TABLE TOPIC DISCUSSIONS- Key Discussion Points and Feedback

CUSTOM DEVICE EXEMPTION AND EXPANDED ACCESS REQUESTS

Moderators: Christopher Ferreira, MS *FDA* and Brianna Prindle, *OSMA*

Chris provided a handout with the FDA definition of custom device and overview of expanded access pathways, including emergency use, compassionate use and treatment investigational device exemption (IDE). There remains some confusion on the differences, including why a patient-matched device is not a custom device (using a device to treat a unique pathology/physiology can be a gray area). The group was polled as to their current usage of these pathways. The results indicated a mix of experience. FDA is currently tracking and trending these requests and has seen a growing number of complex joint replacements, cutting guides and oncology applications.

FDA receives over 800 individual submissions each year. Individual requests place a significant administrative burden on manufacturer and FDA resources and FDA is trying to think more strategically with alternative approaches that still allow patient access. As such, FDA is proposing that requests be addressed through an IDE pathway (i.e., group compassionate use request). All criteria for compassionate use may still be required, but under an IDE. Small numbers of patients are envisioned (no more than 10 patients and no need to publish on clinicaltrials.gov.) No controls would be required. The IDE would be similar to early feasibility study IDEs, where the focus would be on safety, not necessarily on effectiveness. The manufacturer would need to establish that no other alternative treatments exist and include risk/benefit considerations. Some manufacturers are using the HUD definition (i.e., 8000 cases/year) to meet the "sufficiently rare" threshold. The experience of using a central vs. local IRB was also discussed.

The group questioned whether a limitation of 10 devices was realistic and the proposed mechanism for adding additional patients to the IDE. There may be opportunities to expand the IDE and add multiple arms to accommodate additional patients, based on device application, with a single annual report. The intention of the study (e.g., treatment vs. monitoring for adverse events) should be specified and the extent of follow-up would be dependent on purpose. It was acknowledged that future FDA guidance would be required to define the required IDE content, as well as how to address expanding the study to additional patients (perhaps 10 at a time in IDE supplements), how to address device modifications and how anomalies would be addressed. Data from these studies could be gathered prospectively to support a future premarket submission.

The group discussed whether an "envelope" 510(k) might be a better approach. FDA is open to considering this approach. FDA would need to think about how broadly the envelope is defined. When asked how manufacturers are deciding to go the custom device vs. compassionate use route, a threshold of 5 devices was cited, although this is manufacturer-dependent. The challenge with providing replacement parts for discontinued products under compassionate use was also brought up.

Other discussion topics covered include FDA's expectations for design control (must meet some quality system requirements) and what companies are telling patients about the level of oversight for these devices. It was reiterated that companies do not have direct communication with the patients. That is handled by the physician. It was also noted that companies turn down custom device and compassionate use device requests, as they often require significant company resources and expense. These are often heartbreaking decisions when considering patient need.

BIOCOMPATIBILITY

Moderators: Paul Turner, Ph.D., *FDA* and Teresa Palacios Hernandez, Ph.D., *FDA*

The following questions were raised during the discussion:

What is the reason we are asked to re-do all metal characterizations?

FDA is mostly concerned with surface issues. Asking to repeat characterization may be a condition of the product- e.g., porous coating, additive, machine oils and is done on a case-by-case basis. The concern is with chemical controls and the risks of adverse events. Choosing the correct solvents is important. The correct polar or non-polar solvents must be carefully considered. Chemical relevance is what FDA is concerned with. This is not easy to answer.

If exhaustive extractions are not working, then is animal testing an acceptable option?

Yes. It is an acceptable option. Chemical tests are the harder way to go. Because there are so many special polymers, animal testing is the best option.

What if solvents destroy the implant?

Try other solvents or mixtures. If it is still not working, come in and ask FDA.

Can you discuss what you see as best practices?

Be forthright rather than having the FDA find out. We don't like being detectives. We look at what you don't tell us, and that brings concerns. Don't waste our time. Tell us the issues. Don't complicate it. Help us all save time. Help us know the testing lab's rationale. This saves time and credibility.

What are common questions in biocompatibility?

How is this test relevant to your device? What are the reactive materials? What standards are used and why?

Is there a difference between adolescent vs adult testing?

There is no difference in general from the FDA's perspective. The biggest issue is the type of risk. Use the newest standard. Think about the total report and what are the main issues. Primarily the CRA.

Can chemical characterization be an issue?

Start first with design, intended use and then move to materials. Cleaning validation issues are frequent. In addition to cleaning validation, manufacturing processes and source materials need to be considered.

For limited contacting devices, chemical identification is obviously important. Big 5 and good to go. Consider biocompatibility of the materials in direct contact, as well as the processing materials, cleaning materials and the storage conditions.

What reservations do you have about new standards?

You need to adjust to the specifics of the product. Each test lab has different techniques and standards. It is a tall order to standardize. You need to consider how are the standards and testing devices are relevant to your device. It is hard to have a check box for every product. Working on guidance is good. For an existing device with a new component or material or chemical, consider your processes, the chemicals and parameters used.

What if the FDA indicated that for specific materials, use certain chemicals and thereby standardize them for submissions? Or vice versa, if industry standardized chemicals used for specific materials?

No clear answer was given. It was noted that industry will not follow a competitor's process, if not dictated in a guidance or standard. Cooperation between industry and the FDA would be needed.

What is the difference between guidance vs standards?

FDA doesn't have control of standards, whereas the FDA can choose guidance documents.

MEDICAL DEVICE DEVELOPMENT TOOLS (MDDTs)
Moderators: Jessica Mavadia-Shukla, Ph.D., *FDA* and Lisa Boyle, *OSMA*

Does anyone use MDDT?

Feedback and discussion:

- OSMA: Not so relevant in our industry as a specific regulatory science tool
- FDA: It's intended to address a specific problem; safety, effectiveness and performance. The use of qualified tools is optional. If you choose to use one, please do a pre-sub
- OSMA: Any tool would be best used to cast a wide net and apply across a broad range of devices
- FDA: Then you would get a range of feedback from many different reviewers

How are PROs (patient reported outcomes) validated?

Feedback and discussion:

- FDA: They are validated tools – technically they are MDDTs. FDA has looked at clinical data to make sure they're clinically validated and so on.

Are there areas outside of orthopedics that MDDTs are being used?

Feedback and discussion:

- FDA: Yes. There are around 17 qualified tools. About 6-7 are PROs. They've varied in the cardiac, ophthalmology, plastic surgery, and diabetes space. Non-clinical assessment models like MR heating simulations also exist. There's a tool in the biomarker space and databases. There are no restrictions to developing a tool – you just need to have a value proposition as to how the tool will facilitate regulatory decision making. FDA is working on tools in the craniomaxillofacial, cancer, drug abuse, etc.

Does anyone use MDDT in their submissions?

Feedback and discussion:

- FDA: No. Does everyone know what MDDT is?
- OSMA: A few have heard of it, but not really sure what it is
- FDA: The MDDT program is a way for the FDA to qualify tools that medical device sponsors can choose to use in the development and evaluation of medical devices. Any tool developer, medical device sponsor, or others, such as research organizations and academia, can voluntarily submit a proposal for a tool. An MDDT is a method, material, or measurement used to assess the safety, effectiveness, or performance of a medical device. An MDDT is scientifically substantiated and can be qualified for use in device

evaluation to support regulatory decision-making. FDA does have a guidance available on MDDT.

How many tools are available for orthopedics?

Feedback and Discussion:

- FDA: There are around 17 qualified tools. There are two orthopedic related tools, both are MRI related.

How do you access an MDDT?

- FDA: Access to the tools can be found on the FDA website. If you are interested in using a tool in your submission, you would contact the sponsor of the tool and they will provide you access to the tool.

What is the benefit of using an MDDT tool?

- FDA: MDDTs can be used in demonstrating safety, effectiveness, or device performance and to support regulatory decision-making by facilitating the efficient provision of supporting evidence in non-clinical or clinical settings. They have the potential to improve efficiency and transparency of the medical device approval process, by facilitating the use of validated and qualified tools across multiple medical device submissions and manufacturers.