

Chemical Issues in Pharmaceutical Supply Chain: A Case of Tamiflu

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Agenda

- The **primary manufacturing site** is responsible for the synthesis of **the active ingredient of a drug**.
- In the manufacture or design of new synthetic routes of a drug, **the logistics cost, availability of starting materials, number of steps and overall yield** are critical factors to be taken into account.

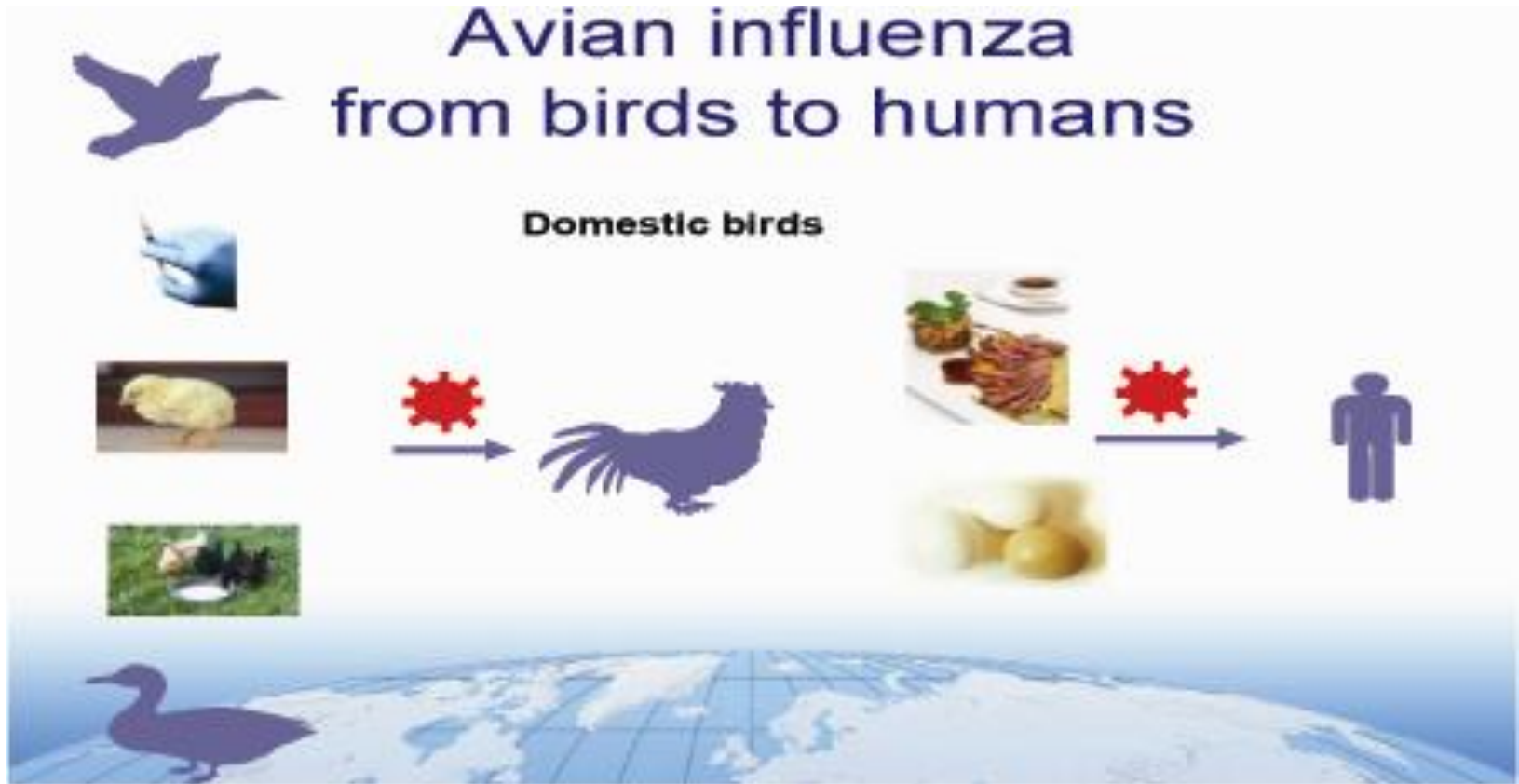
Objectives

- Highlight the concepts of **supply chain management (SCM)** in pharmaceutical industry
- Describe the recent advance in the synthetic chemistry of Tamiflu, focusing on the new approaches **based on inexpensive starting materials.**

Avian Influenza (H5N1)

- Influenza virus: Type A
 - Cause severe illness
- Bird to bird
- Bird to animals
- Bird to humans
- Human to human

Avian Influenza (H5N1)



Source: Tang, O., & Lau, Y.Y. (2013). of avian influenza pandemic in Hong Kong.
International Journal of Logistics System Logistics aspects s and Management, 14(1), 110-130.



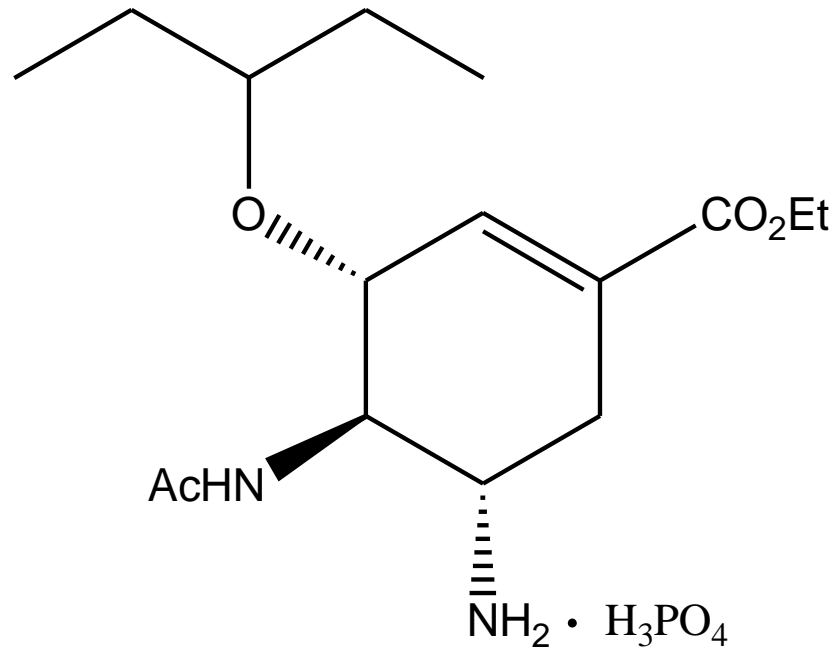
Source: online source: yahoo and google

Cumulative Number of Confirmed Human Cases for Avian Influenza (H5N1), 2003-2015

Country	2003-2009		2010		2011		2012		2013		2014		2015		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	Deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	0	0	2	0	3	0	1	1	0	0	0	0	7	1
Cambodia	9	7	1	1	8	8	3	3	26	14	9	4	0	0	56	37
Canada	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1
China	38	25	2	1	1	1	2	1	2	2	2	0	5	1	52	31
Djibouti	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt	90	27	29	13	39	15	11	5	4	3	37	14	136	39	346	116
Indonesia	162	134	9	7	12	10	9	9	3	3	2	2	2	2	199	167
Iraq	3	2	0	0	0	0	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	2	2	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Myanmar	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Nigeria	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	0	0	0	0	3	1
Thailand	25	17	0	0	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	0	0	0	0	12	4
Vietnam	112	57	7	2	0	0	4	2	2	1	2	2	0	0	127	64
Total	468	282	48	24	62	34	32	20	39	25	52	22	143	42	844	449

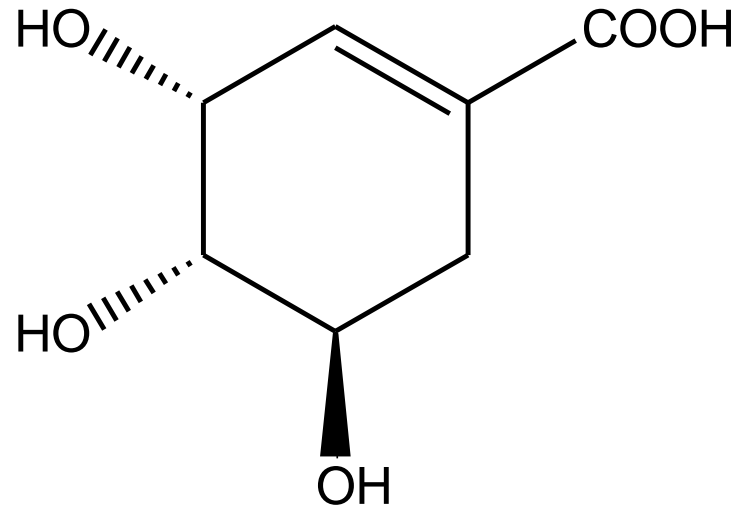
Source: World Health Organization (2015). Website: <http://www.who.int/en/>

Structure of Oseltamivir Phosphate (Tamiflu)



Oseltamivir phosphate (Tamiflu)

Structure of Shikimic Acid



Shikimic acid

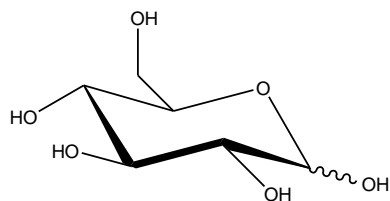
Recent Synthetic Approaches for Tamiflu

- Thailand
 - Kasetsart University
- Singapore
 - Nanyang Technological University
 - The Institute of Chemical and Engineering Sciences
- Japan
 - Shionogi & Co., Ltd.
- South Korea
 - Ewha Womans University

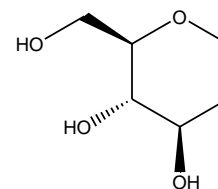
Recent Synthetic Approaches for Tamiflu

- Hong Kong
 - The Hong Kong Polytechnic University
- China
 - Sun Yat-sen University
- The United States
 - Stanford University

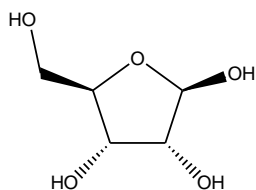
Recent Synthetic Approaches for Tamiflu (Structure of Starting Material)



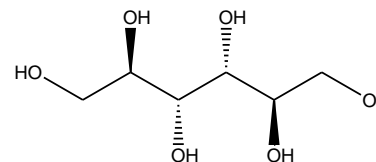
D-glucose



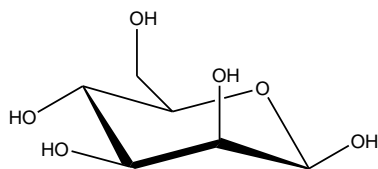
D-glucal



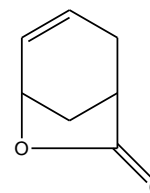
D-ribose



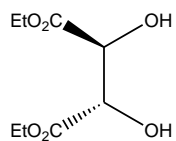
D-mannitol



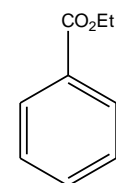
D-mannose



Lactone



Diethyl d-tartrate



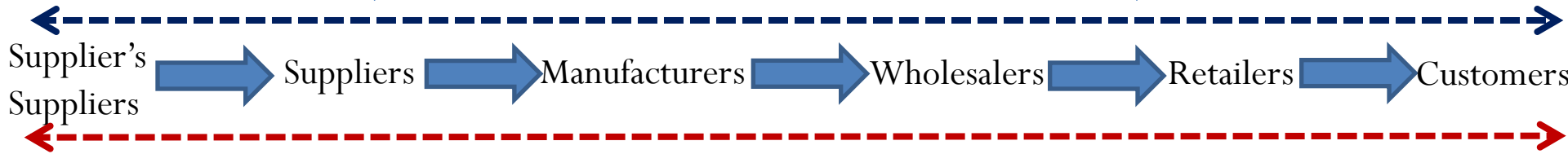
Ethyl benzoate

Supply Chain Management: An Overview

Value Added Solutions

Physical supply materials management
inbound logistics

Physical distribution
outbound logistics



Information Flow
Product/Service
Finance

Sustainable Supply Chain Management (SSCM)

- “The management of material, information and capital flows as well as cooperation among companies along the supply chain while taking goals from all three dimensions of sustainable development, i.e., **economic, environmental and social**, into account which are derived from customer and stakeholder requirements”.

Sustainable Supply Chain Management (SSCM)



Strategic Orientation

- Drug industry requires placing **equal importance** on all three dimensions (i.e., **economic, social and environmental**) of sustainability for their decision making

Continuity

- Select **qualified supply chain partners** and establish **long-term relationships** with supply chain partners in the drug industry

Collaboration

- Integrate the key information and partners in the process level of SSCM. In the drug industry, **joint development** could contribute to **developing new technologies, processes and products**

Risk Management

- **Individual monitoring** of specific suppliers, pressure group management and **standardization** of standards and certification to minimize the supply chain risk

Pro-activity

- Stakeholders are **actively engaged and learning** from each other in the supply chain.
- **Innovation** is the core elements in the dynamic environments of sustainable markets.

The End

Q & A