

SINCE ABOUT THE 1930S PHTHALATES HAVE BEEN USED FOR A VARIETY OF PURPOSES, INCLUDING PERSONAL-CARE PRODUCTS (E.G., PERFUMES, LOTIONS, COSMETICS), PAINTS, INDUSTRIAL PLASTICS, ..

Background

.. AND CERTAIN MEDICAL DEVICES AND PHARMACEUTICALS

Background

PHYSICAL PROPERTIES AND THEREFORE THEIR FIELD OF APPLICATION DEPEND ON THE LENGTH AND BRANCHING OF THE DIALKYL OR ALKYL/ARYL SIDE CHAINS (THE ALCOHOL PORTION OF THE ESTER).

Background

SOME PHTHALATES ARE COMMONLY ADDED TO THESE COMMERCIAL PRODUCTS TO HOLD COLOR OR FRAGRANCE, TO PROVIDE A FILM OR GLOSS, OR, ..

Background

..IN
THE CASE OF SOME PHARMACEUTICALS, TO PROVIDE
TIMED RELEASING.

Background

HOWEVER, PHTHALATES ARE PRIMARILY USED AS PLASTICIZERS TO IMPART FLEXIBILITY TO AN OTHERWISE RIGID POLYVINYLCHLORIDE (PVC)

Background

TO MAKE THE PLASTIC FLEXIBLE AND APPROPRIATE FOR DIFFERENT USES.

DEHP

DI-[2ETHYLHEXYL]-PHTHALATE [DEHP] IS THE MOST COMMONLY USED PLASTICIZER.

Background

- **THESE PLASTICIZERS HAVE BEEN SHOWN TO ELUTE AT A CONSTANT RATE FROM PLASTIC PRODUCTS TO THE ENVIRONMENT.**

Background

CONSEQUENTLY THEY ARE WIDELY DISTRIBUTED IN THE ECOSYSTEM AND HAVE BEEN DESCRIBED AS BEING AMONG THE MOST ABUNDANT MAN-MADE ENVIRONMENTAL POLLUTANTS.

Background

GLOBALLY, MORE THAN 18 BILLION POUNDS OF PHTHALATES ARE USED EACH YEAR AND WELL ABOVE TWO MILLION TONS OF DEHP ALONE ARE PRODUCED ANNUALLY WORLDWIDE

Background

OTHER IMPORTANT PHTHALATES PRODUCTION- AND APPLICATION-WISE ARE:

Background

DIETHYLPHTHALATE (DEP), DIBUTYL PHTHALATE (DBP), DI-ISO- AND DI-N-BUTYLPHTHALATE (DIBUP, DNBUP), BUTYL-BENZYLPHTHALATE (BBZP), DI-ISONONYLPHPTHALATE (DINP) OR DI-N-OCTYLPHTHALATE (DNOP)

Phthalate exposure

HUMANS ARE EXPOSED TO THESE COMPOUNDS THROUGH INGESTION, INHALATION, AND DERMAL EXPOSURE FOR THEIR WHOLE LIFETIME...

Phthalate exposure

...SINCE INTRAUTERINE LIFE!

Latini G, De Felice C, Presta G, et al. Exposure to Di-(2-Ethylhexyl)- Phthalate in humans during pregnancy: a preliminary report. Biol Neonate 2003;83:22-24.

Phthalate exposure

DERMAL AND INHALATIVE EXPOSURES ARE CONSIDERED TO BE THE MAJOR ROUTE OF EXPOSURE TO DEP THAT IS FOUND IN HYGIENE PRODUCTS SUCH AS SOAP, SHAMPOO, AND CONDITIONERS.

Phthalate exposure

IN CONTRAST, FOR PHTHALATES THAT ARE USED MAINLY AS PLASTICIZERS, SUCH AS DEHP, ORAL EXPOSURES PREDOMINATE

Phthalate exposure

FOR CERTAIN SUBSETS OF THE GENERAL POPULATION NON-DIETARY INGESTION (MEDICAL AND OCCUPATIONAL) OR MEDICAL EXPOSURE IS IMPORTANT.

Phthalate exposure

EXPOSURE OF THE GENERAL HUMAN POPULATION TO DEHP HAS BEEN STUDIED MORE IN DEPTH THAN OTHER PHTHALATES.

Phthalate exposure

ESTIMATED TO BE IN THE RANGE OF 3-30 µg/KG/DAY (EXCLUDING OCCUPATIONAL EXPOSURE, MEDICAL EXPOSURES, AND NONDIETARY INGESTIONS IN CHILDREN), THE MAJOR SOURCE BEING FROM RESIDUES IN FOOD

Phthalate exposure

THESE ESTIMATES EXCEED CHRONIC EXPOSURE LEVELS BELIEVED TO BE TOLERABLE FOR THE GENERAL POPULATION.

Phthalate exposure

PREVENTIVE LIMIT VALUES, SUCH AS REFERENCE DOSE OF THE US. EPA AND TDI OF THE EU ARE 20 µG/KG/DAY AND 37 µG/KG/DAY, RESPECTIVELY

Phthalate exposure

GENERAL POPULATION CAN BE EXPOSED TO DEHP TO A MUCH HIGHER EXTENT THAN PREVIOUSLY BELIEVED AND..

Koch HM, Drexler H, Angerer J. Internal exposure of nursery-school children and their parents and teachers to di(2-ethylhexyl)phthalate (DEHP). Int J Hyg Environ Health. 2004;207:15-22.

Phthalate exposure

..AN EXPOSURE OF CHILDREN, TWICE AS HIGH AS THE EXPOSURE OF ADULTS WITH RESPECT TO THEIR BODY WEIGHT HAS BEEN OBSERVED

Koch HM, Drexler H, Angerer J. Internal exposure of nursery-school children and their parents and teachers to di(2-ethylhexyl)phthalate (DEHP). Int J Hyg Environ Health. 2004;207:15-22.

DEHP exposure risk

CHILDREN AND PARTICULARLY INFANTS HAVE TO BE CONSIDERED A POPULATION AT INCREASED RISK,..

DEHP EXPOSURE RISK

..AS THEY ARE EXPOSED SINCE EARLY IN LIFE TO SEVERAL DIFFERENT SOURCES, INCLUDING..

DEHP EXPOSURE RISK

BREAST MILK, INFANT FORMULA, BABY FOOD, INDOOR AIR, AND BY DERMAL AND ORAL EXPOSURE VIA INDOOR DUST CONTAINING DEHP.

Center for Devices and Radiological Health U.S. FDA (September 2001)

SAFETY ASSESSMENT OF DEHP RELEASED FROM PVC MEDICAL DEVICES

Center for Devices and Radiological Health U.S. FDA

1) 1) CHILDREN RECEIVE A
2) GREATER DOSE OF DEHP, ON A
3) MG/KG BASIS, THAN ADULTS
4) DO

Center for Devices and Radiological Health U.S. FDA

2) PHARMACOKINETIC DIFFERENCES BETWEEN CHILDREN AND ADULTS MAY RESULT IN GREATER ABSORPTION OF DEHP,

Center for Devices and Radiological Health U.S. FDA

2)... GREATER CONVERSION OF DEHP TO MEHP AND REDUCED EXCRETION OF MEHP IN CHILDREN COMPARED TO ADULTS

Center for Devices and Radiological Health U.S. FDA

3) CHILDREN MAY BE MORE PHARMACODYNAMICALLY SENSITIVE TO THE ADVERSE EFFECTS OF DEHP THAN ADULTS ARE.

Phthalate exposure

IN ADDITION, THE TRANSGRESSIONS OF TDI FOR DEHP ARE ACCOMPANIED BY CONSIDERABLE UBIQUITOUS EXPOSURES TO DNBP AND BBZP, TWO PHTHALATES UNDER SCRUTINY FOR SIMILAR TOXICOLOGICAL MECHANISMS

Phthalate exposure

EXPOSURES TO OTHER PHTHALATES, INCLUDING DINP AND DIISODECYLPHTHALATE (DIDP), ARE USUALLY ASSUMED TO BE LOWER PRIMARILY BECAUSE PRODUCTION VOLUMES ARE LOWER

Phthalate exposure

HOWEVER, INCREASING EXPOSURES TO THESE PHTHALATES HAVE TO BE ASSUMED FOR THE FUTURE, SINCE THEY ARE USED AS REPLACEMENTS FOR DEHP AND PRODUCTION NUMBERS RISE

PHTHALATES TOXICITY

PHTHALATES ARE ANIMAL CARCINOGENS AND CAN CAUSE FETAL DEATH, MALFORMATIONS, TESTICULAR INJURY, LIVER INJURY, ANTI-ANDROGENIC ACTIVITY, TERATOGENICITY,..

PHTHALATES TOXICITY

..PEROXISOME PROLIFERATION AND ESPECIALLY REPRODUCTIVE TOXICITY IN LABORATORY ANIMALS

PHTHALATES TOXICITY

TOXICITY PROFILES AND POTENCY VARY BY SPECIFIC PHTHALATE. THE EXTENT OF THESE TOXICITIES AND..

PHTHALATES TOXICITY

..THEIR
APPLICABILITY TO HUMANS
REMAINS
INCOMPLETELY CHARACTERIZED
AND CONTROVERSIAL

PHTHALATES TOXICITY

A GREAT DEAL OF CONCERN HAS BEEN RAISED ABOUT THE HEPATO-CARCINOGENIC EFFECT AND THE DEVELOPMENTAL AND REPRODUCTIVE ONE.

PHTHALATES TOXICITY

WITH REGARD TO THE FORMER, IT IS WELL KNOWN THAT SOME PHTHALATES ARE RODENT CARCINOGENS, BUT THE RELEVANCE OF CARCINOGENICITY IN HUMANS IS UNSETTLED

PHTHALATES TOXICITY

RECENTLY, AN INCREASED HEPATOBLASTOMA (HB) RISK. AMONG CHILDREN WITH VERY LOW BIRTH WEIGHT HAS BEEN REPORTED.

Reynolds P, Urayama KY, Von Behren J, Feusner J. Birth characteristics and hepatoblastoma risk in young children. Cancer 2004;100:1070-1076

PHTHALATES TOXICITY

EMERGING EVIDENCE SUGGESTS AN ENVIRONMENTAL RATHER THAN A GENETIC ETIOLOGY FOR HB, AN EMBRYONAL TUMOR RESULTING FROM DEVELOPMENTAL DISTURBANCES DURING ORGANOGENESIS.

Latini G, Gallo F, De Felice C. Birth characteristics and hepatoblastoma risk in young children Cancer 2004;101:210.

PHTHALATES TOXICITY

IN ADDITION, IT IS WELL KNOWN THAT THE LIVER IS THE MOST RESPONSIVE TARGET OF THE DEHP ADVERSE EFFECTS IN ANIMAL MODELS AND DEHP IS A RODENT HEPATOCARCINOGEN

Latini G, Gallo F, De Felice C. Birth characteristics and hepatoblastoma risk in young children Cancer 2004;101::210.

PHTHALATES TOXICITY

THE CHILDREN WHO DEVELOPED HB HAD RECEIVED PERINATAL TREATMENTS FOR A SIGNIFICANTLY LONGER TIME, THUS SUGGESTING THAT…

PHTHALATES TOXICITY

... PERINATAL INTENSIVE AND LONG-TERM MEDICAL TREATMENTS MAY BE INVOLVED IN THE TUMORIGENESIS IN THE HIGHLY SENSITIVE IMMATURE LIVER

PHTHALATES TOXICITY

IN PARTICULAR, MECHANICAL VENTILATION AND OXYGEN-THERAPY DURATIONS SEEM TO BE IMPORTANT RISK FACTORS IN PREDICTING THE DEVELOPMENT OF HB

Center for Devices and Radiological Health U.S. FDA (September 2001)

SAFETY ASSESSMENT OF DEHP RELEASED FROM PVC MEDICAL DEVICES

Center for Devices and Radiological Health U.S. FDA

NEONATES IN THE NICU ENVIRONMENT ARE EXPOSED TO DEHP FROM MULTIPLE DEVICES.

DEHP and PVC

Literature reports that DEHP leaks out from:

- **FEEDING TUBES**
- **INFUSION TUBING SYSTEMS**
- **UMBILICAL CATHETERS**
- **PVC BLOOD BAGS**
- **TRANSFUSION TUBING SYSTEMS**

DEHP and PVC

Literature reports that DEHP leaks out from:

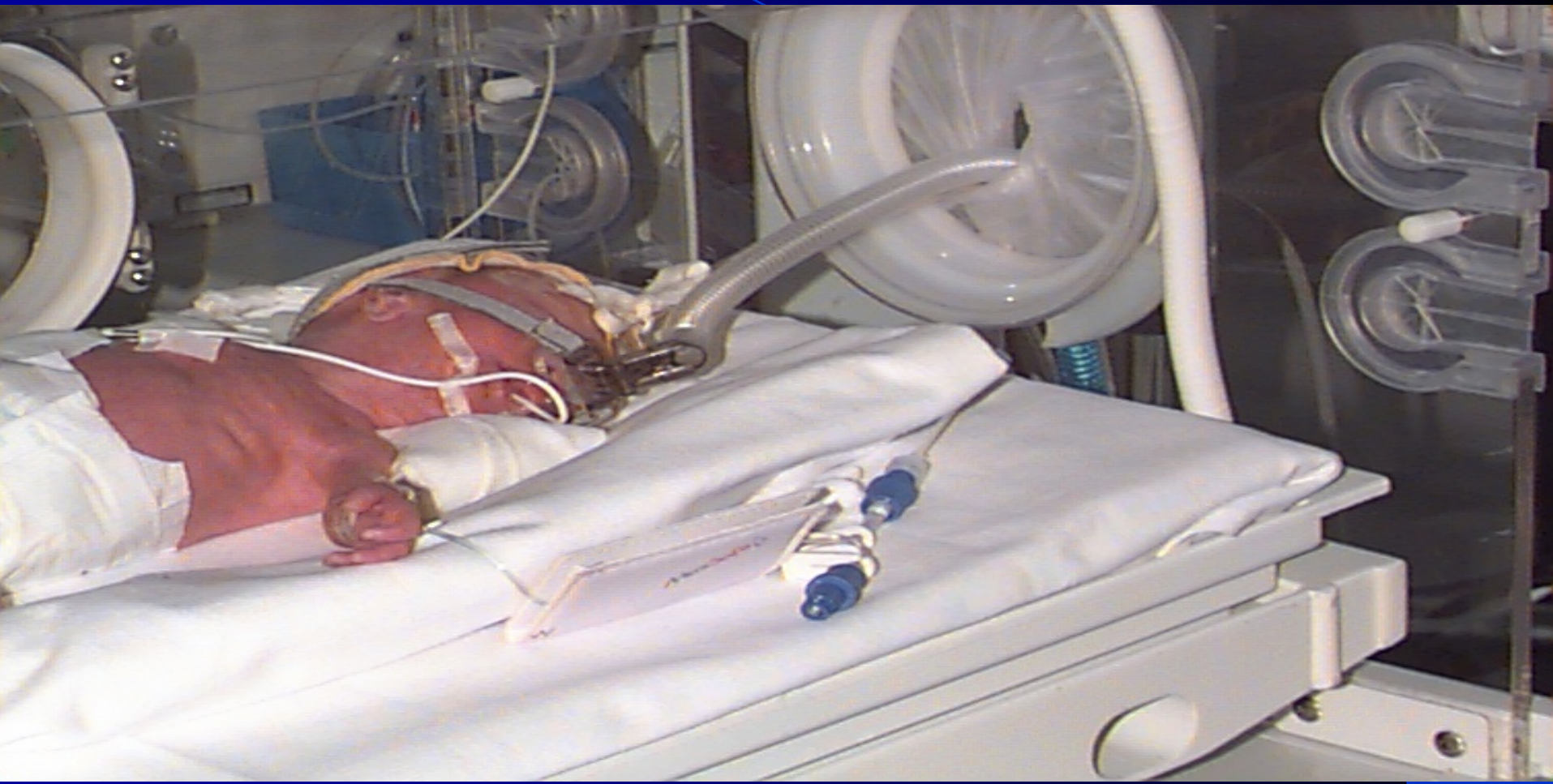
- **HEMODIALYSIS SYSTEMS**
- **PERITONEAL DIALYSIS SYSTEMS**
- **RESPIRATORY TUBING SYSTEMS**
- **CARDIOPULMONARY BYPASS SYSTEMS**
- **ECMO CIRCUITS**

DEHP and PVC

Literature reports that DEHP leaks out from:

- **ENDOTRACHEAL TUBES**

Latini G, Avery GB. Materials Degradation In Endotracheal Tubes: A potential contributor to Bronchopulmonary Dysplasia. Acta Ped. 1999;88;1174-1175.



Center for Devices and Radiological Health U.S. FDA

NEWBORNS MAY REPRESENT A POPULATION AT INCREASED RISK FOR THE ADVERSE EFFECTS OF DEHP.

PHTHALATES TOXICITY

NEWBORNS WHO UNDERGO INTENSIVE THERAPEUTIC MEDICAL INTERVENTIONS ARE EXPOSED TO HIGHER CONCENTRATIONS OF DEHP THAN THE GENERAL POPULATION.

Calafat AM, Needham LL, Silva MJ, Lambert G. Exposure to di-(2-ethylhexyl) phthalate among premature neonates in a neonatal intensive care unit. Pediatrics. 2004;113:e429-34.

PHTHALATES TOXICITY

HUMAN EXPOSURE TO DEHP AND/OR ITS PRIMARY METABOLITE MEHP BEGINS DURING INTRAUTERINE LIFE AND PHTHALATE EXPOSURE IS SIGNIFICANTLY ASSOCIATED WITH A SHORTER PREGNANCY DURATION

Latini G, De Felice C, Presta G, et al. In Utero exposure to Di-(2-Ethylhexyl)-Phthalate and Duration of Human Pregnancy. Environ Health Perspect 2003;111:1783-1785.

PHTHALATES TOXICITY

PRENATAL AND POSTNATAL EXPOSURES MAY HAVE SYNERGISTIC AND CUMULATIVE ACTIONS IN PRODUCING ADVERSE NEONATAL EFFECTS, ESPECIALLY FOR VLBW INFANTS.

PHTHALATES TOXICITY

PERINATAL PHTHALATE EXPOSURE MAY PLAY A ROLE IN INCREASING HB RISK AMONG CHILDREN WITH VLBW, ..

PHTHALATES TOXICITY

ALTHOUGH FURTHER STUDIES ARE CERTAINLY NEEDED IN THE FUTURE TO VALIDATE THIS HYPOTHESIS AND TO DETERMINE IF LESS INVASIVE PERINATAL TREATMENTS MAY REDUCE HB RISK.

Latini G, Gallo F, De Felice C. Birth characteristics and hepatoblastoma risk in young children Cancer 2004;101::210.

PHTHALATES TOXICITY

SEVERAL PHTHALATES AND THEIR METABOLIC PRODUCTS HAVE BEEN SHOWN TO BE DEVELOPMENTAL AND REPRODUCTIVE TOXICANTS AFFECTING PARTICULARLY MALE REPRODUCTIVE DEVELOPMENT

PHTHALATES TOXICITY

AND ARE SUSPECTED OF HAVING ENDOCRINE DISRUPTING OR MODULATING EFFECTS

PHTHALATES TOXICITY

HUMAN STUDIES ARE SCARCE, BUT SUGGESTIVE, AS FREQUENTLY REPORTING AN ASSOCIATION BETWEEN PHTHALATE EXPOSURE AND HEALTH RISKS.

PHTHALATES TOXICITY

THE PRESENCE OF PHTHALATE METABOLITES IN HUMAN BODY FLUIDS DOES NOT BY ITSELF MEAN THAT PHTHALATES CAUSE DISEASE.

PHTHALATES TOXICITY

PHTHALATE EXPOSURE HAS BEEN SHOWN TO BE ASSOCIATED WITH ALTERED SEMEN QUALITY IN HUMANS

Duty SM, Singh NP, Silva MJ, et al. The relationship between environmental exposures to phthalates and DNA damage in human sperm using the neutral comet assay. Environ Health Perspect. 2003;111:1164-9

PHTHALATES TOXICITY

EMERGING EVIDENCE SUGGESTIVE OF HARMFUL EFFECTS OF PHTHALATE EXPOSURE ON THE REPRODUCTIVE SYSTEM AND RELATED OUTCOMES HAS GRADUALLY ACCUMULATED IN RECENT YEARS

Doull J, Cattley R, Elcombe C, et al. the new U.S. EPA Risk Assessment Guidelines. Regul Toxicol Pharmacol. 1999;29:327-57.

PHTHALATES TOXICITY

DEVELOPMENT OF A MAMMALIAN FETUS INTO A PHENOTYPIC MALE FIRSTLY DEPENDS ON TESTIS FORMATION AND SECONDLY ON HORMONE PRODUCTION BY THE FETAL TESTIS

Sharpe RM. Hormones and testis development and the possible adverse effects of environmental chemicals. Toxicol. Lett. 2001;120:221-232.

PHTHALATES TOXICITY

ABNORMAL DEVELOPMENT OF THE TESTIS IN FETAL OR NEONATAL LIFE CAN HAVE LIFE-TIME CONSEQUENCES ON ALL ASPECTS OF REPRODUCTIVE FUNCTION IN ADULTHOOD, INCLUDING SPERM COUNTS

PHTHALATES TOXICITY

DEVELOPMENTALLY TOXIC PHTHALATES (E.G. DBP, BBP, DEHP) ADVERSE EFFECTS ARE RELATED TO ALTERATIONS IN GENE AND PROTEIN EXPRESSION AND A CORRESPONDING REDUCTION IN TESTOSTERONE SYNTHESIS

PHTHALATES TOXICITY

FETAL TESTICULAR TESTOSTERONE PRODUCTION IS ESSENTIAL FOR NORMAL MALE REPRODUCTIVE TRACT DEVELOPMENT AND…

PHTHALATES TOXICITY

..IMPAIRMENT OF FETAL TESTICULAR TESTOSTERONE PRODUCTION, OR BLOCKADE OF THE ANDROGEN RECEPTOR LEADS TO CRYPTORCHIDISM, HYPOSPADIAS, AND REDUCED FERTILITY

PHTHALATES TOXICITY

SOME PHTHALATES HAVE BEEN SHOWN TO DISRUPT SEVERAL GENE PATHWAYS, INCLUDING CHOLESTEROL TRANSPORT AND STEROIDOGENESIS, AS WELL AS ..

PHTHALATES TOXICITY

.. PATHWAYS INVOLVED IN INTRACELLULAR LIPID AND CHOLESTEROL HOMEOSTASIS, INSULIN SIGNALING, TRANSCRIPTIONAL REGULATION, AND OXIDATIVE STRESS.

Liu K, Lehmann KP, Sar M, Young SS, Gaido KW. Gene Expression Profiling Following In Utero Exposure to Phthalate Esters Reveals New Gene Targets in the Etiology of Testicular Dysgenesis. Biol Reprod. 2005 Feb 23

PHTHALATES TOXICITY

ADDITIONAL GENE TARGETS INCLUDE ALPHA INHIBIN, ESSENTIAL FOR NORMAL SERTOLI CELL DEVELOPMENT, AND GENES INVOLVED IN SERTOLI CELL AND GONOCYTE COMMUNICATION

PHTHALATES TOXICITY

PHTHALATES CAN DIRECTLY AFFECT FETAL AND NEONATAL TESTIS DIFFERENTIATION, INDUCING MALE RAT REPRODUCTIVE TRACT MALFORMATIONS,

…

PHTHALATES TOXICITY

AS WELL AS TESTICULAR CHANGES REMARKABLY SIMILAR TO TESTICULAR DYSGENESIS SYNDROME (TDS) IN HUMANS

PHTHALATES TOXICITY

TDS INCLUDES INTERRELATED DISORDERS, SUCH AS LOW SPERM COUNTS, HYPOSPADIAS, CRYPTORCHIDISM AND TESTICULAR GERM CELL CANCER

PHTHALATES TOXICITY

AND MAY
DEVELOP DURING FETAL LIFE
UNDER THE
INFLUENCE OF ENVIRONMENTAL
FACTORS

PHTHALATES TOXICITY

EXPERIMENTAL AND EPIDEMIOLOGICAL STUDIES SUGGEST THAT TDS IS THE RESULT OF DISRUPTION OF EMBRYONAL PROGRAMMING AND GONADAL DEVELOPMENT DURING FETAL LIFE

PHTHALATES TOXICITY

- **FOR THE FIRST TIME A STUDY**
- **LOOKED AT SUBTLE PATTERNS OF**
- **GENITAL MORPHOLOGY IN**
- **HUMANS IN RELATION TO ANY**
- **PRENATAL EXPOSURE.**

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, et al. Decrease in anogenital distance among male infants with prenatal phthalate exposure. EHP doi:10.1289/ehp.8100 Online 27 May 2005

PHTHALATES TOXICITY

- IT WAS MOTIVATED BY
- TOXICOLOGIC STUDIES
- SHOWING THAT GENITAL
- MORPHOLOGY IS ALTERED BY
- ANTIANDROGENS,
- INCLUDING SOME PHTHALATES.

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, et al. Decrease in anogenital distance among male infants with prenatal phthalate exposure. EHP doi:10.1289/ehp.8100 Online 27 May 2005

PHTHALATES TOXICITY

- AGI, THE MOST SENSITIVE
- MARKER OF ANTI-ANDROGEN
- ACTION IN TOXICOLOGIC
- STUDIES, IS SHORTENED AND
- TESTICULAR DESCENT IMPAIRED,
- IN BOYS..

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, et al. Decrease in anogenital distance among male infants with prenatal phthalate exposure. EHP doi:10.1289/ehp.8100 Online 27 May 2005

PHTHALATES TOXICITY

- **..WHOSE MOTHERS HAD**
- **ELEVATED PRENATAL PHTHALATE**
- **EXPOSURE.**

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, et al. Decrease in anogenital distance among male infants with prenatal phthalate exposure. EHP doi:10.1289/ehp.8100 Online 27 May 2005

PHTHALATES TOXICITY

SINCE THE BLOOD-TESTIS BARRIER FORMS JUST BEFORE PUBERTY IN HUMANS, PERMEABILITY OF THE BLOOD-TESTIS BARRIER IS INCREASED IN CHILDREN AND..

PHTHALATES TOXICITY

PARTICULARLY IN NEWBORNS, WHOSE TESTICLES ARE STILL DEVELOPING

PHTHALATES TOXICITY

“AS A CONSEQUENCE, MALE NEWBORNS ARE THOUGHT TO BE AT THE GREATEST POTENTIAL RISK

Conclusion

THUS, IT WOULD BE ADVISABLE IN THE FUTURE TO REPLACE CURRENT PVC PLASTICISERS, ESPECIALLY IF THEY COME INTO CONTACT WITH BABIES, WITH BETTER-QUALITY MATERIALS.

Conclusion

DURING THE MARCH 1, 2000 – MARCH 1, 2004 TIME PERIOD, NEW PLASTICISERS FOR PVC FORMULATIONS HAVE BEEN STUDIED IN THE FRAME OF A FOUR YEARS BRITE-EURAM PROJECT, APPROVED AND FUNDED BY THE EU (CONTRACT N. QLK5-CT-1999-01355).

Conclusion

THE OVERALL GOAL OF THIS RESEARCH PROJECT WAS TO DEVELOP INDUSTRIAL TECHNOLOGIES FOR THE PRODUCTION FROM RENEWABLE RESOURCES OF POLYMERIC PLASTICISERS CAPABLE OF…

Conclusion

..REPLACING PHTHALATES IN FLEXIBLE PVC FOR MASS-CONSUMER APPLICATIONS INVOLVING CONTACT WITH HUMAN FLUIDS AND TISSUES, PARTICULARLY MEDICAL DEVICES.

Conclusion

THE NEW PLASTICISER IS A VERY INNOVATIVE, AND HIGHLY BIOCOMPATIBLE PRODUCT WITH NO DEMONSTRATED TOXICITY.

Conclusion

ALTHOUGH ITS PRICE IS NOT YET COMPETITIVE AT THE MOMENT, IT COULD SIGNIFICANTLY DECREASE IN THE FUTURE, BY ADOPTING A NEW PLANT PROCESS FOR PRODUCTION OF ALTERNATIVE PLASTICIZERS.

Conclusion

Latini G. Monitoring phthalate exposure in humans. Clin Chim Acta (in press)

Brindisi, 17-19 Novembre 2005

NEW TRENDS IN NEONATOLOGY


GRAZIE PER
L’ATTENZIONE