I started here at the Portage site with The Upjohn Company in 1980 as an analytical chemist and retired in October 2017 after 37 years. Today I want to show you that this site has a lot of special history.

- <u>Timeline of the Portage Site</u> Here are the company names associated with the Portage Site. Pfizer has owned the site for the last 17 years.
- WE Upjohn It all started with a man called William Erasmus Upjohn who was born in Richland during 1853. We know him better as WE Upjohn. He was awarded a medical degree at the University of Michigan in 1875 and became a country physician, based in Hastings. Back then a country physician went to see all his patients on horse-back. He moved to Kalamazoo in 1887. W.E.Upjohn owned the first automobile in Kalamazoo County. It was an 1899 Locomobile that was built in Newton, Massachusetts. A man in Kalamazoo called George Taylor actually bought it new but after 5 months he sold it to W.E.Upjohn. Back in 1900 there were only 8,000 automobiles in the whole country but there were 17 million horses.
- Not Just a Businessman This was an era when business leaders were also community leaders. In 1918, WE Upjohn wrote the charter for the new city government and he served as mayor. He was a very generous man, funding the Civic Auditorium, parks and exercise fields around the city. He was a fanatic about the flower called the peony. He cultivated hundreds of varieties, wrote a book on them and funded a peony garden at UOM that you can walk through today. He built one of the world's first electric clocks. He was one of the first business leaders to offer medical insurance to his employees. Clearly, he was a man with tremendous drive and inexhaustible energy.
- The Friable Pill In the 1800s, pills were so hard they usually travelled right through the patient without dissolving. This is because clay was used as the binder. Clay starts out hard and then gets harder over time. You could take

a hammer and pound these pills into a plank of pine wood and they would not break. This fact became part of Upjohn advertising. Obviously, the efficacy of these hard pills for the patient was zero. There was no FDA back then so there were no standards at all. This situation really bothered W.E.Upjohn and he started experimenting with ways to create a pill that would dissolve within the body. He became quite obsessed and one day he succeeded.

- <u>First Price List</u> The Upjohn Pill and Granule Company began in 1886. Here is the first Upjohn price list in 1886. It was one large page that listed 110 different friable pills and 50 granules. Those are impressive numbers for a brand-new pharmaceutical company.
- <u>Upjohn Products Contained</u> here are some of the active ingredients in those 1886 products. What they all have in common is they come from natural sources, either plant extracts or minerals. They were no chemical or biological syntheses back then. None. There was no chemical or biological testing either. When active ingredients arrived at the company, the three tests performed on each batch were (1) Does it look the same as the last shipment; (2) Does it smell the same; and (3) Does it taste the same. That was it!
- Cannabis also known as marijuana, was a very popular medication in the 19th and early 20th centuries, and every pharmaceutical company sold it. It can be very effective for pain relief. This Upjohn product was made from 1900 to 1931. From the batch number of 47092 I would date this one to the early 1920s. This particular bottle was originally in the collection of a country doctor. When that doctor died 7 years ago his family auctioned it on eBay and I really wanted it for my own Upjohn bottle collection. I bid \$100 for it but it sold for \$450.

So, would the cannabis in those pills still be enjoyable? It would be far too risky to take any. A hundred years has likely produced some toxic impurities inside these pills.

- Cocaine, Heroin, Opium and Morphine Cocaine, heroin, opium and morphine were also well-known and popular drugs in the 19th and early 20th centuries. Every pharmaceutical company made them simply because they were so profitable. Upjohn made cocaine and morphine products from 1886 to after 1950. They made opium products from 1893 to later than 1950 and heroin elixir was made from 1902 to 1923. These were all very addictive of course but nobody worried about that back then.
- Aphrodisiac Now let's talk about love. Upjohn sold these Aphrodisiac pills from 1886 to 1933. The batch number of 28307 on the lower right of the bottle label dates this one to 1916. Damiana is a wild shrub that grows in Mexico, Central America, and the West Indies. The leaf and stem are both used in tablets and are said to increase sexual desire. However, we have no scientific proof that it works for this.

The better-known name for Cantharides is Spanish Fly. Spanish Fly has been was in use as far back as the Romans 2,000 years ago. It is made from crushed blister beetles and this substance does cause an inflammation of the genital organs. It works but the inflammation can be painful and the dose needed to cause it is close to being fatal. Used over time it can cause liver and kidney damage. Yes, the price of love can be high.

Interestingly, at the very end of The Upjohn Company, a product called Caverject was approved by FDA in July 1995 for erectile dysfunction. Caverject contains Alprostadil, also known as Prostaglandin E1. Alprostadil acts as a vasodilator, allowing more blood to rush to the penis. It does require an injection with a small needle but it works well. Even in the era of Viagra and Cialis, Pfizer still sells this former Upjohn product today. Think of it as a modern version of Cupid's arrow.

• **Products Containing Mercury**

Mercury has been used by humans for thousands of years. Medically, it was used to treat syphilis, typhoid fever, yellow fever, parasites, constipation, mental health conditions and others. From the 17th to the 19th century, a mercury formulation called Blue Mass was sold throughout this country. It was taken in either pill or syrup form and was 33% mercury in either elemental form or mercury chloride.

Many companies and formularies made Blue Mass products. Here is an Upjohn bottle from the 1890s. The strength is 3 grains of Blue Mass. 1 grain equals 65mg so 3 grains of Blue Mass is about 65mg of mercury per pill. People who took two of these pills per day had a mercury level in their bodies that was 1000 times higher than today's safe limit. That is mercury poisoning and when poisoning symptoms occurred they were usually blamed on a worsening of the original disease. This particular product was made by Upjohn from 1886 to 1925. A 39-year lifespan indicates this was a good seller for the company. You can see on the label the original name of the company, which was "The Upjohn Pill and Granule Company". They used this name until 1902.

It's well-known that Abraham Lincoln took Blue Mass pills for several years to treat what was then called melancholy. Today we would call it depression. However, when taking Blue Mass, he was prone to erratic behavior and violent outbursts. He recognized this and stopped taking the pills, which was a good thing. Nobody wants a president prone to erratic behavior and outbursts.

Mercury was also formulated in ointments for rubbing onto the skin. Here are a few examples. Note the top one contains 30% mercury. These were used to soothe skin irritations such as eczema, psoriasis, impetigo, also sores caused by syphilis, herpes viruses and others. In 1890, Upjohn offered 16 different ointments containing mercury, the highest level of mercury being 50%.

<u>Corrective Infants</u> – Mercury wasn't just for adults. Oh no, It was given to infants too, as shown here. The term Corrective on the bottle simply means correcting a health problem. Looking at the other ingredients on the label it seems like if an infant had an upset stomach this was a treatment option. Mercury was used for teething pain also. Hopefully those infants got over their problems quickly before mercury poisoning hit them.

I looked through an 1890 Upjohn catalog and found 43 products containing mercury, the amount of mercury ranging from 1/1000 of a grain to 5 grains. A couple of interesting combinations were mercury and opium, and mercury and rhubarb extract. In a 1942 Upjohn catalog, there were 62 mercury-containing products. Thankfully by 1960 there were none.

• Quinine Pills (QUY-NINE)

Quinine used to be the first choice for treating malaria, which is a bad fever caused by the bite of a mosquito that has the disease. Quinine pills were huge sellers for the Upjohn Company and many other companies. At one point, quinine pills were 40% of total Upjohn sales. They sold so much that Upjohn was known as the quinine company.

In the 1800s, almost everyone in Michigan had malaria because of all the wetlands in the state. It was said on the East Coast at that time "Don't go to Michigan, that land of ills, the word Michigan means aches, fever and chills." It was not until most of the wetlands were drained that malaria was no longer seen in Michigan.

Malaria was a world-wide problem at that time, making quinine pills a global seller. Every explorer heading out to Africa, Asia or South America was sure to take a good supply of these pills. The small metal cases you see here helped to securely transport the pills across rough country.

Upjohn sold 41 different formulations of quinine pills and 24 different formulations of quinine tablets between 1895 to 1949. However, quinine has some serious side effects so it's now the third-choice option for treating malaria.

• Eczema lotion

Eczema, also known as dermatitis, is a group of diseases that causes inflammation of the skin. Symptoms that people get include itchiness, redness or rash. I know when my skin is irritated, I really appreciate a soothing lotion to rub on it. Alas, there isn't much soothing in this 1925 bottle of Upjohn Eczema lotion. It contains hydrocyanic acid, which is the liquid form of hydrogen cyanide, a deadly gas. It also contains nitric acid, which is a powerful acid. Then there's mercuric chloride. Thank goodness for glycerin. At least that would be soothing. I really think this is chemical warfare on tender skin. The bottle is labeled poison but patients were supposed to rub it on their skin anyway. They were tough, tough people back then!

By the way, I found the exact date that this bottle was filled. There are half-a-dozen Upjohn production log books that survived from the 1920s and 1930s. From the batch number on the label I could track it to a manufacturing date of January 3rd, 1925.

• Hematic tonic – the word hematic refers to blood. A tonic is supposed to perk you up, right? At the top of the ingredient list here is Blaud, which is a formulation of ferrous sulfate. It is named after Pierre Blaud, a French doctor who introduced iron pills in 1832. Also on the list are arsenous acid, mercuric chloride and strychnine sulfate. So, this tonic, which was supposed to perk you up, contained arsenic, mercury and strychnine, which are two toxic metals and a deadly poison. This particular Upjohn product was made from 1920 to 1929.

Why would anybody take these pills? A major homeopathic principle back then was that a very small quantity of poison will really stimulate your immune system. Fortunately for us, that principle has been long debunked. Since there used to be no clinical testing and no FDA to regulate products, companies could sell anything they wanted. It didn't matter if a product worked or not, or what the side effects were. There were no rules at all

until 1906 when the Pure Food and Drugs Act was enacted. However, FDA in its current form did not exist until 1920 and only then was there the start of a big push to eliminate all the harmful products and products that had no therapeutic effect. It took until the 1980s to complete this.

Chocolate Coated Tablets – I love chocolate, especially Ghirardelli. Upjohn chocolate-coated a number of products, such as these creosote and iodine tablets. This particular product was made from 1905 to 1946. The ingredients were bitter tasting and the chocolate coating was intended to get children to swallow the tablets. It amazes me how well the chocolate coating has lasted. This bottle is at least 70 years old but the chocolate looks to be in perfect condition.

• Pantomime Candies

Upjohn's entrance into the world of candies was done with the help of noted Kalamazoo candy maker Bert Kitchen in late 1920. The box was colored a rich brown and shows a group of partiers but I'm not aware of any of these boxes having survived. Alas, only one batch of Pantomime Candies was ever made in the Upjohn factory. The chocolates were said to be tasty but had a hint of "pharmaceutical odor". The project was promptly cancelled and the 800 pounds of chocolates created never made it to store shelves. They were instead given to employees on May 6th 1921 to celebrate the birth of a daughter to company treasurer John S. McColl.

- <u>Early Expansion</u> With pills that dissolved in the body, Upjohn became very successful. By 1904 the company price list was 192 pages long. More buildings in Downtown Kalamazoo were either bought or built by the company. Eventually the Upjohn triangle was formed downtown, which was all the land between Lovell St, South St and Portage Rd. This included a company power plant. All the buildings shown here are Upjohn buildings.
- Major New Buildings Shown here are the production tower, Building 25,
 with the headquarters building in front of it, Building 24. They were both

built in 1934-5. These were major buildings and both paid for entirely out of earnings. No loans were needed. That tells you how successful the company had become. B25 was demolished in 2007 and B24 is now used by Bronson Hospital. Do you see The Upjohn Company spelled at the top of the lower building? That's still there today.

- <u>Late 1930s Production</u> However, you can see from this late 1930s photo, production in the tower during that era was cramped. During World War II it became obvious the company needed a major expansion of manufacturing facilities. Company leaders considered building upwards in Downtown Kalamazoo but decided to buy a spacious site in the country.
- <u>Building of the Portage Site (7 slides)</u> In 1946 1,500 acres of land were bought on Portage Road, the location of our current manufacturing site. At the time the city of Kalamazoo stopped at Cork St and there was no city of Portage, just Portage Township. On postcards from that era the new site is described as being near Vicksburg.

This is the first conceptual drawing of the major buildings on the site. Construction started in 1946 and it took 5 years to complete it. It cost \$32 million to build the entire site, all paid for out of earnings. No loans were needed. Building 38 opened in 1948 and the site was fully opened by April 1951, so we have been manufacturing here for 71 years.

• Grinding Adrenal Glands – the Portage site was now in operation but chemical and biological syntheses were not here yet. In the early 1950s photo we have an Upjohn employee in Building 39 grinding adrenal glands from cows. This was the first step in extracting cortisone from them. It took a huge number of glands to make a little cortisone and the final product was very expensive. I can't help but wonder how bad this grinding operation smelled. I'm pretty sure the newest employee got this job.

During the 1950s Upjohn brought in chemical syntheses and biological fermentations on a large scale. This was truly a revolutionary advance. Suddenly, steroids could be made in large amounts at low cost. For the first time, patients could afford them. By 1960 the big products of the company at this time were steroids like cortisone, progesterone, methylprednisolone, prednisone and hydrocortisone. It also made antibiotics like neomycin, streptomycin and lincomycin. Business was booming. BTW, we started making Gelfoam in 1946, Heparin in 1950 and Solu-Medrol in 1957.

- <u>Upjohn Buses</u> every employee at the new Portage plant lived in the City of Kalamazoo, which stopped at Cork St, and not everyone had an automobile in the early 1950s. Thus, the company bought buses to shuttle people from Kalamazoo to work at the new plant in Portage. The fleet of Upjohn buses eventually grew to 15.
- <u>Barbers Shop</u> Because the Portage Site was so far from the city, a barbers shop, a pharmacy and a check cashing service were provided on site. All of these lasted into the 1980s and I can remember using them. I got my hair cut in the basement of Building 41.
- The Upjohn Airforce in 1956 Upjohn bought their first plane and build a company hanger at the Kalamazoo Airport. The goal was to fly executives and high-level employees around the country as needed. In 1959 a Grumman Gulfstream that held 16 passengers was added. By the mid-1980s there were 4 planes and 7 pilots. 1100 employees per month used the planes. Everyone called it the "Upjohn Airforce". You can still see the hanger today as you drive north on Portage Road.
- <u>Upjohn Awards</u> When W.E.Upjohn died in 1932, he set aside a large block
 of Upjohn stock to fund an annual award for employees. These were the
 Upjohn Awards. It truly was an honor and the high-point of a career to get
 one. In the 1980s there were 40 to 50 awards made each year, and each

recipient would have received a check for as much as 7 thousand dollars.

- <u>Public Tours</u> From 1960 to 1989 there were organized tours of Building 41 that the public could take. Tour participants started in a museum at the west end of the basement (right next to the concourse), climbed to the first floor and walked to the East end through manufacturing, then returned to the museum via the basement. They viewed sterile filling, tablet compressing, fluid production, packaging, sterile inspection and all the supporting shops. Participants ended up in the cafeteria for refreshments. These tours were very popular. Busloads of people arrived daily to take a tour and part of orientation for new employees was taking a tour. The top photo is of the tour guides in the mid-1960s.
- Upjohn in Disneyland Walt Disney was a neighbor and close friend of Donald Gilmore, the CEO of Upjohn during the 1940s and early 1950s. It was natural when Walt was planning the construction of Disneyland in California, he would include an old-time pharmacy run by Upjohn. This was not a real pharmacy. It featured a lot of historic items. Disneyland opened in July 1955 and the Upjohn pharmacy was a popular exhibit. The pharmacy closed in 1972 when the company felt it had served its purpose.
- <u>Centenary in 1986</u> The centenary of The Upjohn Company was in 1986.
 There were 19 nights of parties for employees at the Hilton Hotel in
 Downtown Kalamazoo. The Hilton later became the Radisson. At this time,
 the definitive book on The Upjohn Company "A Century of Caring" was
 published. Nine years later in 1995 The Upjohn Company ended when it
 merged with Pharmacia to form Pharmacia & Upjohn.
- <u>Consumer Products</u> In the 1980s the consumer products some of your parents or grandparents may still talk about were being made here in Portage – Kaopectate, Mycitracin, Unicap, Cheracol, Cortaid, Motrin and

Pyroxate were the most popular ones.

- <u>Vanilla</u> Vanilla is a unique Upjohn product. It was only for sale to company employees. The story I was told was that Martha Parfet, wife of 1970s Upjohn CEO Ted Parfet, used a lot of vanilla in her cooking but could never find a good quality source of it in town. You know that saying "Happy wife, happy life"? Ted needed to do something and since The Upjohn Company already used large quantities of vanilla-flavoring in products like Kaopectate, the materials were already in-house. It didn't take much effort to formulate and bottle it. This Vanilla product was made available to all employees across the world. It really was a popular product because batches were made through the 1970s and 80s. It was discontinued in 1990.
- Rennet Here's a more recent unusual product. Rennet is an enzyme used to coagulate milk in order to form a thick curd. It is used primarily in cheese-making. A maker of kosha cheese products in Wisconsin contracted with Upjohn in the 1990s to produce rennet by fermentation at the Portage plant. Before any batches were made, a rabbi arrived on site to koshercertify all the fermentation equipment and all the ingredients used. A tanker truck was driven down from Wisconsin to pick up each batch of kosher rennet. This contract lasted for 2 years.
- <u>Rogaine</u> I'm going to end with Rogaine. The active ingredient in Rogaine is Minoxidil, which was originally used to treat hypertension. Surprise those hypertensive patients started growing hair and The Upjohn Company took notice. It was claimed at the time that 35 million men and 20 million women in the US were losing their hair, a huge market to sell to. Some analysts believed that Rogaine could be one of the biggest selling drugs ever.

It became available for men in 1988 and for women in 1992, both by

prescription. In 1996 Rogaine was made available over-the-counter, so no prescription was needed anymore. Alas, it never became a true blockbuster product and in 2006 Pfizer sold Rogaine to Johnson & Johnson.

Everything I've shown you is on the website www.upjohn.net. This site has 800 web pages, over 15,000 images and 19 videos. Anyone in the world who can access the internet can see it and I'm always adding more information to it. Any questions?

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