

Project Columbus

Nonclinical and Clinical Development of Health Products: Opportunities and Challenges

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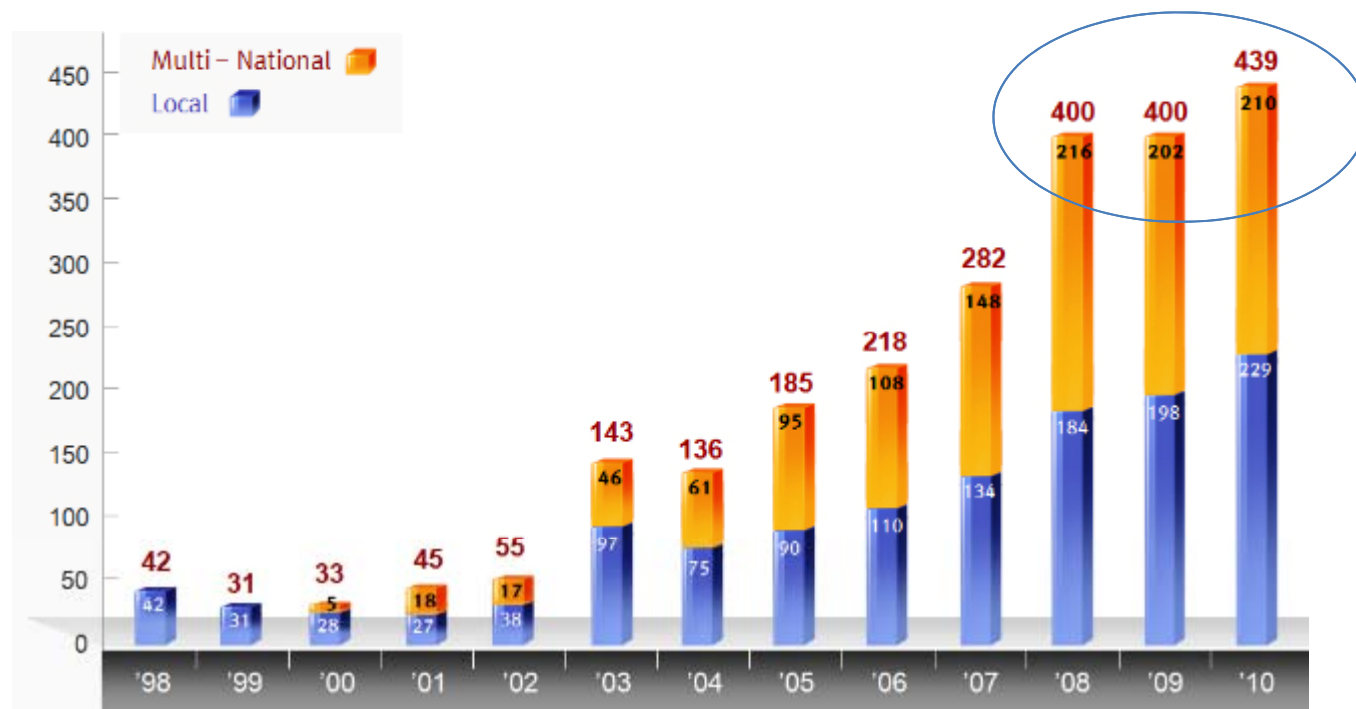


Project Columbus

**Strong foundation has been laid and
much progress achieved in Korea.**

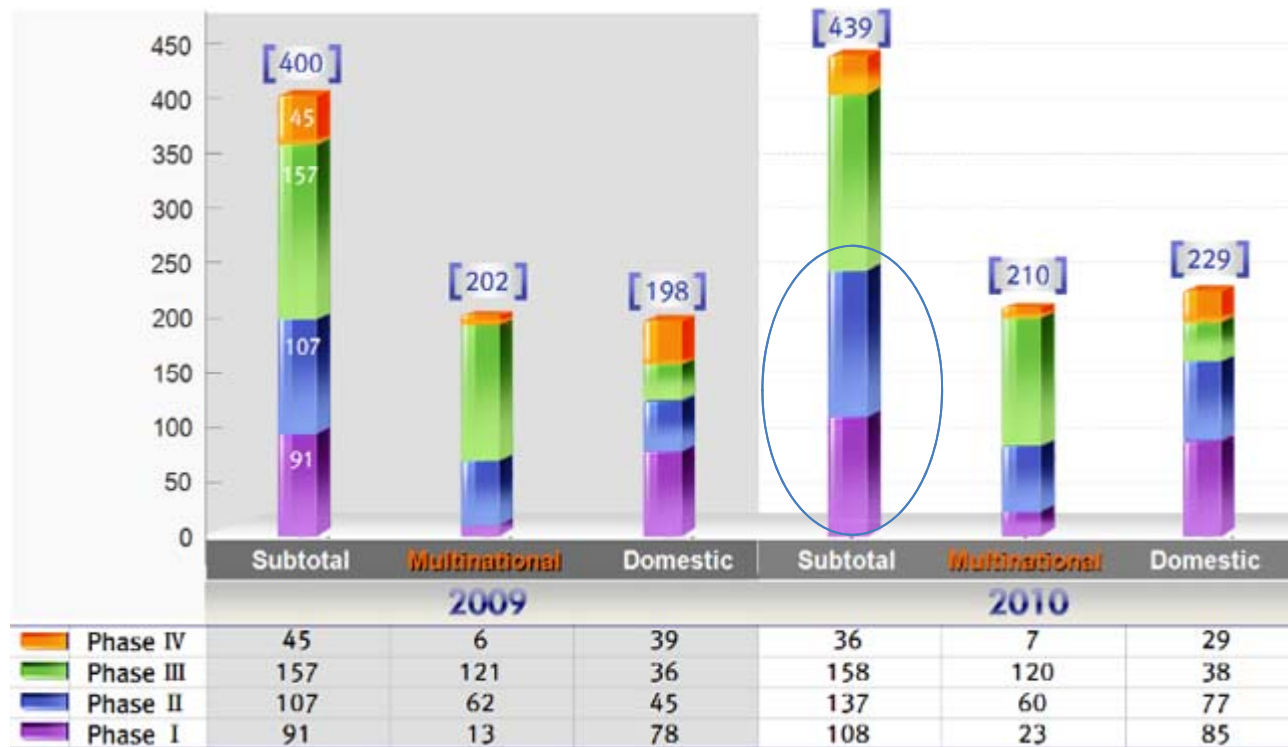


Korea's Impressive Growth in Global Clinical Trials



Source: www. KoNECT.or.kr

Korea's Growth in Phase 1 & Phase 2 Clinical Trials



Key Therapeutic Areas Include Oncology, Circulatory, and Endocrine

For Health Product R&D and Commerce:
***These are the Best of Times and
the Worst of Times***

Opportunity: moving towards a single global market with global standards for R&D

- Challenges—
 - Increasing global competition
 - Increasing regulatory expectations
 - Increasing cost pressures and payer expectations
 - Increasing media and investor scrutiny
 - Increasing market complexity, demand for safety, and individualized medicine pressure

One World— One Set of International Standards

ICH
INTERNATIONAL
CONFERENCE ON
HARMONISATION
GUIDELINES



International
Organization for
Standardization



One Set of International Standards— Yet Many Implementations



One Global Objective Around Safety— Yet Many Different Approaches and Results

Nonclinical Examples:

- Reproductive Toxicity Testing
 - Generally must be completed sooner in Europe than in US for 2 trials to include women of reproductive potential
- Interpretation of Toxicology Study Results
 - Frequently more conservative in the US than in Europe. Examples : Liraglutide (GLP-1 analog) licensed in Europe but held up in the US because of thyroid tumors in animals

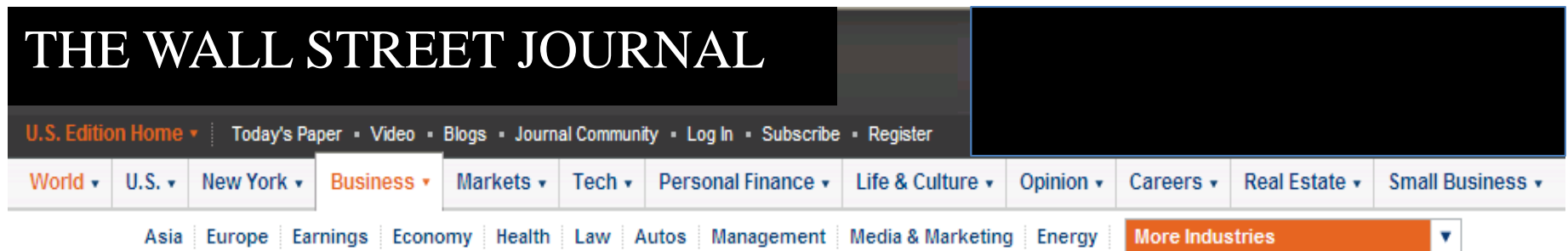


One Global Objective Around Safety— Yet Many Different Approaches and Results

Clinical Examples:

- QTc Evaluation
 - Applied more conservatively by FDA
 - Byetta (Amylin's long acting GLP-1 agent) is held up by QT issue at FDA, but now approved in Europe
- Cardiovascular Safety Trials
 - Now required for all T2 diabetes drugs by FDA but required on a selective basis in Europe
 - May soon be required by FDA for all obesity drugs

Consequence: U.S. Company Abandons FDA Development Program — Pursues Other Global Markets



Orexigen To Halt US Obesity Program As It Disputes FDA Contrave Request

DOW JONES NEWSWIRES

Orexigen Therapeutics Inc. (OREX) said it plans to suspend clinical development of its U.S. obesity programs as it disputes a decision by the U.S. Food and Drug Administration regarding its Contrave weight loss pill.

Shares plunged 36% to \$2.04 in recent premarket trading.

The drug maker had indicated it would provide a regulatory update Friday on the drug, which the FDA rejected in February, requesting another clinical trial to study its long-term cardiovascular risk. The rejection was a major setback and raised questions over whether development of Contrave, which Orexigen is developing with

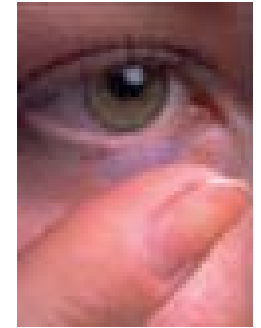
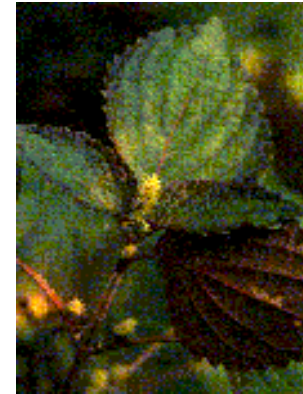
Shared Objective for Affordable Products → Biosimilars

- Follow on Biotech Products
 - Europe has a “biosimilar” pathway, which will allow for more exchangeability with branded products
 - In US, FDA will allow 505b2 pathway but this does not provide easy pharmacy exchangeability with branded products
- Market exclusivity resulting from licensing
 - 10 years in Europe vs. 5 years in US



Common Desire to Expand Health Product Choices

- Conventional drugs
- Biotech drugs/biologics
- Botanical drugs
- Nutraceuticals
- Medical foods
- Traditional medicine products
- Homeopathic medicines
- Over the Counter (OTC) products



Major Differences in Regulation of Dietary Supplements and Traditional Medicines



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Herbal medicinal products

End of transition period set out in Directive
The European Commission's Directorate General (SANCO) has published a question and answer document on traditional herbal medicinal products and the end of the transition period set out in Directive 2004/24/EC, member states are responsible for applying

Guidance for Industry Botanical Drug Products



Copies of this Guidance are available from:

Division of Drug Information (HFD-240),
Office of Training and Communications,
Center for Drug Evaluation and Research (CDER),
Food and Drug Administration
5600 Fishers Lane, Rockville, MD 20857, (Tel) 301-827-4573

Internet at <http://www.fda.gov/cder/guidance/index.htm>

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Current Subject

Drugs & Health Products

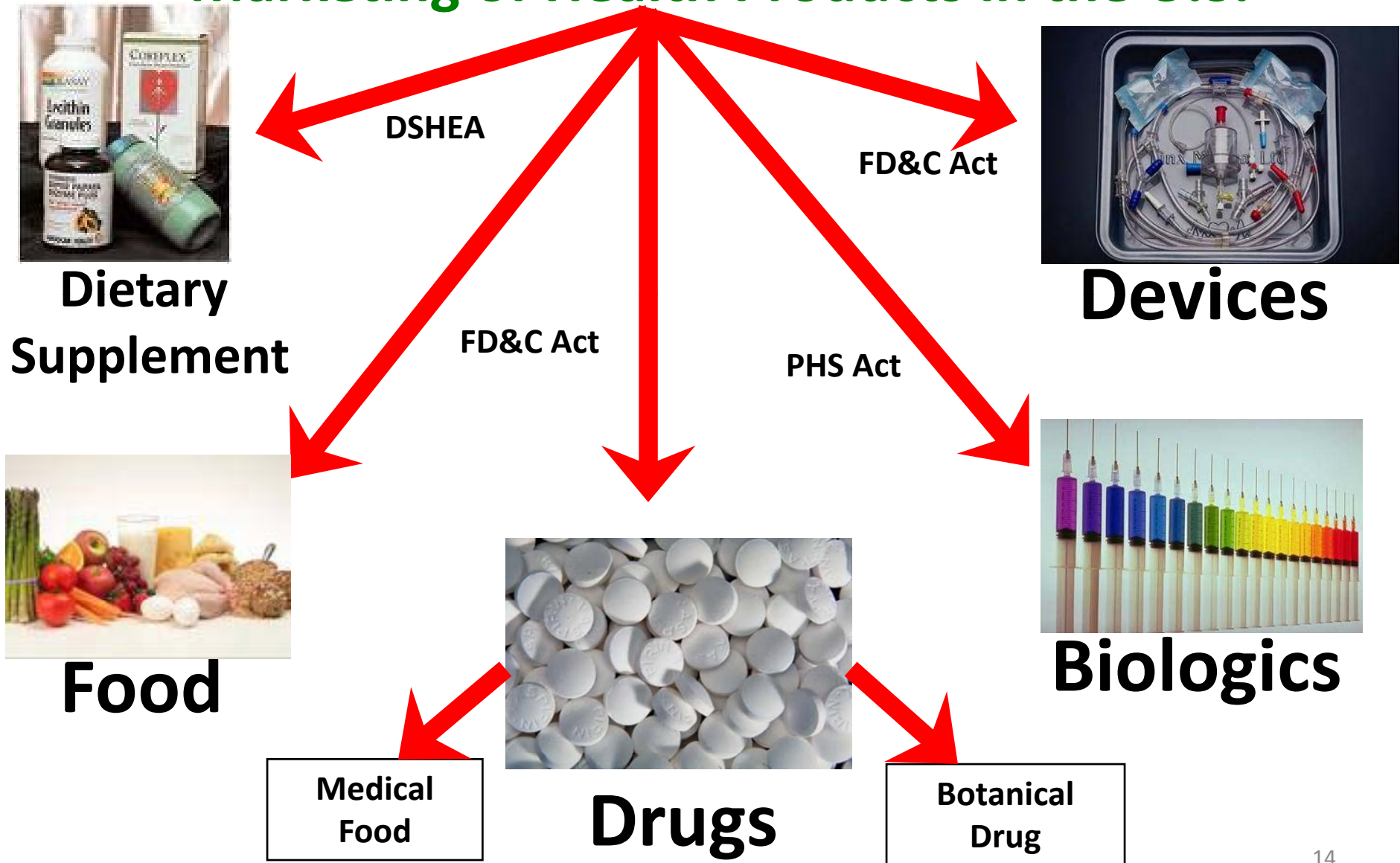
Natural Health

Drugs and Health Products

Natural Health Products

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Regulatory Pathways for Marketing of Health Products in the U.S.



In Short.....

**The Global Environment Provides Great
Opportunity But Carries Many
Challenges.**

**Then, How Do We In Project Columbus
Achieve Global Success Together?**



Proposed Understandings for Working Together in Project Columbus—

- Traditional pharma and biotech paradigms should not be emulated—they should be re-invented
- Our competitors are smart and hardworking—what will be our edge?
- There are many good ideas, but few workable strategies.
- A new product must be developed to compete in the future—not in the present.
- Management of R&D resources is key to reducing time, costs, and risks—and maximizing return on investment.

Traditional Pharma and Biotech Paradigms Should Not be Emulated— They Should Be Re-invented

- Large pharma companies are in a race to re-invent themselves—but suffer from deeply engrained habits and thinking, short timeline
- Project Columbus companies have the advantage of—

...an infrastructure built on today's best practices

...a coordinated long term strategic vision

...an integrated commitment for success



Competitors Are Smart And Hardworking

India, Israel, Singapore, China are formidable competitors in healthcare product development.....**What Will Be Our Edge?**

Project Columbus Companies Can Build Upon -



- South Korea's strong record of growth and global integration to become a high-tech industrialized economy
- Coordination, collaboration, and resource sharing with global product development and regulatory expertise
- Acceleration of innovation that grows exports of products and services and benefits Korea's aging population

There Are Many Good Ideas... But Few Workable Strategies

- Possible scientific approaches for addressing unmet clinical need are nearly unlimited
- Fewer approaches can practically be translated into a product
- Careful evaluation, goal setting, and planning are required in the beginning



A New Product Must Be Developed To Compete In The Future— Not In The Present

- Health products—drugs in particular—can require many years before commercialization
- A full understanding of clinical positioning, competition, project cost and regulatory environment at targeted launch time is essential and should be continually re-evaluated during product development cycle
- Global product design may have nuances necessary for commercial success



Management of R&D Resources Is Key To Reducing Time, Costs, And Risks—And Maximizing Return On Investment

- Every function of health product development (discovery→marketing) has been commoditized
- Selection and management of these vendors are very challenging

Project Columbus companies should invest their resources in acquiring knowledge, devising strategies, and managing execution



Good Intentions Can Lead To Bad Results

Examples of lessons learned:

- Alternate delivery of injected product identified as having high value → Was true at one time but no longer true after \$billion investment.
- Use of home glucose monitors in trial of a diabetes drug → Resulted in large placebo effect among patients who had not used a monitor before.

Examples Of Lessons Learned- Continued

- A contractor in China was selected for an animal study because of close connection to SFDA. → Study was not acceptable to FDA
- Academic experts who do not understand FDA expectations recommended a clinical trial design → FDA rejects design, 6 months' time lost
- Premature selection of lead compound and manufacturing process → Large ex-US program investment, FDA found product form unacceptable

Project Columbus: A Long But Gratifying Journey

시작이 반이다

천릿길은 한 걸음부터

