body systems. It’s not that the core protein is changed, but the modifications that happen to that protein make it a slightly bigger, more branched molecule that’s slower to break down. Bayer has also introduced human heat shock protein 70, a natural chaperone protein. This helps with better folding of the protein as well as reducing premature cell death.

**HT:** Are there any other ways in which these two products are different?

**Dr. Mahdi:** Kovaltry does not use any human or animal derived raw materials in the cell line, purification process or in the formulation process to manufacture Kovaltry. We also introduced a 20-nanometer filtration step that reduces the theoretical risk of contamination. Think of it as a sieve that removes potential viruses and clumps of misfolded proteins from the final product.

**HT:** What have recent clinical trials shown with regard to developing inhibitors, first in previously treated patients (PTPs) and, secondly, in previously untreated patients (PUPs)?

**Dr. Stoffman:** The RODIN study (See Hemophilia Today, Vol 49, No 3, November 2014) and the more recent SIPPET study (see page 24) did not look at PTPs, so from a scientific point of view, we can’t comment, but based on what we understand of inhibitors, there would be no increased risk of inhibitors in PTPs with a recombinant product like Kovaltry. These patients have been frequently treated, they haven’t developed an inhibitor, and there’s no concern of inhibitor development when switching from one product to another.

However, there is a real concern that previously untreated patients starting on Kovaltry, or any of the other recombinant products on the market right now, are exposed to a higher risk of an inhibitor compared to starting on a plasma-derived FVIII with von Willebrand factor. At least, that’s what SIPPET seems to suggest.

**HT:** Tell us about formats and storage.

**Dr. Mahdi:** It is administered via intravenous injection after reconstitution with a diluent supplied in two pre-filled syringe volumes: 2.5 mL for the 250, 500 and 1000 IU nominal dose strengths and 5 mL for the 2000 and 3000 IU nominal dose strengths. These are the same as Kogenate FS, as is the administration device or vial adapter. Kovaltry needs to be refrigerated between 2°C to 8°C and never frozen. Once removed from the fridge, it cannot be re-refrigerated. You can store Kovaltry at room temperature up to 25°C for a single period of up to 12 months. After reconstitution it must be used within three hours.

**HT:** What are the plans for making the transition from Kogenate to Kovaltry?

**Dr. Mahdi:** The plans are to ship across the country from June to October with Atlantic Canada being the first to transition. We’ve left this to Canadian Blood Services and the clinics to manage. By the end of October, the transition should be finished.

**Dr. Stoffman:** The plans are to ship across the country from June to October with Atlantic Canada being the first to transition. We’ve left this to Canadian Blood Services and the clinics to manage. By the end of October, the transition should be finished. – D.P.

Hemophilia Today (HT): What has led to the development of this next generation of rFVIII?

**Dr. Mahdi:** Kovaltry is not a new molecule but its development reflects Bayer’s commitment to continually improving its products. Kovaltry is produced with advanced manufacturing technologies that enhance the production of rFVIII.

**HT:** In what ways are Kogenate FS and Kovaltry similar?

**Dr. Mahdi:** Compared to Kogenate FS, Kovaltry is similar in terms of efficacy and safety. They are both made using a copy of the same natural unmodified FVIII molecule that we find in human blood. They’re also both recombinant molecules with an identical factor VIII amino acid sequence and molecular formula, which are produced in the same baby hamster kidney cell line.

**Dr. Stoffman:** Kovaltry has the same clinical efficacy and it’s indicated for all the same uses as Kogenate: prophylaxis, on-demand therapy and surgery.

**HT:** In what ways are Kogenate FS and Kovaltry different?

**Dr. Stoffman:** Study data showed a slightly longer half-life, a mean of 14 hours versus 12 with Kogenate.

**HT:** If it’s the same molecule from the same cell line, how do you explain that the half-life appears to be longer?

**Dr. Stoffman:** Kovaltry uses great big sugars on the side of the molecule to hide the key part of the protein from the natural