Non-Thermal Effects of Radio Frequency Exposure on Biologic Pharmaceuticals for RFID Applications

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Abstract— **Radio frequency identification (RFID) has been an emerging technology over the past decade with applications ranging from simple supply chain utilizations to sensory monitoring of heat and humidity sensitive products during transportation. RFID has direct implications for the area of pharmaceutical distribution especially for temperature sensitive products where they are tagged and tracked in their shipping environment. Per FDA CPG Sec.400.210, Drugs, Radiofrequency Identification, the FDA has not allowed RFID technology to be used for drugs covered under a Biologics License Application or protein drugs covered by a New Drug Application since the potential impact of radio frequency (RF) radiation on biologics and proteins is not well documented. The intent of this study is to determine the non-thermal effects on the protein structures of biopharmaceuticals by constant exposure to radio frequency energy at different wavelengths using twice the equivalent isotropically radiated power (EIRP) allowed by FCC in the United States. As a contribution of this study, the test setup and protocol provide a fundamental and universally applicable methodology which combine the hardware to generate and radiate high power RF signals at different frequencies and a temperature controlled dark anechoic chamber where the temperature and light sensitive products can be exposed to RF radiation. Five different frequencies are used which account for the majority of commercially available RFID systems adopting high frequency (13.56 MHz) or ultra-high frequency (433 MHz, 868 MHz, 915 MHz, and 2.4 GHz) radio waves as well as active or passive tags for communication. Multiple products from different pharmaceutical companies falling under three major protein groups and their integrity after exposure to 8 Watts EIRP RF radiation for a full 24 hours are investigated. The results show that even at twice the EIRP as regulated by FCC, the effects of RF energy on the purity of all the tested biopharmaceutical proteins remain undetectable after purity and potency stability-indicating assays.**

I. Introduction

Radio frequency identification (RFID) is a technology tool which holds great promise of enhancing or in some cases replacing current identification technologies such as the bar code [1]. Just like the universal product code (UPC) in bar codes, RFID systems use electronic product codes (EPC) in tags that are unique to individual items, cases or pallets, unlike UPC which is unique to a product. RFID tags are being used to improve visibility through supply chains to monitor and control the product flow. At specific check points throughout the supply chain, tags are interrogated by RFID readers to get information about the shipment which is only limited by the capabilities of the tag. In other words, the information can range from the item ID, production date and first day of shipment to the entire temperature or humidity profile of the environment that the product is exposed to. Every object in the supply chain is characterized by a unique serialized number that can be tracked in real time, which provides an invaluable advantage for pharmaceutical supply chain in particular by augmenting the e-pedigree requirement introduced by the FDA to prevent counterfeit drugs on the market [2].

Furthermore, recent years have seen an increase in research and development of sensor based RFID systems such as tags that sample and log temperature during the shipment of a product [3]. Especially for temperature sensitive products like fresh produce and pharmaceutical drugs, knowing the environmental profile of a specific shipment is important. In the case of fresh produce, this enables multiple scenarios which include intelligent rerouting of goods based on the remaining shelf life or product quality. In the case of temperature sensitive pharmaceutical drugs, an even bigger challenge exists, where one needs to know the quality of the drug to prevent a life threatening situation. Currently most pharmaceutical companies and distributors use non-RF based solutions, such as simple temperature loggers, to monitor their supply chain temperatures. However, RF temperature tags would enable real time access to temperature information and events that can otherwise be downloaded and analyzed offline only after the shipment takes place.

Currently, FDA has not allowed the biologic drugs covered under a Biologics License Application (BLA) or protein drugs covered under a New Drug Application (NDA) to use RFID

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applications due to concerns that RF radiation would affect the integrity of the protein structure of these biopharmaceuticals [4]. However, our hypothesis suggests that the wavelength of RF radiation is too large to create a resonance big enough to alter the protein structure of the drug [5]. In this paper, we investigate the effects of RF radiation on various biologic drugs which include either of the three major protein structures–vaccines, hormones and immunoglobulins–at 5 different frequencies using 8 Watts of equivalent isotropically radiated power (EIRP) which is twice the power approved by FCC for radio frequencies. In order to accomplish this, we present a test setup and protocol to determine the impact of RF radiation on the purity of biologics using techniques such as high-pressure liquid chromatography and immunoelectrophoresis [6].

The remainder of this paper is organized as follows. In section II we state the hypothesis that drives the research in this paper. In section III, we discuss the hardware to generate RF signals and the overall test setup to be used in the anechoic chamber for a product's optimal exposure to RF radiation. The methodology, test protocol and specific system parameters are explained in more detail in section IV. Section V provides further information on the types of drugs and proteins used in the experiments and briefly describe the purity test after exposure. Finally, the results and conclusions are presented in sections VI and VII.

II. Radio Frequency Exposure and Biologics

The effects of radio frequency exposure on biologics, similar to other types of electromagnetic (EM) radiation, can be analyzed in two groups: thermal and non-thermal [7]–[9]. The thermal effects arise from a noticeable change in the temperature of the product under RF exposure which is comparable to a change in temperature caused by conventional heating. In the case of pharmaceuticals, the correlation between temperature and drug stability and subsequently the thermal effects of RF radiation are well understood.

Product heating depends on a few factors such as the frequency of the EM source, the dielectric constant, the contents of the water and the overall thickness. For instance, products greater in conductivity are more likely to absorb greater amounts of radiation which in turn generates more heat. Recent research documents the thermal effects of RF exposure on drugs at various frequencies in greater detail [10].

In addition, some studies suggest that there are reactions to RF exposure on substances that cannot be explained by thermal heating, since these non-thermal effects occur without a significant increase in the product temperature after the exposure [11]. The goal of this paper is to study the non-thermal effects which arise in the protein structure of biologic drugs using three major protein categories under RF exposure at different frequencies and various types of purity and stability testing such as immunoelectrophoresis (IEP), high performance liquid chromatography (HPLC), etc. to analyze the purity of the drugs before and after the RF exposure.

Since the purity analysis of the protein cannot differentiate between different types of effects (thermal, non-thermal), in order to study non-thermal effects specifically, one must ensure the change in product temperature during the exposure remains within the required limits to not cause any thermal effects on the drug. Figure 1 shows the change in temperatures of 3 vaccine products (a type of protein used in the experiments) for a 24-hour exposure to 915 MHz RF radiation at 8W EIRP which is twice the amount allowed by FCC for radio frequencies. The impulses in the plot show the cold cycles of the chamber. The chamber sensor measures the temperature of the chamber at the furthest point from the thermal unit whereas the products are located in the middle of the chamber. As the plot shows, after a full 24 hour exposure to RF radiation, the temperature of each vaccine remains within acceptable limits to not cause any thermal effects. The same experiment has been performed for each tested frequency from 13.56 MHz to 2.4 GHz and the results were similar, indicating that there won't be a measurable thermal effect in any of the tested products.

In order to understand the effects of EM radiation on biologics, one needs to look at the structure of a protein and the relation between the frequency of the EM wave and the dimensions of the protein. The largest dimension in a typical protein is 50 Å in size where $1\mathring{A} = 10^{-10}\ meters$. Figure 2 shows a typical sinusoidal wave defined by its amplitude and wavelength. In order for an EM radiation to affect the protein, it needs to create a resonant reaction in the structure of the protein which requires the wavelength to be in the same order of magnitude with the dimensions of the protein or less. The relation between the wavelength and the frequency of an RF signal is defined by the following formula;

$$f = \frac{c}{\lambda}\ or\ \lambda = \frac{c}{f}$$

where f is the frequency in Hz, c is the speed of light in meters per second and λ is the wavelength in meters.

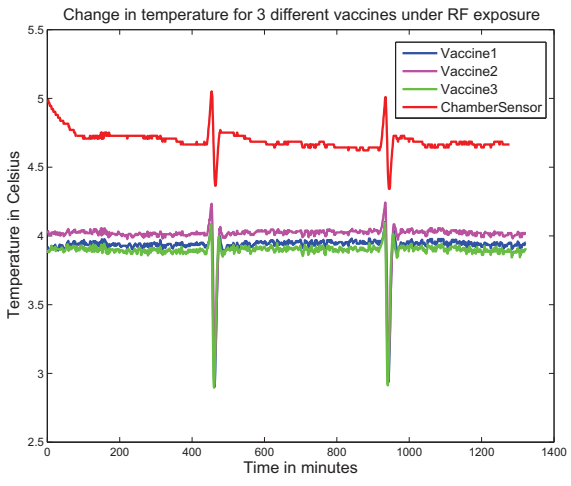

Fig. 1. Change in product temperatures at 915 MHz frequency with 8W EIRP when compared to the control temperature of the chamber

As one moves up the EM spectrum the frequency of the signal increases and the wavelength decreases. For the extreme example of Gamma ray radiation and a typical frequency of $10^{20} Hz$, the wavelength is;

$$\lambda = \frac{3x10^8}{10^{20}} = 3x10^{-12}\ meters = 0.03\mathring{A} \ll 50\mathring{A}$$

which is much less than the typical size of a protein of 50Å which supports the well-known fact that Gamma ray radiation will result in cell genomic alteration [12]. In comparison, the highest frequency used by some of the common RFID systems is 2.4 GHz. Similarly, the wavelength of such a signal is;

$$\lambda = \frac{3x10^8}{2.4x10^9} = 1.25x10^{-1}\ meters = 1.25x10^9\mathring{A} \gg 50\mathring{A}$$

which is much bigger than the typical size of a protein of 50Å to cause any resonant changes in the overall structure integrity.

This discussion supports the hypothesis that RF radiation, especially within the EIRP levels regulated by FCC won't have an impact on the purity of the biopharmaceutical products. In this paper, we describe an experimental protocol and methodology to test this hypothesis and provide results on the non-thermal effects of RF exposure on biologic pharmaceuticals.

III. Test Setup

The overall test setup is composed of four building blocks:

- Overall hardware responsible for generating high power RF signal at 5 different frequencies (13.56 MHz, 433 MHz, 868 MHz, 915 MHz, 2.4 GHz)
- Five antennas to propagate these signals to expose biopharmaceuticals to RF radiation
- A temperature controlled anechoic chamber as the test environment
- A test table with two adjustable planar surfaces to house the antenna and hold the products within the antenna's radiation field.

Since all the products to be tested are temperature (and in some cases light) sensitive, a special anechoic chamber has been employed which is also a dark temperature controlled room as shown in figure 3.

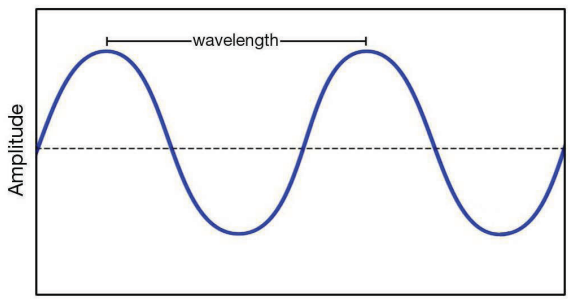

Fig. 2. A sinusoidal wave as defined by its amplitude and wavelength

The remainder of this section presents these individual components in more detail.

A. Hardware Setup

The main goal of the hardware is to create an RF signal at a specific frequency with a desired power spectrum to imitate a commercial RFID reader output but at a much higher power to generate twice the EIRP at the output of the antenna allowed by FCC in the United States. The setup of electronic hardware follows a similar outline with the one in [13] with a few differences based on the physical location of the hardware and the temperature controlled anechoic chamber. Figure 4 shows the block diagram for hardware selection and connections in greater detail.

1) Function Generator: This device is responsible for creating the baseband signal to model the data encoding and modulation done by the reader to communicate with the tag. Even though every protocol uses a different way of encoding, in terms of power spectrum they can all be modeled in a similar fashion. For instance, in the non-return to zero (NRZ) encoding scheme, the signal moves between a high and a low logic level depending on the data input at positive clock transitions. If the data is 0, output's logic level is switched, whereas if the data is 1 output's logic level remains the same.

In a typical communication setting it is safe to assume that throughout the entirety of transmission the probability distribution of high and low logic levels will be uniform, which means the encoding scheme in this case can be modeled by a pulse train with a 50% duty cycle. In this experiment, we have used a 120 MHz programmable direct digital synthesis function generator manufactured by BK Precision (model number BK 4087).

2) Signal Generator: The signal generator serves as the real source of the RF signal by taking the baseband signal coming from the function generator and carrying it to high (HF) and ultra-high frequency (UHF) range to create a low power

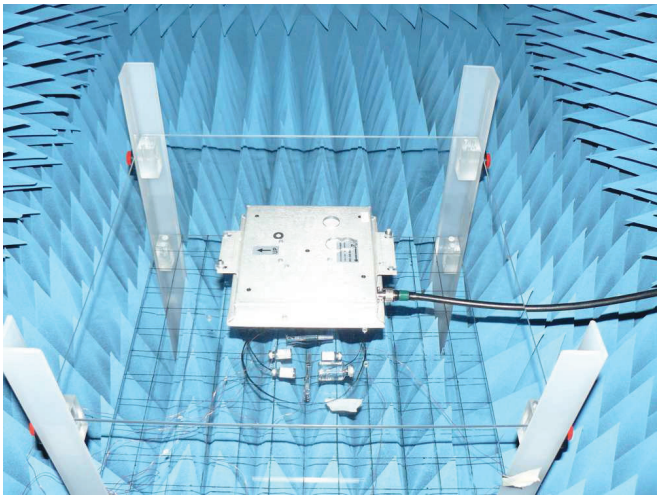

Fig. 3. The temperature controlled anechoic chamber that is used as the test environment in this experiment

representation of an actual RFID reader signal. The baseband signal coming from the output of the function generator is supplied to the pulse modulator input of the signal generator to provide a pulse train input with a 50% duty cycle. In this experiment, we have used Agilent's N9310A signal generator with a 9 kHz-3 GHz range to cover all 5 frequencies (from 13.56 MHz to 2.4 GHz) that will be applied to the different types of pharmaceutical products.

3) Power Amplifier: As one of the most crucial elements of the overall system, the power amplifiers amplify the low power RF signal coming from the signal generator before inputting it to the antennas. The goal of the experiment is to expose biologic drugs to RF radiation of at least 8W EIRP, twice the EIRP allowed by the Federal Communications Commission (FCC), and accordingly the power amplifiers need to be able to supply the required power levels to the antennas. Since the experiment protocol covers a very wide range of frequencies from 13.56 MHz to 2.4 GHz, two different power amplifiers were used to amplify different frequencies successfully. In order to amplify frequencies between 13.56 MHz and 915 MHz, we used a custom made 50W linear power amplifier with 1-1000 MHz frequency range from OphirRF (model number 5803039A-001). Similarly, in order to amplify the highest frequency RF signal, 2.4 GHz, another custom made amplifier from OphirRF (model number 5803081) with a 10W linear gain between 1-2.5 GHz was used. In order to minimize the cable loss between the power amplifiers and the antennas, they were connected with a 50 foot LMR400 cable (to cover the distance between the hardware station and the anechoic temperature chamber).

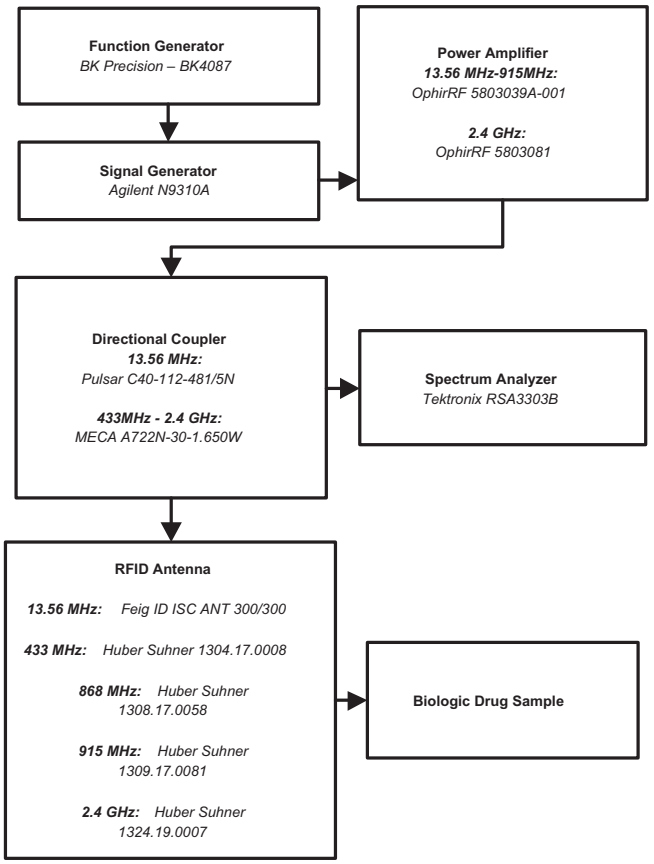

Fig. 4. The overall block diagram of the hardware used to generate RF signals at different frequencies with different power spectrums

4) Directional Coupler: The directional coupler, as its name implies, couples the same high power RF signal between the power amplifier and the antenna to the spectrum analyzer (power meter), to ensure that throughout the 24-hour exposure, there is no loss in the RF power level that might affect the outcome of the experiment. Similar to power amplifiers, due to the wide range of frequencies covered by the experiment, two different directional couplers have been used to cover all 5 frequencies. A 722N-30-1.650W model coupler from MECA Electronics has been used to cover frequencies between 433 MHz and 2.4 GHz, while a C40-112-481/5N coupler from Pulsar Microwave was used for the HF signal of 13.56 MHz.

5) Spectrum Analyzer: The purpose of the spectrum analyzer is to detect peak power levels at any given frequency, and with the help of the directional coupler, to record the RF signal going into the anechoic chamber for the duration of exposure. A Tektronix, 0-3 GHz, real time spectrum analyzer (RSA3303B) with 65.5 million sample deep memory has been used for measurement and recording in the experiment.

6) RFID Antennas: For each UHF experiment, we used circularly polarized antennas, whereas for HF exposure we used a square loop antenna manufactured by FEIG to ensure it can withstand input power levels of up to 8W.

- For 13.56 MHz, a square loop antenna from FEIG Electronics with model number ID ISC ANT 300/300 was used which allows for a maximum of 8W transmitting power
- For 433 MHz, a circularly polarized Huber Suhner antenna with 9dBi gain was used (model number 1304.17.0008)
- For 868 MHz, a circularly polarized Huber Suhner antenna with 8.5dBi gain was used (model number 1308.17.0058)
- For 915 MHz, a circularly polarized Huber Suhner antenna with 8dBi gain was used (model number 1309.17.0081)
- For 2.4 GHz, a circularly polarized Huber Suhner antenna with 8.5dBi gain was used (model number 1324.19.0007)

Due to the fact that each antenna has a different gain factor, the output of the signal generator must be separately adjusted for each frequency. In the methodology and system parameters section, this process will be described in further detail.

B. Chamber Setup

Since most biologic drugs typically have very specific environmental requirements during their transportation and storage, such as light and temperature the test environment had to possess three important properties:

1) It should be anechoic, or in other words RF proof. This means that no outside RF radiation (such as local Wi-Fi

network communication or Global System for Mobile Communications or radio waves) can come in and no RF radiation created inside can leave the chamber. In addition, the RF radiation created by the antenna is absorbed by the walls and not reflected.

2) When the chamber door is closed, it should be completely dark inside to ensure that the light-sensitive drugs are properly stored during RF exposure.
3) It should be temperature controlled such that different drugs with varying temperature requirements can all be tested within the NDA or BLA requirements.

The ultimate goal of this research is to explore the changes in the protein structure of different biologic drugs only due to RF radiation while eliminating the effect of other factors such as heat and light. In order to achieve this we used a validated cold room in the Center for Food Distribution and Retailing labs of the University of Florida with variable temperature controls and a light-proof door. To make the chamber anechoic, we used ECCOSORB VHP-NRL, a very high performance broadband material which is a solid, pyramidal shaped, carbon loaded urethane foam absorber from Emerson & Cuming Microwave Products. As shown in figure 3 the walls, the ceiling and the floor of the chamber is covered entirely with this anechoic material to absorb RF radiation inside the chamber.

IV. Methodology and System Parameters

In this section we will discuss the overall test protocol, methodology and how we decided on important system parameters such as the signal generator power level for different frequencies.

A. The Dimensions and Distance of the RF Exposure Plane Relative to the Antenna

We designed an RF-lucent table with two adjustable parallel planes to place the products on the bottom plane and to affix the antenna on the top plane as shown in figure 5.

In regards to the antenna and product placement there are two critical parameters that need to be adjusted such that the drugs are exposed to the maximum possible RF power while still allowing for as many products to be tested as possible at one 24-hour cycle exposure:

- The distance between the parallel planes, i.e., the vertical displacement between the antenna and the products.
- The area of optimal exposure on the bottom plane, i.e., the radius beyond which the RF power falls below 90% of its peak value in the center of the plane.

After taking measurements for all five frequencies using the spectrum analyzer, it was found that the peak power had a significant roll-off after 20cm confirming the previous results of other researchers [10]. Hence, the distance between the two parallel planes has been fixed at 22cm where 2cm accounts for the antenna thickness which is quite uniform between frequencies.

Figure 5 shows the isometric view of the table configuration used for the measurements. With vertical distance fixed at 20cm, we placed a 12 x 12 grid on the bottom table to measure the RF power at 144 unique points along the plane. The goal was to find the peak power and the points beyond which the power fell below 10%, 15% and 20% of the peak power. Table I shows the radial distance of the points that correspond to the above power drops:

TABLE I

RF POWER MAPPING TEST RESULTS FOR FIVE DIFFERENT FREQUENCIES SHOWING THE RADIAL DISTANCE BEYOND WHICH THE POWER FALLS BELOW 10%,15%,20% OF ITS PEAK VALUE OVER THE PLANE

Frequency \ % of peak power	80%	85%	90%
13.56 MHz	16cm	14cm	12cm
433 MHz	14cm	12cm	10cm
868 MHz	18cm	15cm	12cm
915 MHz	17cm	15cm	11cm
2.4 GHz	19cm	15cm	12cm

Based on the findings in Table I, we have decided to pick a circle of 20cm diameter to place the products on the bottom plane in order to ensure at least 90% of the peak 8W EIRP RF power is applied to all the pharmaceuticals on the table. Hence, both the vertical distance from the table and the diameter of the radius in which the products will be placed have been chosen as 20cm for all frequencies. This is a safe assumption for a typical use case concerning an RFID system application, as well, since even in the worst case scenario where the case or the pallet stops on the conveyer belt right next to the antenna, the total distance between the belt and the antenna will be greater than 20cm.

B. Signal Generator Output Power Tuning

This section deals with how we tune the signal generator output power for the five different frequencies that will be used in the tests, to make sure the EIRP at the antenna is exactly

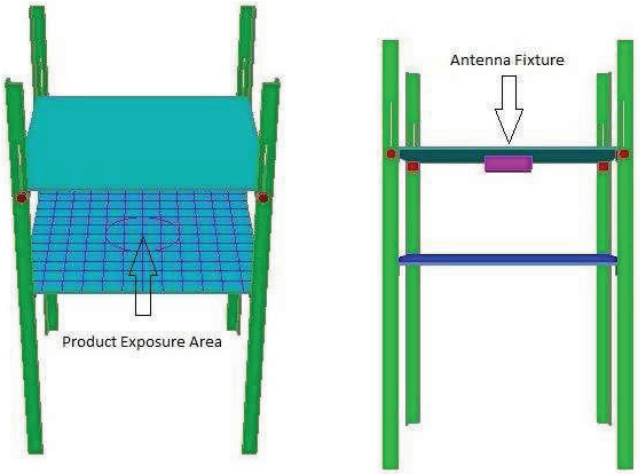

Fig. 5. The isometric view of the table configuration used for the RF power measurements across the test plane

8W (double the amount of 4W that is currently allowed in the US). It is necessary to remember that:

- FCC has approved a maximum of 4W EIRP for RF frequencies for commercial applications.
- The goal of this experiment is to show that even at double the power level (8W EIRP) there will be no non-thermal effect on the protein structures of hormones, vaccines and immunoglobulins.
- The product of the transmitter power times the antenna directivity is called EIRP.
- The calculation of EIRP is performed as follows:
  1) $EIRP = P_t - L_c + G_a$, where P_t is the power of the transmitter (output power of the RFID reader in case of a commercial application), L_c is the cable loss and G_a is the antenna gain in decibels over isotropic (dBi).
  2) Since we need 8W EIRP this equals $10 * log(8) = 9dB$ which in turn is equal to 39dBm.
  3) In other words, including the antenna gain for each frequency, we need an output power of 39 dBm.
  4) Instead of a commercial reader we have set up our own system consisting of a function generator (for the RF baseband signal), a signal generator and two RF amplifiers so that we can successfully simulate a typical RFID reader signal and adjust the output power as we need by using the signal generator variable amplitude.
- We have set up the experiment such that the spectrum analyzer is connected to the end of the coaxial cable which is connected directly to the antenna. By doing so we are including the overall cable / connector loss in the whole system in our measurements without the actual need to measure them separately.
- Hence, we expect our $EIRP = PSA + G_a + 30dBm$ where PSA is the power measured by the spectrum analyzer in dBm. The reason we are adding 30 dBm is because of the fact that we are using the 30 dBm attenuated output of the directional coupler for the spectrum analyzer in order to prevent damage to the device (spectrum analyzer).
- Since the antenna gains will be different for each frequency setup, we had to calculate the exact output power of our signal generator in order to satisfy the 8W (39 dBm) EIRP requirement.

Based on the above test setup and protocol, the signal generator output power levels were adjusted accordingly for each frequency such that the output of each antenna is exactly 8W EIRP.

The final part of the testing protocol involves the specifics of the transportation of products between the pharmaceutical companies that are participating in this experiment and the University of Florida. The temperature of each product is monitored during each shipment and both the anechoic temperature chamber and the chamber used for storing the products between tests have been validated.

C. Test Procedure

Based on the information discussed in Section III.A and III.B, the complete test procedure can be summarized as follows. Please note that the below procedure is specified for each product type and must be followed for all five frequencies separately.

1) Pharmaceutical company ships six samples (one for each of the five frequencies) for RF exposure testing to the University of Florida (UF) with non-RF temperature loggers. 5 of these samples are exposed to RF and one of the samples is used as a non-exposed control sample.
2) UF receives the samples and controls the logged temperature data to confirm the products stayed within their required temperature range.
   - IF the temperature log data indicates otherwise, UF ships the products back to the company and request new samples.
   - ELSE the products are placed in temperature validated storage chambers until their RF exposure test.
3) Validate the temperature controlled, dark anechoic chamber where the RF exposure tests will take place.
4) Place the products inside the chamber on a table as described in detail in section III.A.
5) Seal the chamber and turn on the RF hardware for a specific frequency, say 13.56 MHz.
6) Adjust the signal generator output power level as described in section III.B and check the spectrum analyzer to observe the required power output level at the input of the antenna such that at the output you observe 8W of EIRP.
7) Run the test for a full 24 hours before turning off RF hardware. Log the antenna input signal for the duration of the test.
   - IF the logged data shows continuous power application throughout the test, remove the products from the chamber and put them in the storage room.
   - ELSE request new samples from the pharmaceutical company to re-administer the test.
8) For each of the five samples, follow steps 4 through 7 for the other frequencies, in this case, 433 MHz, 868 MHz, 915 MHz and 2.4 GHz.
9) Ship the exposed products back to the pharmaceutical company using non-RF temperature loggers.
10) The company checks the non-RF temperature logger for verification.
    - IF the temperature log data is within required limits, send products for purity testing.
    - ELSE, send new products to UF for a new test.
11) Administer the protein purity test for each product exposed to RF radiation.
12) Send the results back to UF in pass-fail format showing which products were affected (or not affected) by RF exposure for each frequency.

V. Sample Information and Analysis

Proteins are grouped in different categories and the three major groups that cover the majority of biologic pharmaceuticals are vaccines, immunoglobulins and hormones. Brief descriptions of the tested protein groups and the type of analysis to be performed for each drug to analyze the purity are provided below.

1) Vaccine: Vaccines are biological preparations that serve to confer some type of immunity to the recipient using an inactive or attenuated form of an infective agent. Following administration, the body's own immunological response will develop an immunity to the delivered microbe which provides a resistance to subsequent infections. Typical preparations can be comprised of killed microorganisms, less virulent strains, inactive toxic components, or proteins both separate and linked to polysaccharides in order to allow for immunological identification of antigens.

2) Immunoglobulin: Also referred to as antibodies, immunoglobulin is a protein which allows for the identification and elimination of foreign agents in the body. The most ubiquitous form is comprised of two "heavy-chains" linked to two "light-chains", both of which consist of constant and variable regions. The variable regions determine the specificity of the protein and allow for binding to a specific antigen. Once bound, the antibody serves as a tag, directing other parts of the immune system to attack the bound agent.

3) Hormones: Hormones serve as chemical signals throughout the body, allowing for an action at a distance. Typically they are released from a cell or tissue and elicit a response in other parts of an organism. Most commonly, only small amounts of hormones are required for action, acting as messengers in the body. Many hormones are derived from amino acids, either using a functional group transfer, or wholly consisting of peptide chains. Others may be derived through lipid metabolism, including steroid-based hormones. Side-chains and added groups may resemble a combination of all of these classes as well, further diversifying this class of biologics.

4) High pressure liquid chromatography: The purity analysis of each product before and after exposure to RF radiation is performed by each participating company for their own drugs. Even though pharmaceutical companies utilize proprietary test setups in order to accomplish this, they are all specialized derivations of the same type of purity analysis commonly referred as high-pressure liquid chromatography (HPLC) and immunoelectrophoresis.

In basic terms, HPLC is a process by which biological compounds can be separated and quantified. HPLC operates by passing a mobile liquid containing a number of compounds through a stationary substrate column. The rate at which compounds pass through the column will be determined by their affinity for binding to the column. The solution is typically analyzed as it exits the column and different compounds are seen as the process continues. Use of a high-pressure pump allows for fluid movement through a more densely packed column. In doing so, a better resolution is obtained, and allows for a more accurate analysis of a solution.

VI. Experimental Results

The participating pharmaceutical companies; Abbott and Pfizer have provided the biopharmaceuticals to be tested in this experiment. All the products supplied by the manufacturers fall into one of the three major protein groups described in section V. Due to confidentiality agreements, the names of the tested products and respective associations with the companies will not be stated explicitly in the results. However, they will be grouped under one of these major categories as the results created by the purity analysis from each company are provided to the University of Florida in a pass-fail format for each individual drug.

TABLE II
Results of the protein purity test for biologic pharmaceuticals for frequencies commonly used by active RFID systems

Product \ Frequency	433MHz	2.4GHz
Hormones (4 products)	Pass	Pass
Immunoglobulins (7 products)	Pass	Pass
Vaccines (4 products)	Pass	Pass

The results are presented in two tables for frequencies commonly used by active and passive RFID systems. If there is a purity change in only one sample from any company, the entire protein group will be labeled as "fail".

TABLE III
Results of the protein purity test for biologic pharmaceuticals for frequencies commonly used by passive RFID systems

Product \ Frequency	13.56MHz	868MHz	915MHz
Hormones (4 products)	Pass	Pass	Pass
Immunoglobulins (7 products)	Pass	Pass	Pass
Vaccines (4 products)	Pass	Pass	Pass

As shown in table II and III, there was no change in protein purity for any of the hormone, vaccine or immunoglobulin products from any of the companies at all five frequencies. Remembering the fact that the temperature of the products were held within required limits, it is possible to conclude that any non-thermal effect from RF exposure at various frequencies is undetectable.

VII. Conclusions

In this paper we analyze the non-thermal effects of RF radiation on the protein integrity of biologic drugs and pharmaceuticals. In order to achieve this, a complete experimental procedure and test protocol have been developed which include the collaboration of major pharmaceutical companies for the protein purity tests to analyze any non-heat effect after exposure. State-of-the-art hardware is used to generate high

power RF signals with twice the EIRP approved by FCC at the antenna end to provide a 24-hour RF exposure for temperature and light sensitive biologic drugs in a temperature controlled, dark anechoic chamber. The exposed drugs are then shipped back to the participating pharmaceutical companies for a thorough analysis of their protein integrity. The overall protocol provides an objective and universally applicable methodology to investigate non-thermal effects of RF exposure on pharmaceutical products. The results show that even at a power level of 8W EIRP at five different and most commonly used RF channels, none of the three major protein groups, including hormones, vaccines and immunoglobulins, showed degradation in their structural properties which suggest that, for the tested protein categories and associated biologic pharmaceuticals, there is no detectable non-thermal effect due to RF exposure. In light of these findings, it is recommended that FDA reconsiders its statement in CPG Sec.400.210 concerning RF radiation and BLAs.

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