Quality in the 19th and 20th Centuries

Jeremy Winkworth

19th Century Products

More 19th Century Products

First Upjohn Building in 1886

Pills were made by hand

Quality Testing in the 19th Century

- The Upjohn Pill and Granule Company performed only three tests on incoming materials and active ingredients
  - Does it look the same as the last shipment?
  - Does it smell the same as the last shipment?
  - Does it taste the same as the last shipment?
- No results were written down.

Legal Requirements in the 19th Century

- The United States Pharmacopeia (USP)
- National Formulary (NF)

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ELIXIR BUCHU ET POTASSII ACETATIS.

Elixir of Buchu and Potassium Acetate.

	Metric.	*Apothecaries'.*
Potassium Acetate	85 Gm.	2¾ troy ounces.
Elixir of Buchu (N. F.), a sufficient quantity		
To make	1000 Cc.	32 fluidounces.

Dissolve the Potassium Acetate in sufficient Elixir of Buchu to make 1000 Cc. (or 32 fluidounces) and filter, if necessary.

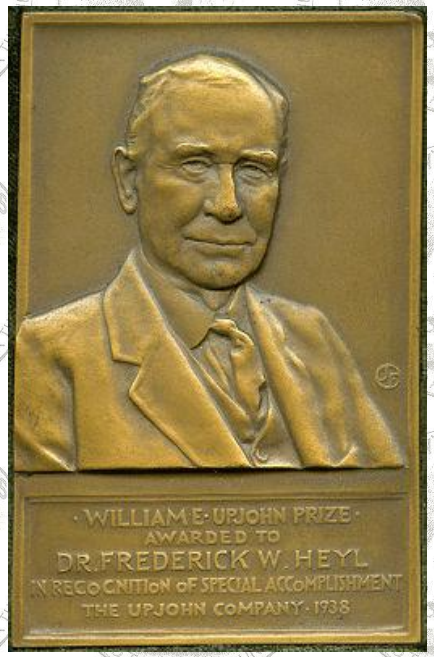
4 Cc. (1 fluidrachm) represent 0.34 Gm. (5 grains) of Potassium Acetate and about 0.5 Gm. (7½ grains) of Buchu.

Average dose: 4 Cc. (1 fluidrachm).

The Start of Quality at Upjohn

- 1899 – Arthur Crooks, a self-taught chemist
- 1905 – Fred Staley, had a correspondence degree in chemistry
- 1910 - William Perkins, the first bacteriologist
- 1913 – Fred Heyl, the first scientist

A Champion for Science and for Quality



Fred Heyl went on to be called the "Father of Upjohn Science." During his career, he launched Upjohn's chemical control efforts, published more than 80 scientific papers, helped to develop hundreds of new products, and served as vice president of the company's Research Division.

After his retirement in 1944, Heyl continued to work on projects at his lab bench until 1955. He died in 1968.

1914-1915 Quality Report

REPORT OF THE DEPARTMENT OF

ANALYTICAL CHEMISTRY

1914 - 1915.

S. R. Light, M.D.,

The Vice-President,

The Upjohn Company.

Dear Sir:-

The following is a report, written for the purpose of proving the quality of the finished products of these laboratories in so far as such products are amenable to chemical examination. Physiological or Biological work is entirely excluded from the discussion, although the standard solutions of ergot, digitalis, etc., were prepared in the chemical laboratory and then forwarded to the Biological department. This report includes analytical data upon all outgoing products for one year, beginning from July 1st, 1914. The report on incoming products is therefore abridged in order that the greater emphasis may be placed upon the former subject.

Legally Required Quality Standards

- 1906 - The Pure Food and Drug Act was passed, prohibiting the sale of misbranded and adulterated foods and drugs and giving oversight to the Bureau of Chemistry
- 1927 - The Bureau of Chemistry was renamed the Food, Drug, and Insecticide Administration
- 1930 - The name was shortened to the present Food and Drug Administration (FDA)
- 1938 - The Federal Food, Drug, and Cosmetic (FDC) Act is passed by Congress

QUININÆ SULFAS

Quinine Sulfate

Quin. Sulf.

$(C_{20}H_{24}N_2O_2)_2 . H_2SO_4 . 2H_2O$ Mol. wt. 782.92

The sulfate of an alkaloid obtained from cinchona.

Description—Quinine Sulfate occurs as white, fine, needle-like crystals, usually lusterless, making a light and readily compressible mass. It is odorless, and has a persistent, very bitter taste. When exposed to light, Quinine Sulfate acquires a brown tint.

Solubility—One Gm. of Quinine Sulfate dissolves in 810 cc. of water, and in 120 cc. of alcohol, at 25° C. One Gm. of it dissolves in 35 cc. of water at 100° C., and in about 10 cc. of alcohol at 80° C. It is slightly soluble in chloroform and in ether, but is freely soluble in a mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol.

Identification—

A: Acidify a saturated, aqueous solution of Quinine Sulfate with diluted sulfuric acid: the solution develops a vivid blue fluorescence.

B: Add 1 or 2 drops of bromine T.S. to 5 cc. of an aqueous solution of Quinine Sulfate (1 in 1000), and follow with 1 cc. of ammonia T.S.: the liquid acquires an emerald green color due to the formation of thalleioquin.

C: An aqueous solution of Quinine Sulfate (1 in 50) made with a few drops of hydrochloric acid, responds to the tests for sulfate, page 592.

D: A solution of Quinine Sulfate (1 in 50) in normal sulfuric acid is levorotatory, page 601.

Loss on drying—When dried to constant weight at 100° C., Quinine Sulfate loses not more than 5 per cent of its weight.

Ash—Quinine Sulfate yields not more than 0.05 per cent of ash, page 556.

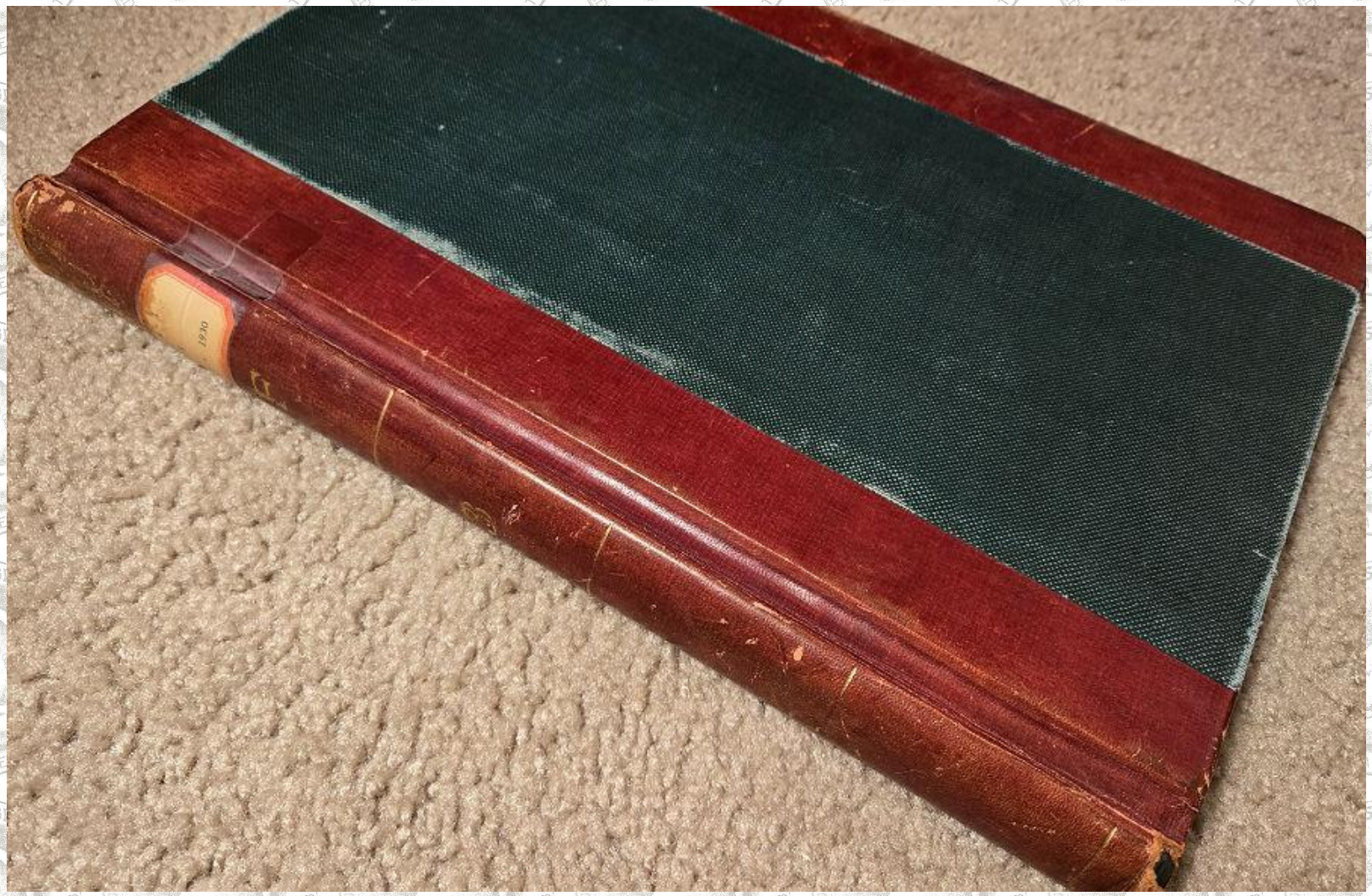
Carbonizable substances—Dissolve 0.2 Gm. of Quinine Sulfate in 5 cc. of sulfuric acid: the solution has no more color than matching fluid M, page 563.

Reaction—A saturated, aqueous solution of Quinine Sulfate is neutral or not more than slightly alkaline to litmus paper.

Inorganic salts—Heat 1 Gm. of Quinine Sulfate to 50° C. with 7 cc. of a mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol: it dissolves completely and the solution remains clear on cooling.

1920s USP Monograph for Quinine Sulfate

Fluids Department Production Logbook 1923 - 1930



Fluids Production Logbook 1923 - 1930

FLUID RECORD

28

Aug 23, 1924

5 gals. 59207 Sodium Bromide + Chloral Comp.

59208 " " "

Aug. 25, 1924

12 gals. 59209 Spirits Camphor Usp IX

100 gals. 59210 Fluct. Opium Camphorated Usp IX

12 gals. 59211 Fluct. Ferric Chloride Usp IX

59212 " " "

59213 " " "

59214 " " "

2 gals. 59215 Chloroform Liniment Usp IX

25 gals. 59216 Soap Liniment Usp IX

" " "

Aug. 27, 1924

25 gals. 59247 Fluct. of Citro-Chloride of Iron N.F. IV

39 gals. 59248 Rose Water

59249 " "

59250 " "

Aug. 28, 1924

25 gals. 59251 Fennel Water Usp IX

600# 59252 Fl. Ext. Nux Vomica

2 gals. 59253 Fehlings Solution "A" Usp IX

2 gals. 59254 Benedicts Solution

59255 " "

100 gals. 59256 Syrup White Pine Comp. N.F. IV

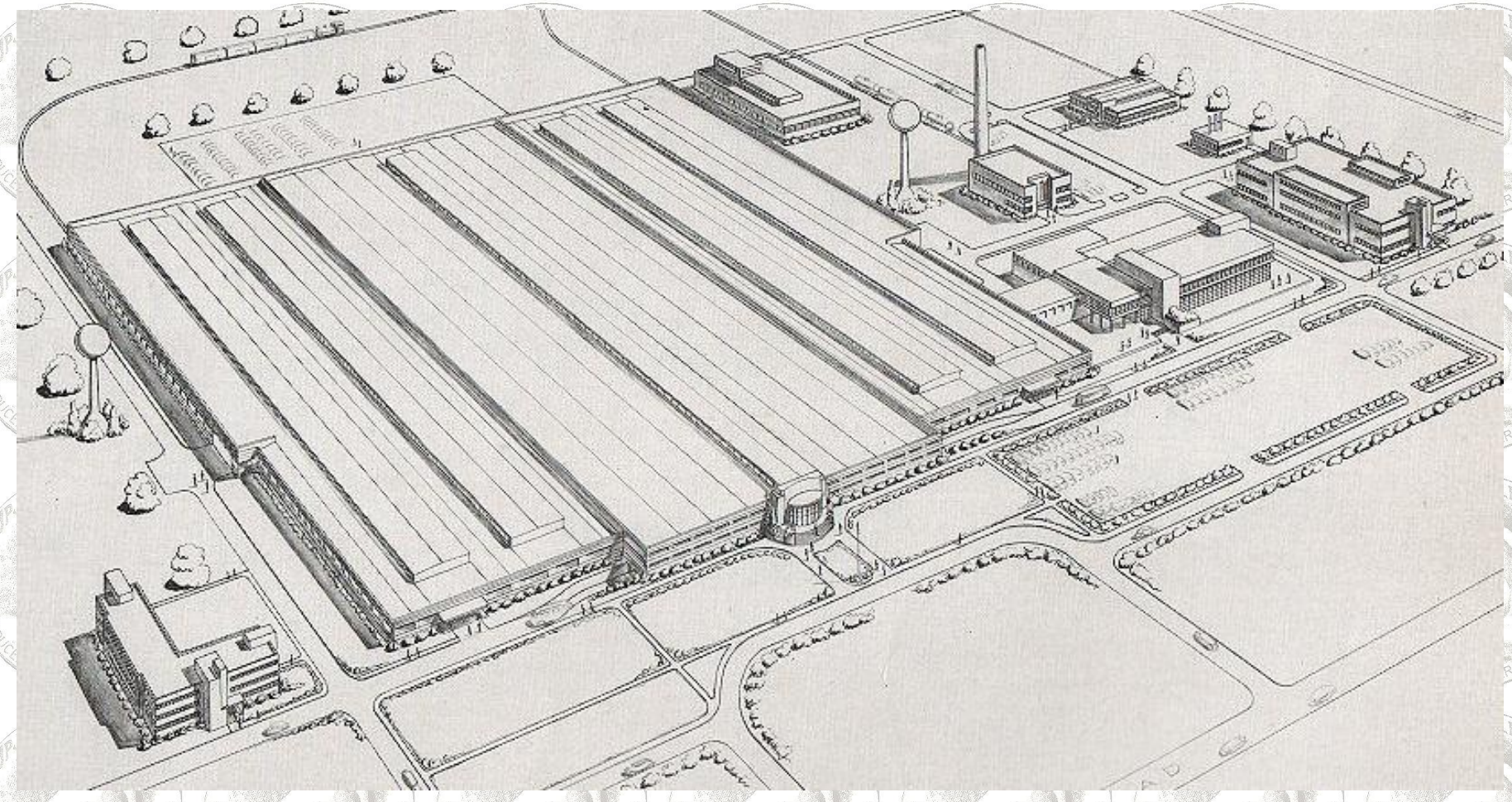
Aug. 29, 1924

5 gals. 59257 Fluct. Gambier Comp. Usp IV

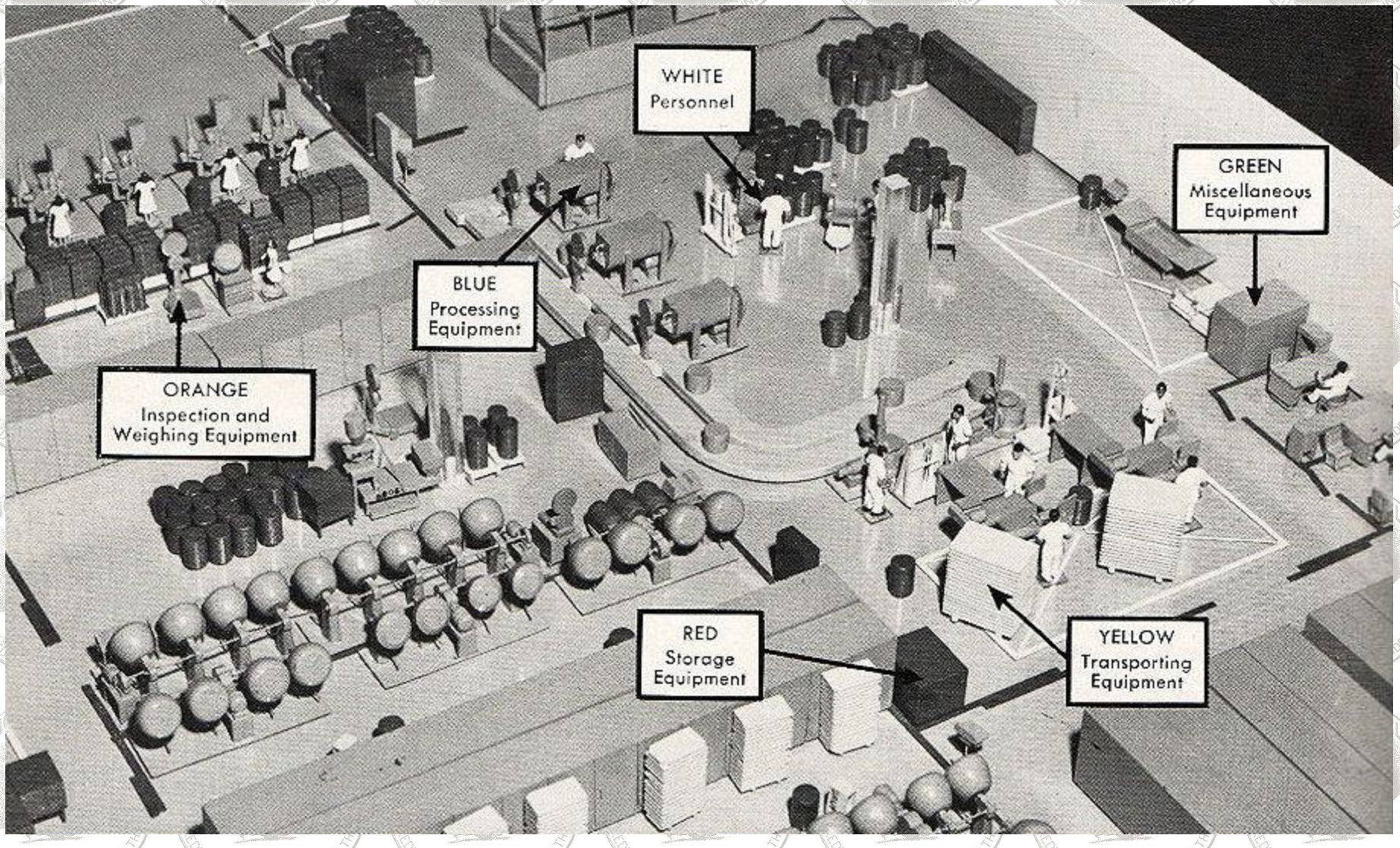
Manufacturing in the late 1930s

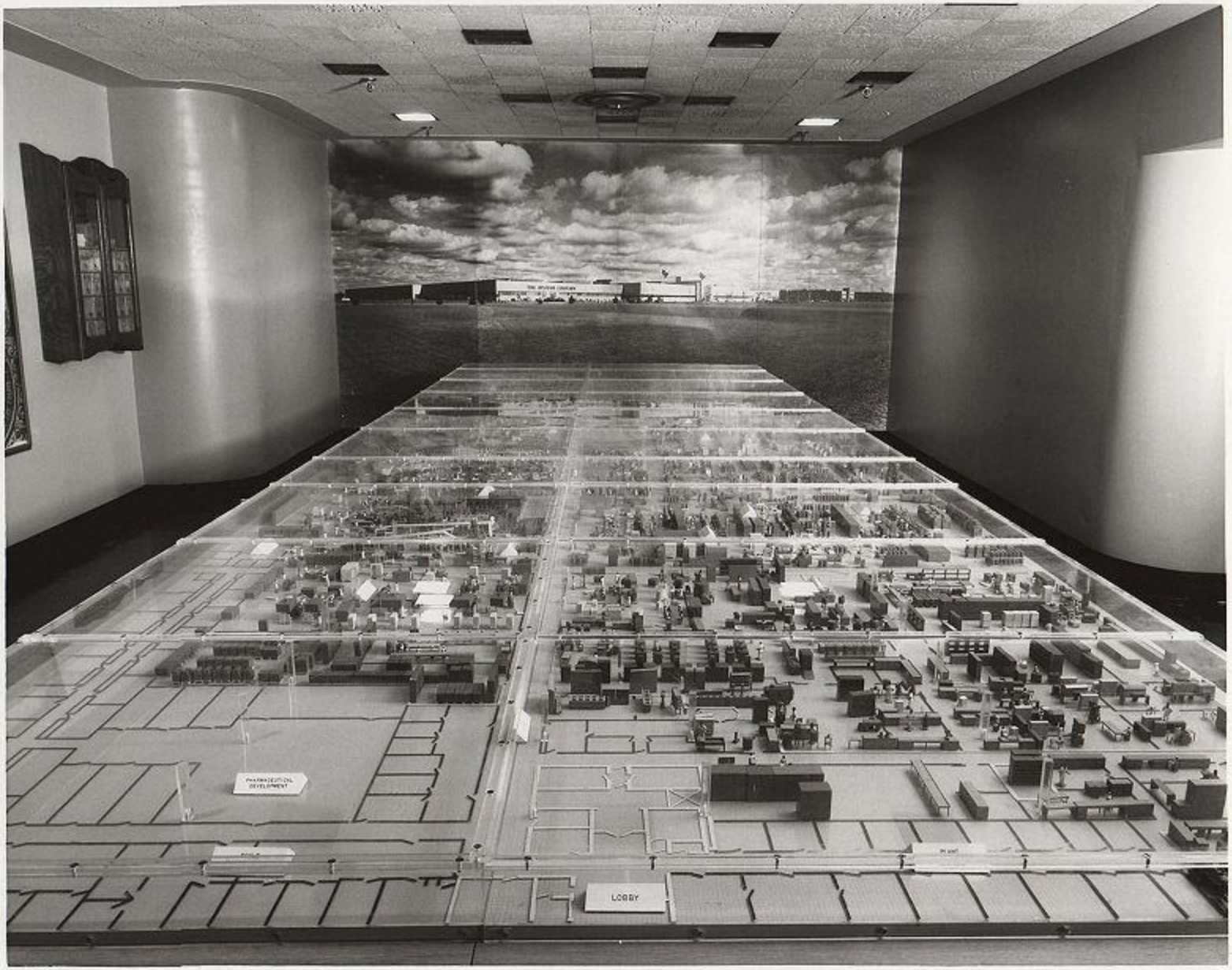
Packaging in the late 1930s

New Manufacturing Plant in Portage

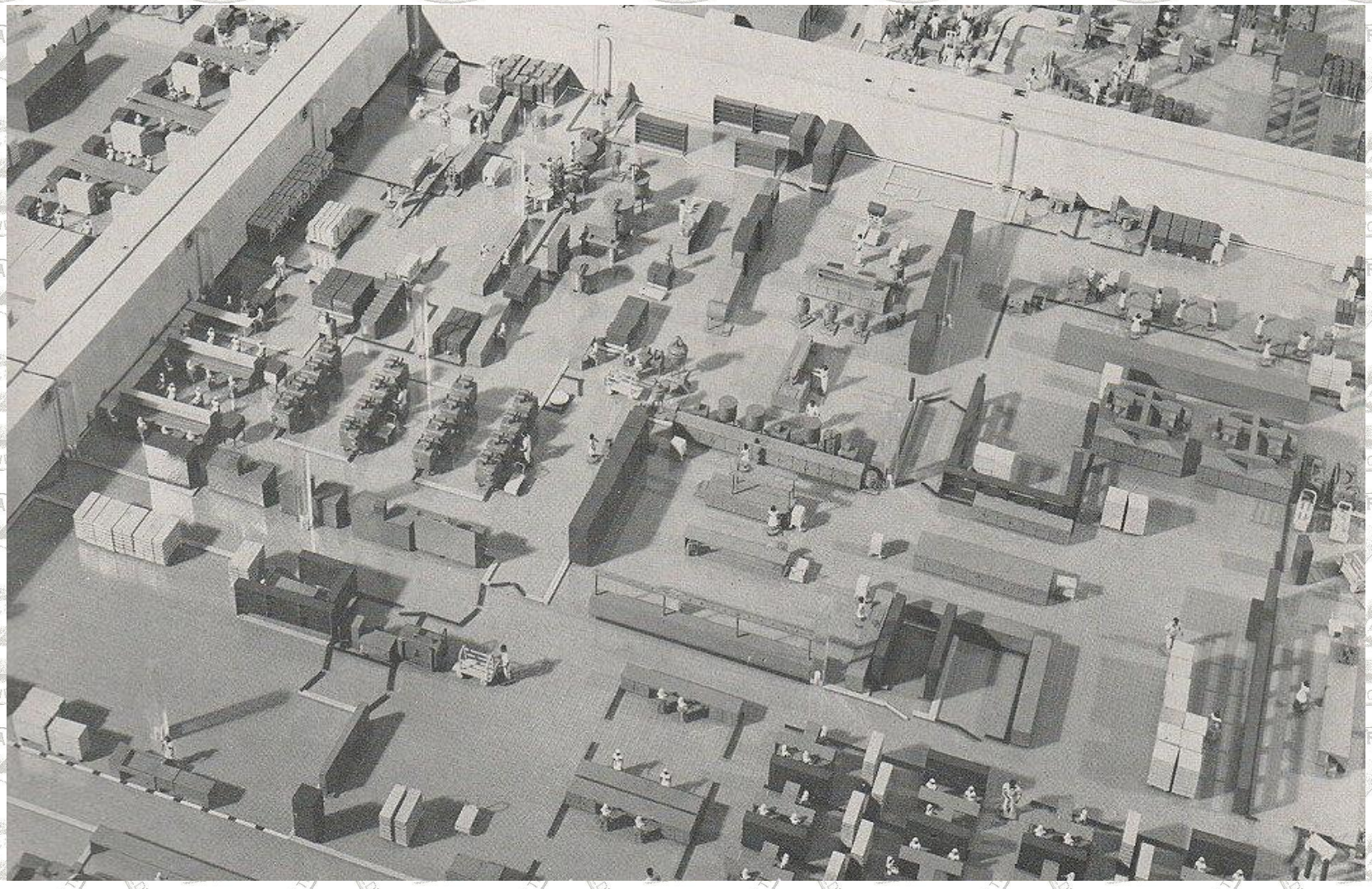


Modeling B41 Production




LOBBY

Model of the Sterile Manufacturing Department



Big Advances in Quality after WW2

- Automated production equipment was being installed
- Written instructions and documentation became standard
- Separation technologies were being introduced in the analytical laboratories
- Statistical techniques were being used to help justify a pass/fail decision

Bill Clement sends messages on their way through the pneumatic tube system.

Moving Important Paper Records in Building 41

Dangerous Ingredients Removed/Restricted

Antimony
Arsenic
Belladonna
Calomel
Cannabis
Henbane
Heroin
Mercury
Opium
Quinine
Strontium
Strychnine
Turpentine

Arrival of Computer Systems

- First mainframe computer arrived here in 1959
- By the 1980s, quality and production documents were being managed using computers
- Analytical laboratory information was gathered and processed on computers
- Quality information for production batches is stored on computer and batches are released from that information
- Computer control of equipment in production starts

The Cost of Quality

Animal protein
Brewer's feed east
Bone meal
Calcium phosphate
Ferrous gluconate
Wheat germ oil
Lecithin
Cephalin
Inositol phosphatides
Soy bean oil
Choline
Vitamin A
Vitamin D
Thiamine hydrochloride
Riboflavin
Pyroxidine hydrochloride
Niacinamide
Folic acid
Vitamin B-2

In Summary

- In the 1800s there was low quality
- Through the early 1900s, national standards and requirements for quality were put in place
- After WW2 the new Portage Plant was the catalyst for higher quality operations and products
- Automation and computers helped us achieve greatly improved quality