Report to FDA of PQRI RFID Working Group

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Executive Summary

In its report, Combating Counterfeit Drugs, issued in February 2004 (1), the FDA stated that “Radiofrequency Identification (RFID) tagging of products by manufacturers, wholesalers, and retailers appears to be the most promising approach to reliable product tracking and tracing.” The Agency, while clearly indicating in the same report (1) that none of the contemplated track and trace technologies, including RFID, represents a “magic bullet”, has encouraged regulated industry to consider RFID as a potential tool in anti-counterfeiting efforts.

A concern has been raised about the potential impact on product quality due to exposure of drug products to radiofrequency radiation which would occur if RFID is adopted. This issue was assigned to the Drug Product Technical Committee (DPTC) of PQRI. The DPTC requested a study design for exposure of biological/biotech drug products to RF radiation; in the course of discussing the proposed study, the DPTC unanimously requested that a risk assessment for such exposure be done. This report is that assessment.

There are three main components to the risk assessment performed: 1) a summary of the results from the industry sponsored, FDA reviewed Accenture Jumpstart test of the impact of RF exposure on product quality and product temperature specifically (2,3), 2) a review of the scientific literature on the impact of RF exposure on biomolecules, and 3) a discussion of the perspective on risk provided by high-field NMR studies of biomolecules.

The key finding of the Accenture Jumpstart effort in regard to any potential product quality impact from exposure to up to 16 hours of RF is a temperature rise of between one half and one degree Celsius and no change in strength, purity, and potency (2,3). Given that the ICH stability studies allow a ±2ºC variability in chamber temperature, such a temperature rise should be considered negligible.

A review of the current literature on RF exposure of biomolecules indicates that the effects noted in both the theoretical and experimental papers (5,6) are understandable as extremely localized thermal effects. To extrapolate these effects to the situation of RF exposure through the use of RFID track and trace technology would require a drug product that is sufficiently thermally labile and concentrated so that these potential highly localized effects could propagate through the sample to a sufficient extent to create a measurable impact. Under the conditions anticipated in the drug distribution environment, this is most unlikely.

A recent paper from FDA’s Center for Devices and Radiological Health (CDRH) is a simulation of RF exposure under theoretical worst case scenarios (7). Although the abstract and the paper state that the modeled exposure is for insulin, a careful reading of the paper reveals that insulin was modeled by a gel of 0.9% saline with

hydroxyethylcellulose. This study produced results that are entirely consistent with the Accenture Jumpstart study (2,3); that is, exposure to RF under a worst case scenario will not increase the temperature of a pharmaceutical by more than 2°C, again a negligible change.

The key to an in-depth risk assessment of drug products, in particular, biomolecules, exposed to RF due to the use of RFID is the realization that the extremely high magnetic fields used in current NMR studies of biomolecules require similarly high RF input in the 800-900 mHz range, precisely the range anticipated for most US RFID systems. This means that NMR structural studies of biomolecules provide an appropriate comparator to RFID for the purpose of determination of relative risks. The field strength of the NMR is more than a million fold greater than that experienced by a biomolecule exposed to RF from an RFID tag. The drug will typically also be exposed to this miniscule field for less than one millionth the time that biomolecules are exposed to RF in NMR structural determination experiments. That exposure to RF in this energy range does not cause non-thermal damage to biomolecules is born out by a number of recent studies that used NMR to examine the active site(s) of several proteins, including the binding of ligands to those proteins (10-15). In these peer-reviewed papers, NMR studies on several different proteins are presented, including: human acetylcholinesterase (10), small ubiquitin-related modifier (SUMO) proteins (11,15), human factor Xa protein (12), and heme oxygenase of both human (13) and bacterial origin (14).

The adoption of a radiofrequency identification track and trace system may contribute significantly to public health by making it harder for counterfeiters to slip into the legitimate distribution system. There have been concerns raised regarding the possibility of damage to drugs, particularly biological/protein based drugs, due to exposure to the RF energy that such a system would entail. This paper examines the risks involved and characterizes them as thermal or non-thermal. The thermal risks have been determined to be negligible by the Accenture Jumpstart study which showed only a very small temperature rise on exposure to several hours of RF from an RFID system.

The non-thermal risks are assessed by examining representative articles from the peer-reviewed literature and by considering the NMR structural studies of biologicals and proteins which employs RF in the same energy range as RFID. It is seen that what the current literature presents as so-called non-thermal effects are, in fact, highly localized thermal effects. Concerns over such effects are unwarranted, as they are improbable for any biological or protein-based drug that is stable at either controlled room temperature or 2-8ºC. Further, a recent paper from FDA's Center for Devices and Radiological Health (7) simulated exposure of liquid drugs in vials to RF under worst case conditions and observed a less than 2ºC rise in temperature, consistent with the Accenture Jumpstart results.

It was further seen that the relative time risk of exposure to RF due to RFID is greater than 2.5 million times higher for NMR than for RFID, except in the artificial worst case

scenario of a package stuck for 16 hours in an RFID reader that remains on. Consideration of the relative distance involved in NMR vs. RFID led to a relative risk greater than 1 million times NMR.

And yet, as noted above, NMR can and has been used not simply for protein structural determination, but to actually measure binding at the active site of the protein, in other words, as a bioassay.

All of the above, taken together, provide ample evidence that exposure to RF energy due to the implementation of an RFID track and trace system represents a negligible risk to drug product quality, whether of small molecules or biological or protein-based drugs.

Report to FDA of PQRI RFID Working Group

Background & Problem Statement

In its report, Combating Counterfeit Drugs, issued in February 2004 (1), the FDA stated,

> *Because the capabilities of counterfeiters continue to evolve rapidly, there is no single "magic bullet" technology that provides any long-term assurance of drug security. However, a combination of rapidly improving "track and trace" technologies and product authentication technologies should provide a much greater level of security for drug products in the years ahead. Similar anti-counterfeiting technologies are being used in other industries, and FDA intends to facilitate their rapid development and use to keep drugs secure against counterfeits.*

Specifically, in regard to RFID, the same report indicated that:

> *Radiofrequency Identification (RFID) tagging of products by manufacturers, wholesalers, and retailers appears to be the most promising approach to reliable product tracking and tracing. Significant feasibility studies and technology improvements are underway to confirm that RFID will provide cost-reducing benefits in areas such as inventory control, while also providing the ability to track and trace the movement of every package of drugs from production to dispensing. Most importantly, reliable RFID technology will make the copying of medications either extremely difficult or unprofitable. FDA is working with RFID product developers, sponsors, and participants of RFID feasibility studies to ensure that FDA's regulations facilitate the development and safe and secure use of this technology. FDA is also working with other governmental agencies to coordinate activities in this area.*

Thus, the Agency, while clearly indicating in the same report (1) that none of the contemplated track and trace technologies, including RFID, represents a “magic bullet”, has encouraged regulated industry to consider RFID as a potential tool in anti-counterfeiting efforts. As a follow-up the Agency released a Compliance Policy Guide (CPG), Section 400.210 Radiofrequency Identification Feasibility Studies and Pilot Programs for Drugs in November of 2004 (4). This CPG stated:

> *To the extent that it may be necessary, FDA intends to exercise enforcement discretion as described below for studies that fall within all of the following parameters:*
> - *A manufacturer, repackager, relabeler, distributor, retailer, or others acting at their direction will attach RFID tags (chips and antennae) to only immediate containers, secondary packaging, shipping containers, and/or pallets of drugs that are being placed into commerce. There is no limit to the number of tags or readers that may be used in the study.*
> - *The drugs involved will be limited to prescription or over-the-counter finished products. The drugs involved will not include those approved under a Biologics*

License Application or protein drugs covered by a New Drug Application. The study need not have a pre-determined time limit or endpoint, except that tag placement for the study will be completed by December 31, 2007.

- *…*
- *The tag readers will work by emitting electromagnetic energy at radio frequencies of 13.56 megahertz, 902-928 megahertz, or 2.4 gigahertz, and at powers in compliance with regulatory requirements of the Federal Communications Commission (i.e., 1-4 watts effective isotropically radiated power).*

In summary then, the FDA has actively promoted RFID use as one component of an overall strategy to secure product integrity and further protect patient safety. One key question was whether exposure to radiofrequency energy in the range contemplated would be expected to have any impact on the quality of the drug products so tagged. Particular concern was expressed by the Agency in regard to Biologics or protein drugs as noted above.

The purpose of the PQRI RFID taskforce was to evaluate to the risk to product quality posed by RF exposure of Biologics and protein based drugs. The DPTC requested a study design for exposure of biological/biotech drug products to RF radiation; in the course of discussing the proposed study, the DPTC unanimously requested that a risk assessment for such exposure be done. This report is that assessment.

Accenture Jumpstart Results

Project Jumpstart was formed in February 2004 by Accenture, a leading business consulting and services firm, to promote pilots of RFID technology in the pharmaceutical industry supply chain. It included consumer goods and pharmaceutical manufacturers, distributors, retailers, and associations. In September 2004, some Project Jumpstart members completed a 12-month EPC pilot project that was unprecedented in its scope and pharmaceutical industry participation (2,3).

The participants spent months designing the pilot then conducted an eight-week trial that tracked 10 products from multiple manufacturers through 16 business scenarios at 15 locations. More than 13,000 products were tagged and read. HDMA participated in the project, as did Abbott Laboratories, Barr Laboratories, Cardinal Health, CVS Pharmacy, Johnson & Johnson, McKesson, National Association of Chain Drug Stores (NACDS), Pfizer, and Rite Aid, with Accenture serving as project administrator.
The project was designed as a proof of concept for using EPC technology in multiple business operations. The main focus was to determine how unit-level item serialization could improve supply chain security. Other goals included:

- Assess RFID suitability to satisfy regulatory mandates such as the Florida pedigree requirement;
- Establish processes to facilitate returns and recalls;
- Develop and execute tests to see if electromagnetic energy from radio frequency affects the efficacy, potency, and strength of solid drugs included in the trial;

- Gain knowledge and develop solutions for labeling, including tag frequency and the color, size, wording, and location of RFID labels.

Jumpstart declared the project a success and reported it demonstrated the potential of RFID technology to provide many benefits specific to the industry, including meeting regulatory transaction history requirements, returns and recall management, improved consumer safety through electronic track-and-trace and authentication capabilities, greater order accuracy, and increased labor productivity. Several obstacles and challenges to widescale implementation also were identified. The project provided many insights and recommendations as to how companies can develop RFID strategies and implement the technology, and how the industry needs to collaborate to further develop EPC systems to meet specific needs.

In particular, the potential impact of RF exposure on product quality was evaluated. The FDA requested that the manufacturers who participated in EPC Jumpstart test a representative sample of the products they intended to tag by exposing them to electromagnetic energy. The FDA requested that these tests should be executed prior to introducing tagged product into commercial distribution. Furthermore, it was requested that the tests be designed so that the effect of the exposure to the electromagnetic energy on the strength, purity, and potency of the exposed product be compared to the strength, purity, and potency of unexposed control product. The FDA indicated that they were primarily concerned about the thermal effects of exposure to the electromagnetic fields emitted by RFID systems. The FDA suggested the following parameters while creating the test protocol:

1. A continuous exposure of the product to electromagnetic energy for the longest period of time that a product would remain in the maximum field strength produced by the RFID antenna. The duration of 16 hours is considered to provide a worst-case scenario simulating a package containing pharmaceutical product being left overnight in the RFID reader field.
2. The product should be placed at the closest possible distance to the antenna and exposure of the product to electromagnetic energy should use equipment and other environmental factors that simulate the worst-case heating conditions expected during commercial use. In considering the 60 degree beam width for the antenna, a distance of 12 inches provided an exposure field approximately 12 inches in diameter.

Using these requested parameters by the FDA and creating additional parameters within the Pharma EPC Jumpstart Protocol the EPC Jumpstart Project exposed each product to a controlled duration of fixed radio frequency energy using 915 MHz Stationary Reader/Antenna Set. This was considered a worst-case in that it provided a maximum gain and power, operating at a full 4 watts power output.

The participating manufacturers exposed their EPC Jumpstart Products (and some additional products including a liquid) to electromagnetic energy. The following conditions existed and equipment was used to capture the effects:

1. The product was exposed to the RF energy in the pharmacy shelf package configuration with the RFID tag affixed to the package (Package information per product tested within EPC Jumpstart is attached).
2. A field strength meter (Agilent 84110EM) was used to confirm that the 915 MHz reader/antenna was performing as expected and was operating consistently across the area where the product was located. This information was recorded periodically through the test along with the ambient field strength.
3. Temperature of the interior of the container with product present was monitored to evaluate temperature observed during the exposure period. A Teflon temperature probe was placed in each package during the exposure to RF energy as well a temperature probe measuring ambient room temperature. Continuous temperature data was captured using a 16 channel evaluation system.
4. Three replicates of each product were exposed to the RF Field.

Once the exposure was complete, the products were returned to the manufacturers to be tested using currently approved analytical methods. Typical stability indicating methods were employed (e.g., physical characteristics, dissolution, assay, degradation, etc.). In cases where the routine release testing and stability testing for a particular test parameter are different, the stability method was used, either in conjunction with or in replacement of the routine release method. Where multiple packages of product were exposed, testing was performed on individual samples taken from each package. All manufacturing companies have reviewed the results, and have determined that there are no apparent effects on strength, purity, and potency of exposed product to electromagnetic energy when compared to the controls. The results have shown the following:

1. Approximately a one-half degree increase in temperature throughout the 16 hour period for solids. Approximately a one degree increase in temperature was noted throughout the 16 hour period for the one liquid product tested.
2. Field Strength remained constant throughout the 16 hour period.
3. Strength, purity, and potency were not affected by the exposure.

While none of the products evaluated in the Jumpstart project were biologicals or protein drugs, it can be concluded from this study that thermal effects of RFID exposure on any drug whether small molecule or biological are not expected to pose any risk to product quality.

A copy of the Jumpstart report was sent to Dr. Paul Ruldolph, then at FDA (2,3).

<u>RF Exposure Papers discussion</u>

In recent years the question of whether exposure to radiofrequency energy could have an effect on biological materials has been raised. While some of what has been put forth can be dismissed as anecdotal at best, there have been peer-reviewed scientific

articles that address this question. It is appropriate to evaluate what is known in this area as the potential impact of RF exposure on the quality of biological and protein based drugs due to the use of RFID technology is considered.

While it is not possible to review the entire literature on this subject, three representative papers will be considered, one theoretical, one experimental, and the third a simulation of RF exposure of insulin vials. In none of the papers is a convincing scenario provided that RF exposure of the type expected for the use of RFID track and trace technology, even a worst case situation, presents a credible risk to product quality.

The theoretical paper is by an Australian group and was published in 2000 (5). The authors state that microwave exposure under “athermal” conditions occurs when no temperature rise can be measured by conventional thermometry. They note that existence of biological effects arising from such athermal exposure is still controversial, significantly because of a lack of the linear dose response relation. They propose a model in which pulsed microwave radiation causes a triggering of the heat shock or stress response by altering the conformation of proteins through a transient heating of the protein and its close environment. In support of this model, the authors use the heat diffusion equation and show that pulsed exposure even when athermal can lead to transient temperature excursions outside the normal range. They thus propose that the power window phenomenon in which biological effects are observed at low power levels may be caused by an incomplete triggering of the heat shock response.

The authors focus on the heat shock response of cells as the mechanism by which non-thermal RF exposure might produce biological effects. This is presumably because the heat shock proteins are exquisitely sensitive to energy input and readily undergo conformation changes. The authors offer the following scenario:

> At low power levels, a partial unfolding of specific target protein(s) occurs, which will be insufficient to induce the stress response, but sufficient to alter protein function. A biological effect (e.g. on cell proliferation) will be observed.
>
> At higher power levels a more unfolded (molten globule) conformation is induced. The stress response will be activated, protecting the protein, and preventing an observable biological effect.
>
> At very high power levels, protein aggregation and precipitation occurs, and despite the activation of the entire stress response, a catastrophic biological effect (e.g. cell death) will be observed.

Thus the theoretical effects the authors consider in a non-thermal situation are, in fact, thermal effects that occur in a highly localized environment on a scale and time frame too small to be observed by measurements of the temperature of a whole sample. In addition, the postulated effects are primarily whole-cell focused and where they do center on specific proteins, only those proteins that are particularly sensitive to thermal effects are likely to be impacted.

In terms of the anticipated risk to biological or protein based drugs from exposure to RF, whole cell effects can generally be discounted as most materials in commerce are either isolated, purified molecules or dead cells in the case of vaccines. Live cell vaccines are theoretically at some risk under this scenario, but the amount of that risk is too small to quantify. The risk to molecules of highly localized thermal effects and unfolding can be evaluated by reference to bulk stability data for the material. The only molecules that one would anticipate to be at risk in this situation are those that are so thermally labile that they could never be formulated or marketed. That is, any localized effect would create an impurity in such small amounts as to be undetectable by any assay.

The second paper attempts to establish experimentally what the first offered in theory: that RF exposure can change protein conformation without bulk heating (6). The authors exposed concentrated solutions of bovine serum albumin (BSA) at various temperatures to microwave radiation and observed protein aggregation as determined by light scattering. In a separate experiment, they observed that a heat shock gene recombinantly expressed in *E coli* was expressed more in microwave exposed cells than in controls.

The concentration of BSA used in the experiments was reported to be 50-100 mg/mL. For perspective, the concentration of insulin in marketed preparations is in the 1-5 mg/mL range. Thus, the effect observed is (intentionally) magnified by the use of a very highly concentrated solution. Also, the authors controlled temperature through the use of incubators and by measuring with a microthermocouple after exposure. What this experimental set up did not do is provide for or document adequate thermal control of the samples intended to be kept at a specific temperature. As will be seen below in the NMR section, RF exposure can and does have a significant local heating effect. It is likely that the effects observed in this study are attributable to local heating rather than a non-thermal effect. The other significant consideration in terms of risk evaluation is the power used. The microwave radiation employed was 1.0 GHz and 0.5 W. While the geometry of the experimental set up was not precisely described in the paper, it is clear that the proximity to the RF source was likely considerably closer than is anticipated in the RFID situation.

The third paper is from FDA's Center for Devices and Radiological Health (CDRH). It presents a simulation of RF exposure under theoretical worst case scenarios (7). Although the abstract and the paper state that the modeled exposure is for insulin, a careful reading of the paper reveals that insulin was modeled by a gel of 0.9% saline with hydroxyethylcellulose. The purpose of the gel was to minimize or eliminate diffusion effects on any temperature rise observed. The modeling conditions used 200 - 350 Watts of power rather than the 1 - 4 Watts typical of RFID devices. This was to enable determination of temperature effects over very short time frames to minimize or eliminate diffusion effects. These results were then extrapolated to the real world situation. The results extrapolate to a 1.7°C temperature rise in the single case of a vial sitting in the position of maximum effect. In any other position, or if the vial were surrounded by other vials as would be the case in a commercial package, the effect was

estimated to be 0.6°C or less. The author's extrapolation applies to a worst case scenario that neglects heat lost to the surrounding environment.

In short, this study produced results that are entirely consistent with the Accenture Jumpstart study (2,3); that is, exposure to RF under a worst case scenario will not increase the temperature of a pharmaceutical by more than 2°C.

In summary, the effects noted in the first two papers (5,6) are understandable as extremely localized thermal effects, while the third paper (7) presents simulated RF exposure under a worst case scenario that results in a temperature rise of less than the ±2ºC variability permissible in stability chamber temperature; such a temperature rise should be considered negligible. . To extrapolate these effects to the situation of RF exposure through the use of RFID track and trace technology would require a drug product that is sufficiently thermally labile and concentrated so that these potential highly localized effects could propagate through the sample to a sufficient extent to create a measurable impact. Under the conditions anticipated in the drug distribution environment, this is most unlikely.

Similarity of RF Exposure in RFID Use to NMR Studies

In evaluating the relative risk to product quality of biologics and protein based drugs exposed to RF energy, a comparison with nuclear magnetic resonance (NMR) studies of biomolecules structure is helpful. NMR has been used to determine the structures of small molecules for half a century and has been applied to larger molecules for the past two decades. The key point to consider here is the Larmor Equation which states that, in the presence of an external magnetic field, the energy of interaction of the proton's own magnetic field is proportional to the strength of the external magnetic field.

The extremely high magnetic fields used in current NMR studies of biomolecules require similarly high RF input in the 800-900 mHz range, precisely the range anticipated for most US RFID systems. This means that NMR structural studies of biomolecules provide an appropriate comparator to RFID for the purpose of determination of relative risks. The following table lays out a comparison of the different factors involved in both high field NMR and RFID (8,9).

Parameter	High Field Protein NMR	RFID
RF Frequency (8,9)	600-900 MHz	13.56 MHz or 902-928 MHz
Power (at antenna) (8)	5-30 W	4 W
Exposure Time (8)	Several days with ~10-25% duty cycle	msec; worst case assumed to be 16 h
Typical Protein Concentration (8)	As close to solubility limit as possible, typically millimolar	Insulin for example, is present in vials at ~ 4 mg/mL
Distance from RF antenna (8)	2-3 mm	2-3 meters
Calculated Field Strength (9)	>2.4 MA/m	< 1A/m

Let us calculate the relative risk factors from the information above. Assume an NMR exposure of 3 days with a 10% duty cycle and a 10 millisecond RFID exposure. The relative time of exposure is 2,592,000 greater for the NMR scenario. Only in the artificial assumed worst case of a 16 hour RFID exposure, would the relative time of exposure become roughly equivalent at 0.45 in favor of the RFID exposure.

A second risk factor is the distance from the antenna. The typical NMR setup has the RF coils as close as possible to the sample. The typical RFID scanner is designed to be used to detect goods passing through a loading dock. The difference is then a factor of a 1000 (millimeters vs. meters). Since the field strength will be determined by the square of the distance this represents a minimum of a relative risk factor of 1,000,000 greater for NMR. Note that a separate calculation in reference 9 produces relative risk factor in terms of field strength that is 2,400,000.

In summary, the field strength of the NMR is more than a million fold greater than that experienced by a biomolecule exposed to RF from an RFID tag. The drug will typically also be exposed to this miniscule field for less than one millionth the time that biomolecules are exposed to RF in NMR structural determination experiments.

NMR Studies and Bioassay

That exposure to RF in this energy range does not cause non-thermal damage to biomolecules is born out by a number of recent studies that used NMR to examine the active site(s) of several proteins, including the binding of ligands to those proteins (10-15). In these peer-reviewed papers, NMR studies on several different proteins are presented, including: human acetylcholinesterase (10), small ubiquitin-related modifier (SUMO) proteins (11,15), human factor Xa protein (12), and heme oxygenase of both human (13) and bacterial origin (14).

What the referenced studies have in common is that they each use high field NMR, with the correspondingly high RF input to study the three-dimensional active structure of the respective proteins. As part of each study involved using NMR techniques to determine binding to the active site of the protein being studied, these reports can be characterized as NMR-based bioassays. In short, exposure to the RF in the same range as is anticipated for an RFID system not only did not cause any detectable non-thermal damage to the proteins involved; that exposure was an integral part in performing a bioassay of those proteins. Further, the work cited includes studies that demonstrate the NMR structure determination provides results fully consistent with crystal structure data (14) and have documented the presence of individual hydrogen bonds at the active site of human acetycholinesterase (10). That last observation is critical; if the hydrogen bonds, weaker than any covalent bond, can be observed in these studies while a highly concentrated solution of the protein is undergoing exposure to high energy RF radiation, it clearly demonstrates that such exposure does not disrupt these interactions.

Conclusion

The adoption of a radiofrequency identification track and trace system may contribute significantly to public health by making it harder for counterfeiters to slip into the legitimate distribution system (1). There have been concerns raised regarding the possibility of damage to drugs, particularly biological/protein based drugs, due to exposure to the RF energy that such a system would entail. This paper has examined the risks involved and characterized them as thermal or non-thermal. The thermal risks have been determined to be negligible by the Accenture Jumpstart study which showed only a very small temperature rise on exposure to several hours of RF from an RFID system (2,3).

The non-thermal risks have been assessed by examining representative articles from the peer-reviewed literature and by considering the NMR structural studies of biologicals and proteins which employ RF in the same energy range as RFID. It was seen that what the current literature presents as so-called non-thermal effects are, in fact, highly localized thermal effects. Such concerns are improbable for any biological or protein-based drug that is stable at either controlled room temperature or 2-8ºC.

It was further seen that the relative time of exposure to RF due to RFID is greater than 2.5 million times higher for the typical NMR experiment versus the normal RFID exposure. Only in the artificial worst case scenario of a package stuck for 16 hours in an RFID reader that remains on was the exposure time comparable to the NMR protein experiment. Consideration of the relative distance involved in NMR vs. RFID led to a relative risk factor for field strength greater than 1 million times for NMR over RFID exposure.

And yet, as noted above, NMR can and has been used not simply for protein structural determination, but to actually measure binding at the active site of the protein, in other words, as a bioassay.

All of the above, taken together, provide ample evidence that exposure to RF energy due to the implementation of an RFID track and trace system represents a negligible risk to drug product quality, whether of small molecules or biological or protein-based drugs.

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