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The Varian story

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ABSTRACT

This *Perspective* offers a personal view of the story of Varian NMR, a courageous initiative that began in the 1950s but came to an abrupt end some 60 years later. Without doubt, Varian leaves behind a priceless legacy, particularly in the field of structural chemistry. The highlights are set out in four main sections, named after the four seasons, but not necessarily in strict chronology. How did the accepted business practices influence the evolution, growth, and eventual demise of this exciting venture? How well did management handle an unconventional group of young scientific entrepreneurs? What does it all mean for the future of magnetic resonance? The subject can be viewed on two different levels, the Varian story itself, and the larger picture – the Silicon Valley phenomenon as a whole, with Varian considered as an interesting microcosm.

1. Springtime

1.1. The beginning

Russell and Sigurd Varian had a profitable business manufacturing microwave devices, based on the invention of the klystron [1]. Russell then looked around for a fresh scientific challenge. He specifically ruled out any profitable commercial venture, but sought something more akin to a hobby (we can now appreciate the unintended irony). Intrigued by the pioneering work of Felix Bloch and Ed Purcell, he chose to explore the new field of magnetic resonance. It fitted neatly with his expertise in radiofrequency electronics, and his continued interest in the related topic of radar.

This offered a fairy tale beginning for a handful of scientists from Stanford University. By a stroke of good fortune they had completed their doctoral work with Felix Bloch in a field of research that was entirely new and unproven, and which seemed to have no limits. Jim Arnold built the original 'high-resolution' permanent magnet. Unfortunately it was not something that could easily be replicated, because it required most of the power supply of Stanford University to energize it. This was the first time that anyone had even attempted to generate a magnetic field with such a fantastically high degree of spatial uniformity. Someone remarked that the resolving power, one part in 60,000,000, could be likened to that of an optical telescope capable of resolving images of 'two cats sitting side-by-side on the moon'.

Martin Packard, Jim Arnold and Wes Anderson then recorded the very first high-resolution NMR spectra in the world. This small core of enthusiasts banded together to form an instrument section within the main Varian operation, comfortably protected from mundane concerns about funding. To these courageous innovators we owe the genesis of Varian NMR. They had the foresight and courage to take the raw experiments performed at Stanford and construct something solid and practical that could be offered for sale. They appeared to be thinking 'NMR is an exciting invention, so let's make it possible for others to use it too'. Profit seemed to be only a secondary consideration. Thanks to Sputnik, the scientific climate at that time was one of boundless optimism.

1.2. The age of innocence

Conventional 'Master of Business Administration' (MBA) wisdom would have insisted that the new group should concentrate exclusively on design and construction of the first commercial NMR spectrometer, thus ensuring continued viability for the venture. But the fledgling Varian scientists enjoyed a remarkable freedom to be flexible in their choice of project. Unstructured 'blue sky' research is *fun*, although mostly restricted to a lucky few. They decided to develop Russell Varian's idea for an Earth's field magnetometer [2], using free precession of proton spins in a water sample. Once the device had been built and tested, the question 'What shall we use it for?'

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produced two diametrically opposed answers, and throws an interesting light on the question of motivation. The first application was to develop a 'magnetic anomaly detector' that could search for submarines in the magnetically quiet environment of the oceans. At the other extreme, Varian scientists working in Switzerland noted that snow was also a magnetically quiet medium, and they embarked on a project verging on pure philanthropy. Avalanches kill dozens of skiers in the Alps every year. Some victims are trapped under the snow but can still breathe, and are not seriously injured. The standard search and rescue operation involves a combination of trained sniffer dogs and a line of human volunteers to probe the snow with long poles. The Varian idea was to exploit their new magnetometer. Although the magnetism of skis can be detected, skis are often thrown far from the victim, so the proposal was to embed small magnets in the ski boots, and install a Varian magnetometer at each ski station. Unfortunately, young skiers, convinced of their immortality, are reluctant to pay for modified ski boots, and the Varian initiative failed. But it does say a great deal about motivation.

1.3. Flowering

By now a critical mass of remarkably talented people had been assembled at Varian, made up of specialists in NMR, EPR, and magnet engineering, and supported by a dedicated 'applications laboratory' that set out the stall for potential customers. To some extent the new group behaved more like a university research department than a commercial enterprise. Often scientists from abroad, having seen a flurry of publications on magnetic resonance from an address in Palo Alto, assumed that this must be one of the many California universities. A post-doctoral program sprang up, attracting some top European candidates. Management adopted a relaxed, visionary approach. In the early 1960s the entire reporting hierarchy was made up of physicists, all the way to the top; not an MBA in sight. Flexibility was the order of the day, offering the freedom to explore new avenues of magnetic resonance that had no obvious direct impact on sales, but nevertheless kept Varian NMR in the spotlight. For example, what seemed at the time to be just a curiosity-driven study of double resonance techniques eventually led to an important general method for internal field/frequency lock derived from a proton or deuterium signal.

1.4. Spreading the word

The very first Varian NMR machines had low-resolution magnets and were largely acquired to explore the broad resonances of nuclei other than protons, or to venture into electron spin resonance studies. But a few imaginative chemists saw that proton NMR could be a powerful tool for determining molecular structure, and this swiftly shifted the focus towards high resolution NMR. Even established infrared spectroscopists now grudgingly admitted that NMR might one day become important. Early enthusiasts had to build their own spectrometers from scratch, not a simple undertaking in a department concerned primarily with wet chemistry. By offering a commercial machine, Varian now provided significantly faster access to this exciting new field. This was the beginning of what later became a veritable revolution in structural chemistry. It was strongly encouraged by Jim Shoolery, who began a Varian campaign to popularize the new chemical applications by publishing regular bulletins called '*This is NMR at Work*' and by organizing 'workshops' to demonstrate this arcane branch of physics to bewildered chemists. It is interesting to note that these teaching sessions deliberately by-passed the rigorous formalism of NMR in favor of a strictly pragmatic understanding of how it impacted on the determination of molecular structure – an unashamedly practical perspective that lives on among chemists to this day.

1.5. An NMR icon

A high-resolution spectrometer of that era was heavy, cumbersome, not an easy beast to operate, and prohibitively expensive for a typical chemistry laboratory budget. Purchase of a spectrometer often involved the appointment of an expert in magnetic resonance to run the machine. Even then, much time could be expended on 'in-house' modifications to improve the temperature stability of the magnet and its cooling water. This was all changed by a stroke of genius – the concept of a 'user-friendly' spectrometer, aimed specifically at the organic chemist. The NMR machine was completely redesigned, stripped down in size, and reduced to the bare essentials. Introduced in 1961, it was called the 'A60' [3]. It was compact, much lighter than earlier machines, and seemed far more at home in a typical chemistry laboratory. It came as a complete surprise to the magnetic resonance community.

Organic chemists, often little concerned with pure physics, naturally found the mystique of magnetic resonance difficult to master, but the A60 was specifically conceived to make everything as simple and intuitive as possible, with only the absolute minimum of operating controls. Of these, only field homogeneity optimization ('shimming') required any real skill; even today this is still a necessary chore. The most important innovation of all stemmed from Wes Anderson's invention of the 'nuclear sideband oscillator', [4] that held the ratio of field and NMR frequency essentially constant. A flatbed recorder was introduced for the first time, with the scan through the spectrum synchronized with the movement of the pen. This permitted precalibrated charts to be employed, allowing the chemist to associate a particular chemical grouping with a specific location on the chart. This can be thought of as a subliminal teaching aid – a direct visual representation of the concept of 'up-field' or 'down-field' chemical shifts. The A60 vastly broadened the general acceptance of high-resolution spectroscopy and brought NMR within the reach of hundreds of eager organic chemists. It enjoyed a surprisingly long life, exemplified by the fact that Paul Lauterbur's historic magnetic resonance imaging experiment [5] in 1973 was carried out on an A60.

2. Summertime

2.1. The golden age

It would have been wrong to say at this stage, 'and the living is easy'. Nevertheless Varian NMR had settled into a less hectic regime, represented by the steady progression from 30 MHz, 40 MHz, 60 MHz, to 100 MHz spectrometers, wider chemical shift dispersion, higher sensitivity, double resonance, and field/frequency lock. The wild exuberance of springtime was now tempered by a fresh exhortation: '*The Virginia City Days are Over*', an allusion to the onset of the California gold rush, when it was claimed that you could stumble over a gold nugget while strolling down main street. Those heady days were long gone, yet there were still some precious NMR nuggets to be discovered, with the important difference that now the search required a great deal of hard work. Two remarkable innovations stand out as prime examples.

2.2. The Fourier spectrometer

This may not be generally appreciated, but the seed of the Fourier transform revolution had been firmly planted by Russell Varian in a patent filed in 1956 [6]. The concept was based on wide-band noise irradiation, but it was later realized that excitation by intense radiofrequency pulses was a better alternative. It was immediately accepted that *at that time* the conversion of a transient time-domain signal into a frequency-domain spectrum presented enormous practical difficulties. The digital computers then available were essentially mechanical adding machines not so far removed from the one invented by Charles Babbage. Extraction of the individual NMR frequencies had to rely on analog Fourier analysis, akin to the procedure used in a spectrum analyzer. Russell Varian proposed recording the free induction signal on audio-frequency magnetic tape, making a closed loop of the tape, and repeatedly scanning it to pick out the desired 'resonances' one at a time. The idea was too far ahead of its time to allow any meaningful reduction to practice.

2.3. 'A plurality of frequencies' [6]

Almost a decade later, Wes Anderson was exploring an alternative concept for boosting sensitivity by multichannel excitation of the high-resolution spectrum using a comb of modulation sidebands, generated by an imaginative new mechanical device related to the prayer wheels favored by Buddhist monks. This project was abandoned once it was realized that Russell Varian's revolutionary Fourier transform concept might now be a realistic proposition [7], even allowing for the fact that the transformation stage would have to rely on a mainframe IBM computer that could only be used at night when the essential Varian management and accounting calculations had been completed. After much diligent work, Richard Ernst and Wes Anderson were able to show that a working prototype Fourier spectrometer could nevertheless be built, and it offered an order of magnitude improvement in sensitivity [8]. However it remained only a 'proof of principle'; a truly practical commercial model was still far into the future. Certainly this seminal paper was so far ahead of its time that even the referees completely failed to appreciate its significance and originality, and twice rejected the manuscript.

In retrospect it is easy to overlook the fact that the Ernst and Anderson initiative was not yet a practical alternative to existing high-resolution spectrometers employing the conventional sweep method. Digitization of the free induction signal was a slow and cumbersome procedure, dedicated laboratory minicomputers were not available, and the Cooley–Tukey fast Fourier transform algorithm [9] had yet to be introduced. Then, suddenly, the Varian Fourier transform project lost its champion when Richard Ernst left the company and returned to academia in his native Switzerland. The torch was passed to a small Varian research group that set out to modify an HA60 spectrometer for FT-NMR, this time incorporating a laboratory minicomputer for the Fourier transformation. It featured an innovative field/frequency regulation scheme in which the tetramethylsilane signal was repeatedly excited in pulsed mode, even when the full proton spectrum was not being acquired. Unfortunately, without the Cooley–Tukey algorithm, transformation of a typical 1 K data set required 20 min. A few potential customers were shown this prototype, but no sales were made. A busy chemist was not prepared to wait through a suspiciously long coffee break to see the first spectrum. A commercial Fourier spectrometer was not top of the agenda.

Market research had indicated that potential NMR customers were dreaming of a brand-new spectrometer that could, at the touch of a switch, investigate *any* magnetic nucleus in the entire periodic table, with decoupling as standard, and with built-in field/frequency lock. It was decided to design and build a machine with 'all the bells and whistles' – the XL-100. This vast engineering enterprise monopolized resources and required years to complete. The resulting 'all-encompassing' machine became the flagship of the Varian NMR fleet. Chemists showed little interest in a putative Fourier transform project that appeared cumbersome and dangerously high-risk. This opened the door for the Bruker company to exploit the Ernst and Anderson initiative, and build a Fourier transform spectrometer, thereby stealing a march on Varian. Too much reliance on the customers' wish list, and not enough real vision? Most chemists were still busy reveling in the seemingly unlimited possibilities of the existing high-resolution spectrometers, so why bother with such an eccentric innovation? Yet within a few years, Fourier transform spectrometers had completely replaced the old-fashioned idea of slow-passage frequency sweep spectroscopy.

2.4. Superconducting magnets

Varian can hardly be accused of complacency with the achievements at that time. It was well understood that more intense magnetic fields offered wider chemical shift dispersion and enhanced NMR sensitivity, but the practical upper limit for the field of an iron-cored magnet corresponded to a proton frequency of 100 MHz. Harry Weaver had designed the suite of Varian electromagnets. He could have been forgiven for resting on his laurels, but instead he took on the daunting challenge of developing a completely new form of magnet – a solenoid of superconducting wire held at the temperature of liquid helium [10]. Would the magnet be persistent, or would there be a slow degradation of field intensity with time? Was there a danger that the magnet could suddenly quench? Could acceptably high field homogeneity be achieved? It is easy to imagine all the practical challenges to be overcome, not least mastering the arcane technology for making superconducting joints. In these early magnets the Dewar vessel was not particularly efficient, and helium boiled away quite rapidly, necessitating a refill every morning; there were no holidays or extended vacations for the unlucky person in charge. Just as in the prototype Fourier transform project, superconducting solenoids were not going to make life easy for the operator. On the other hand, it turned out that they benefitted from an important practical advantage – in the persistent mode the total magnetic flux was essentially constant, offering a welcome increase in field stability. The initial goal was to build a 250 MHz spectrometer, later moderated to 220 MHz for the first machine delivered. This tentative proof of principle eventually led to today's essentially global acceptance of superconducting NMR spectrometers. An invaluable example of the Varian legacy.

2.5. User-friendly superconducting spectrometers

Later, in an initiative reminiscent of the iconic A60 project, a completely new superconducting spectrometer was designed, with help from an expert on cryogenics from Stanford. The new magnet was physically much smaller, and was housed in a rounded enclosure to minimize helium loss; it bore an uncanny resemblance to the character R2D2 in *Star Wars*. This solved the helium problem once and for all. The operator could now direct his full attention to important matters of NMR spectroscopy, relegating the magnet to the role of an innocuous bystander. This great leap in spectrometer design (the XL-200) encouraged the general acceptance of superconducting magnets, just as the A60 had popularized NMR in chemistry.

Another new feature of the XL-200 was to have profound consequences. Reprogramming earlier instruments to perform new experiments had required changes to the instrument software at the machine code level, deterring all but the foolhardy. In the XL-200, pulse programming was carried out using the high level language PASCAL, and for the first time it became possible for ordinary users to try out new pulse sequences. The result of this democratization was a blossoming of pulse sequence development that bore fruit in many of the experimental methods in common use today.

2.6. Governance

Unfortunately it was not long before the heavy hand of management made a catastrophic decision. As it happened, two European scientists were visiting Varian at the time in the guise of outside consultants. Both were absolutely horrified by the simplistic 'logic' of the latest managerial *diktat*.

(1) Very high-field NMR is not profitable.
(2) We do not want to be in an unprofitable business.
(3) Discontinue all work on high-field magnets.

No one seemed to imagine any possible flaw in this reasoning. Had the same managers been in charge in the early days of Varian, nothing would ever have been ventured. Needless to say, the entreaties of the two European academics fell on deaf ears, and Varian abruptly abandoned all development of NMR spectrometers at frequencies higher than 200 MHz. When, much later, this disastrous edict was eventually overturned, Varian had lost the initiative and was forced to procure the necessary high-field superconducting magnets from an outside enterprise, Oxford Instruments. The competitive advantage had been sacrificed, with regrettable long-term consequences. One wonders what Harry Weaver thought of it all.

The loose gossip around Palo Alto sometimes tended to dismiss Varian as a group of competent engineers without any managers. This was certainly not the case in the golden years; there was a firm hand on the tiller, belonging to physicist Ed Ginzton who clearly understood that Varian was a very special enterprise requiring an enlightened approach to management. The first C.E.O. was Merle Stearns, who came from the klystron facility on Long Island and provided funds to support the new NMR venture. It was only very much later that governance became more 'rationalized' – that is to say, dictated principally by short-term profitability. There was a fairly regular replacement of middle management. It could be argued that the root problem lay in the very nature of the conventional business model, because it seems fundamentally unsuited to this type of imaginative enterprise. A young MBA, suddenly placed in charge of a high technology group, understood perfectly well that there was only a year or two to 'turn things around' so naturally concentrated on short-term planning, with scant attention to the long-term future. It is also possible that a newcomer, trained purely in business doctrine, was not really comfortable dealing with unruly and insubordinate staff, armed with their superior knowledge of magnetic resonance. This kind of friction affected company harmony, and a few top scientists drifted away, or were even 'eased out' by the management. Like an inherently unstable heavy isotope, perhaps a nucleus made up of too many prima donnas is doomed to eventual disintegration?

3. Autumn

By now the Varian company as a whole had split off the NMR business and renamed it Varian, Inc. For simplicity in this Perspective it will still be referred to as 'Varian'.

In the now mature NMR business, the early easy-going environment of Varian's golden age was no longer acceptable. Emphasis was placed on growth, market share, and the bottom line. In this phase of the story, initiatives from outside Varian – solid-state NMR, biochemical applications, cryogenically cooled probes, and multi-dimensional spectroscopy – increasingly contributed to the continued expansion of the subject. Magnetic resonance was now a thriving science in its own right, and the initiative had started to pass from the manufacturer to the customer – 'users' were becoming innovators.

3.1. Competition

Innovation alone does not guarantee commercial success. Other technology companies had ventured into the NMR business. By far the most important of these was the Bruker organization, but it was quite a while before Varian began to pay serious attention to the danger posed by this private instrument company, then principally owned by the Laukien family. Managed largely by scientists, it benefitted from much more operational freedom, and was not under pressure from shareholders. Furthermore, Varian was seriously constrained by its practice of preparing detailed documentation for the manufacturing process – hundreds of blueprints for any particular model of NMR spectrometer. This was the norm for any mass-production operation, because it allowed the factory to employ less-skilled personnel, and it supplied exact detailed descriptions for servicing the equipment. But in practice NMR spectrometers were manufactured one at a time; this was not actual mass production. Bruker managed to operate with far simpler documentation that could be modified for each new spectrometer, offering each client an essentially custom-built machine. This more flexible regime employed skilled science graduates who could make any desired modifications on the factory floor. It was less expensive, more efficient, and it permitted progressive improvements to be introduced in a gradual manner. The saving grace of Varian's detailed documentation was that it made their spectrometers ideal for researchers working on NMR methodology, allowing them to adapt instruments in ways undreamt of by their designers. This new pastime became known as 'spin gymnastics' or 'spin choreography'.

3.2. Growth

Imagine a small family company selling mousetraps. Sales are perfectly stable, year-on-year, and the owners are quite content to continue in this comfortable steady-state regime. But business dogma insists that this is not an option; growth is *absolutely* mandatory. Varian was no exception. How did the fledgling NMR business evolve during the next stage, after the turbulence of the initial start-up? Business analysts like to represent growth by a rising exponential curve, tacitly disregarding the inherent limits of this assumption. The problem lies in any attempt to extrapolate. Whatever the exponent, fast or slow, a growth curve of this kind cannot continue to increase indefinitely. [In the 1960s someone remarked that the number of new PhD students joining IBM was rising exponentially, and calculated the date at which *all* new PhDs in America would be swallowed up by IBM.]

Common sense tells us that growth must inevitably slow, and the graph will gradually change into something closer to the shape of a sigmoid curve, possibly reaching a plateau or (horror of horrors) a downward trajectory. How does management react, knowing that the perception of growth is essential? For the market in question, there is a limit imposed by the total number of NMR spectroscopists in the world, so there was little point in putting all the blame on the sales department. The decision was made to broaden the scope of Varian, Inc, either by acquiring related companies (gas chromatography, mass spectrometers) or by investing in the development of new forms of spectroscopy (ion cyclotron resonance). Perhaps the most ill-fated Varian venture at that time was a project to build a suite of low-cost 'table-top' NMR, ESR and mass spectrometers, in the belief that university chemistry departments would purchase these 'a dozen at a time' to equip practical teaching laboratories. The university administrators remained steadfastly unconvinced. These seemingly laudable initiatives largely failed, siphoning off key personnel and funding that would have been better devoted to supporting the core NMR business. Perhaps management indulged in a misplaced over-reliance on the dogma of the 'return on investment' calculation, which implicitly writes off past losses as if they had never happened, thus imparting a false rosy glow to any disastrous project? More importantly, ruthless American business administration methods that work for a shoe factory may be much less successful when applied to an enterprise like Varian NMR.

4. Winter [11]

4.1. The bombshell

It began with what appeared to be positive news. On 14 May 2010 Agilent Technologies acquired Varian, Inc for approximately $1.5 billion in cash. The president and CEO of Agilent was quoted as saying, '*The Varian acquisition – the largest in our company's history – furthers our evolution toward becoming a global leader in bioanalytical measurement. We're gaining tremendous talent and technology*'. Most Varian watchers, after the initial shock, decided that this acquisition was in fact a good thing, arguing that the original Hewlett–Packard (the predecessor of Agilent) was widely regarded as a fine example of a well-run company. It was suggested that the (former) Varian would benefit from the new management.

In any merger one hopes for the best elements to be inherited, but fears the worst. In this case the apparent commercial weaknesses of Varian – central control, long command lines, and rigid processes – seem not to have been remedied, perhaps because the Agilent organization was not particularly well tailored to the supply of relatively small numbers of high-cost NMR spectrometers and MRI scanners. Agilent's progressive withdrawal, first from medical imaging and then from high field NMR, represented the writing on the wall, but it still came as a shock and a bitter disappointment when they announced (on 14 October 2014) the immediate closure of their NMR business, essentially putting an end to the Varian era. Notice the *reprise* of the simplistic mantra (quoted above) for justifying the termination of an unprofitable operation. By closing down the whole NMR, MRI and magnet operation, Agilent has done a great disservice to a distinguished heritage and to a scientific community that had been faithful to Varian through thick and thin.

Those who cannot remember the past are condemned to repeat it. The worst military defeat ever suffered by the Roman Empire was in 9 AD, when a German guerrilla force in the Teutoburg Forest annihilated three entire legions, led by the general Publius Quinctilius Varus. Historians know this as the *clades Variana* [12] – the Varian disaster. Was Varian NMR simply outclassed by nimbler competition? The rivalry between Varian and Bruker undoubtedly helped to drive major improvements in instrumentation, but until very recently it could still be argued that neither company had a clear technical lead. The principal differences between them lay rather in their commercial organizations, with local Bruker operations enjoying higher levels of autonomy, and greater flexibility in responding to customer needs.

It is left to the reader to judge the reasons behind the decision to shut down the Varian NMR operation in this ruthless manner; it is perhaps too soon to reach any meaningful verdict. Future MBA student projects will doubtless examine how it was possible to pay an immense cash sum to acquire another company, and then close it down after just four short years. The wider science community will deplore the massive and irreplaceable loss of personnel and expertise in the key areas of chemistry, structural biology and clinical imaging. Here the most widespread reaction will be incomprehension. There remains an acute sense of loss, resentment, and even betrayal, not least at the lay-off of hundreds of former employees, many of whom were popular and respected members of the NMR family. Scientists in general will mourn the disappearance of an enterprise that contributed so much to research, that worked so hard to popularize NMR in chemistry, that greatly extended the scope and performance of spectrometers, that enabled users to devise a rich field of new pulse programs, and that bequeathed a valuable legacy for future instrument development. Colleagues in other branches of science will feel a chill wind: if a management misjudgment can lead to such a sudden and irreparable loss of personnel and expertise in a field so central to progress in so many areas, we are all losers.

The cornerstone of western business doctrine is the need for competition, but the unexpected demise of Varian NMR creates a virtual monopoly. Will another company (the remaining competitor JEOL for example) take up the challenge? The hope is that the managers of the Bruker organization will realize the enormous responsibility that has now fallen on their shoulders. To sit back and reap the profits would be unworthy of that company. In contrast, to emulate the early Varian 'philanthropic' vision and vigorously promote magnetic resonance would be applauded by the entire community. After all, Varian NMR first evolved in an environment where there was little serious competition, and the story outlined above suggests no evidence that the young company exploited its near monopoly; rather the opposite.

This sad end to a famous company cannot alter the fact that science will continue to benefit from the Varian legacy far into the future. It is surely impossible to conceive of chemistry today without NMR, and the later development of magnetic resonance imaging owes a great deal to its predecessor. The Varian innovations that have been described above add up to an enormous positive contribution to science. Perhaps we may look forward to a new springtime?

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